Gynecological Endocrinology

ISSN: 0951-3590 (Print) 1473-0766 (Online) Journal homepage: http://tandfonline.com/loi/igye20

Abstracts from the ISGE World Congress 2016

To cite this article: (2016): Abstracts from the ISGE World Congress 2016, Gynecological Endocrinology, DOI: 10.3109/09513590.2016.1150635

To link to this article: http://dx.doi.org/10.3109/09513590.2016.1150635

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GYNECOLOGICAL ENDOCRINOLOGY

http://tandfonline.com/igye
ISSN: 0951-3590 (print), 1473-0766 (electronic)

Gynecol Endocrinol, Early Online: 1–163
© 2016 Taylor & Francis. DOI: 10.3109/09513590.2016.1150635

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DOI: 10.3109/09513590.2016.1150635

Bruno Lunenfeld Lecture

Editorial

Gaudeamus igitur, iuvenes dum sumus!
The International Society of Gynecological Endocrinology in now 30 years old! And, there is no better song to celebrate this event than the ''De brevitate vitae'', the international students' anthem.
The ISGE has grown through infancy and puberty, has achieved the growth peak and now looks to the future as a young and bright student. Full of enthusiasm and curiosity ISGE nurtures Science and Medicine and strives to accomplish its aims with eagerness.
And, it is to the young and the newcomers that ISGE is directing its outreach, renewing the under 34 award and organizing a new full day only for residents and younger physicians, to make available to the new generations the wisdom and the experience of those who have lived in person the history of gynecological endocrinology.
But, Gaudeamus Igitur also expresses the joy and the freedom of the goliardic spirit. The spirit that characterizes every university student from the medieval times to the twenty-first century. . .. And this will be the spirit of the 30th anniversary of ISGE! Let's all convene to enjoy science and life in the most beautiful city of the World, Florence! And let's indulge in the happy mood that every ISGE congress creates!
As 30 years mark the passage towards full adulthood, and to our Society is in keeping with this new condition! Science, joy and freedom and the intriguing advancements of gynecological endocrinology, what a fantastic recipe to celebrate!
So. . . Gaudeamus Igitur, iuvenes dum sumus!!

Prof. Tommaso Simoncini
Executive Secretary of the International Society of Gynecological Endocrinology (ISGE)

Prof. Andrea R. Genazzani
President of the International Society of Gynecological Endocrinology (ISGE)

Uterus transplantation with live births

Mats Brännström (SE)
University of Gothenburg

The last frontier to conquer in female infertility is absolute uterine factor infertility (AUFI). The cause of AUFI may be uterine aplasia, hysterectomy at young age, Asherman's syndrome or uterine malformation. Today 11 human UTx attempts have been performed, with the last 9 of by our team in Sweden. In early 2013, our team completed the surgeries of a series of totally 9 human UTx, with live uterus donors. Eight recipients were MRKH patients and one had undergone a hysterectomy because of cervical cancer. Five donors were mothers and others were close relatives and in one case family friend. The age of the donors were between 39 and 62 years. The donor surgery involved uterine isolation with pedicles of the uterine arteries and veins and including large parts of the internal iliacs. Transplantation was by bilateral end-to-side anastomosis to the external iliacs. The recipients received induction immunosuppression therapy. Two patients were hysterectomized during the initial months due to uterine complications (thrombosis, uterine abscess). The other 7 patients experienced regular menses from 2 months after UTx and embryo transfers were initiated 12–16 months after transplantation. So far 4 out of the 7 patients have delivered healthy babies (57% take-home baby rate) and another recipient is pregnant and expected to deliver in January 2016. The babies were delivered by c-sections in week 31 + 5 (no. 1; preeclampsia) and in week 34–35 (no. 3–4). The babies had normal weight for gestational age at birth and have developed normal. A sixth recipient was pregnant but miscarried at week 14 and only one woman has so far (4 ETs) not been pregnant. This gives a total clinical pregnancy rate of 86% in this cohort of 7 UTx patients. Uterus transplantation is a highly successful treatment for the previously untreatable AUFI condition.

Plenary Lectures

The role of KIS peptides in the regulation of the ovulatory cycle

Bruno Lunenfeld (US)
Bar Ilan University

Endocrine, metabolic and environmental inputs provide inhibitory and stimulatory feedback signals to the brain-pituitary axis to maintain gonadotropin secretion within homeostatic boundaries to support normal gonadal function. Emerging evidence supports the idea that neurokinin b neurons (stimulatory role) which coexpress kisspeptin, and dynorphin (inhibitory action) send projections to GnRH terminals within the median eminence to mediate feedback information to modulate pulsatile GnRH secretion. KiSS-1 peptide, the natural ligand of GPR54 stimulates LH and FSH secretion by governing GnRH pulse amplitude and frequency. It appears that in humans, KNDy neurons mediate negative sex steroid feedback as well as changes in energetic resources or signals of energy availability (e.g. leptin). This allows for adjustments of the response to real-time changes in energy availability in the preoptic area by suppressing the secretion of kisspeptin and neurokinin B and stimulating the secretion of dynorphin, which act synergistically to reduce the activity of the GnRH neuronal system, and thus gonadotrophin secretion. Kiss1 neurons in infundibular nucleus are implicated in the sex steroid-dependent positive feedback control of gonadotropin secretion, and are involved in generating the preovulatory rapid high amplitude GnRH pulses responsible for the predominantly LH surge. There is less marked anatomical differentiation of the two feedback pathways in humans; however, the two functions are mediated by different neurons. Kisspeptin also stimulates endogenous release of gonadotrophins in volunteers, and can induce egg maturation and induction of ovulation Therefore, kisspeptin has potential as a novel therapeutic agent.

Uptodate strategies for myoma, endometriosis and adenomyosis

Leila Adamyan (RU)
Russian Scientific Center for Obstetrics, Gynecology and Perinatology

New methods of diagnosis and reconstructive surgical treatment of patients with myoma, endometriosis and adenomyosis were developed and introduced into clinical practice in the Department of Operative Gynecology of Russian Scientific Center for obstetrics, gynecology and perinatology in recent years. Over 8000 patients with endometriosis were treated in the same period of time. Clinical management and surgical treatment is based on the previously proposed of own classification of retrocervical endometriosis and adenomyosis. Particular attention is paid to the reconstructive surgery in patients of reproductive age with nodule forms of adenomyosis. Further development and improvement of myomectomy is continued. For last two decades 6897 reconstructive surgeries (myomectomies) for uterine fibroids were performed. The effect of uterine fibroids on reproduction, restoration of reproductive function after myomectomy, including preparations for assisted reproductive technologies is now in the field of interest. New perspectives for the development of genital

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reconstructive surgery in the next decades would be determined by the success of basic scientific research. Significant influence will be due to the improvement of instrumentation in the reconstructive surgery, the supply of medicines, reagents, hemostatics, new sutures and synthetic meshes, procedures for adhesions formation prevention. However, the development of reconstructive surgery is not possible without improving of the precision surgical techniques.

Plenary Sessions

(PS01) New insight into female-specific factor that influence brain function

Cognitive behaviour therapy as a treatment for VMS: evidence from RCTs and mechanism of action

Myra Hunter (GB)
King's College London

Objective: There is a need for effective and acceptable interventions for women with vasomotor symptoms (VMS) for whom hormonal treatments are contraindicated or for those who prefer non-medical approaches. The results of three RCTs of cognitive behaviour therapy (CBT) for VMS (MENOS1, MENOS2 and EVA) are described.
Methods: These trials include samples of menopausal women (MENOS2 $N = 140$) and breast cancer patients (MENOS1 $N = 90$ and EVA $N = 422$). Analyses include the impact of CBT upon subjective (problem-rating and frequency) and physiological (sternal skin conductance) measures of VMS, mediators and moderators of treatment effects, as well as qualitative interviews at the final 6 month assessment.
Results: Results provide consistent evidence of the effectiveness of the interventions (effect sizes 1.19 MENOS1; 1.18–1.41 MENOS2; 0.39–0.56 EVA) upon the problem-rating of VMS. Group and Self-help forms of CBT had similarly positive effects on VMS (MENOS2) and physiological VMS significantly reduced for well women but not for breast cancer patients. Improvements with CBT were mainly mediated by changes in beliefs and behaviours, and there were few moderators, i.e. the CBT was effective regardless of sociodemographic or clinical factors.
Conclusion: This evidence suggests that these interventions offer women who have problematic VMS a safe and acceptable treatment choice.

(PS01) New insight into female-specific factor that influence brain function

The central autonomic network and premenstrual disorders

Tamaki Matsumoto (JP)
Shitennoji University

A majority of women experience at least some degree of a regular recurrence of various symptoms during the days prior to menstruation, which usually abate quickly at or within a few days of the onset of menstruation. The cluster of symptoms can alter behavior and well-being, and affect family, friends, and working relationships. We commonly know this enigmatic condition appears in the late-luteal phase as premenstrual syndrome (PMS). Researchers have attempted to unveil this unique condition from various perspectives. At the time of writing, however, no consensus had emerged on the etiopathogenesis of PMS. The autonomic nervous system plays vital roles in dynamically controlling the response of the body to a range of external and internal stimuli and ingeniously modulating biological homeostasis in humans. Since the autonomic nervous system plays a crucial role in the integrity of the mind–body connection as the functional driver of general health and wellness, instability, or even a slight disorder of the system could induce broadly ranging psycho-physiological phenomena. The question emerges, as a matter of course, does the autonomic nervous system, which could reflect central commands, contribute to PMS? A series of studies on women's health in my laboratory has measured heart rate variability and salivary chromogranin A as reliable, non-invasive electrophysiological and biochemical indexes of the sympatho-vagal activity, respectively, in eumenorrheic women who report varying degrees of PMS during the menstrual cycle. Based on the findings of the previous research, together with classic and contemporary literature, this presentation will discuss the extent to and the manner in which the menstrual cyclicity of autonomic nerve activity relates to PMS and the enigmatic conditions surrounding it.

(PS02) Neuroendocrinology: from basic science to clinical impact

Creating positive feedback in organ culture of the rat hypothalamus

Alma Levy (US), Luis Miguel Garcia-Segura (US), Abraham Shahar (US), Frederick Naftolin (US)
New York University, NY, USA

Rationale: Male rat hypothalamic are masculinized at birth and cannot undergo estrogen-induced glial spreading and synaptic disconnection [estrogen-induced synaptic plasticity (EISP)] or positive gonadotrophin feedback control. We previously ''masculinized'' perinatal rat hypothalamic slices with estradiol. In the present study we tested *in vitro* for the presence or loss, respectively, of EISP in long-term cultured female and male hypothalamic slices.
Experimental: Newborn male and female rat pups were sexed at birth and on P1–2 their hypothalami were sliced and cultured in estradiol-free culture medium. Estradiol (10^{-7} M) was administered after 31 days. Forty-eight hours later (equivalent of P33) slices were prepared for electron microscopy or freeze-fracture study. Control undifferentiated E15–17 slices were tested at 37 days.
Results: Astroglial spreading and axosomatic synapse numbers in male pup hypothalamic slices did not respond to estradiol. Slice cultures from female pups and undifferentiated fetuses underwent glial spreading and had 39% fewer synapses 48 hours after estrogen treatment ($p < 0.01$ vs. slices from males). Freeze-fracture showed a 55% increase in glial coverage of neural surfaces in females and undifferentiated fetuses ($p < 0.01$).
Conclusions: EISP can be induced *in vitro*, opening up the possibility of direct studies on this critical occurrence during reproduction. Hypothalamic slice culture is a promising method for the study of brain sexual differentiation and synaptic plasticity.

(PS02) PCOS: L'IMPATTO CLINICO E LE SCELTE TERAPEUTICHE

La gravidanza nella paziente con PCOS è da considerarsi ad alto rischio?

Stefano Palomba (IT)
La gravidanza nella paziente con PCOS è da considerarsi ad alto rischio?

Dati recenti di tipo meta-analitico mostrano che donne con sindrome dell'ovaio policistico (PCOS) hanno un rischio doppio di sviluppare

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diabete gestazionale e almeno triplo di ipertensione indotta dalla gravidanza e di pre-eclampsia rispetto ai controlli non-PCOS. Tali dati sono il risultato della sintesi di studi retrospettivi o di studi prospettici su piccolo campione e non-sono stati aggiustati per gli innumerevoli fattori confondenti presenti nelle popolazioni studiate. Ampi studi di coorte, in cui le analisi hanno tenuto conto di tali fattori, hanno comunque confermato l'aumentato rischio di gravidanza complicate nella popolazione con PCOS. Sebbene l'esatto meccanismo etiopatogenetico coinvolto sia ancora sconosciuto, è evidente che donne con PCOS debbano essere considerate ad alto rischio ostetrico poichè aventi caratteristiche genetiche, ambientali, ciniche e biochimiche tutte chiaramente associate a gravidanza complicata. Sfortunatamente, al momento, non-esistono chiare strategie di prevenzione e di managment della complicanza materno-fetale specifiche per la paziente con PCOS. Linee-guida del Royal College of Obstetricians and Gynaecologists consigliano una curva da carico in tutte le donne con PCOS in epoca pre-concezionale per diagnosticare precocemente un diabete pre-gestazionale o alterazioni pre-diabetiche, mentre l'impiego della Doppler velocimetria sulle arterie uterine, così come la somministrazione di metformina, sono ancora argomenti controversi e dibattuti.

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(PS03) Breast cancer risk and hormones part 1

Dependency on dosage, duration, regimen and type?

Xiangyan Ruan (CN)
Beijing Obstetrics & Gynecology Hospital, Capital Medical University

Women using any hormones most fear the risk of breast cancer. Until now,we could not get any conclusion dependency on dosage, duration, regimen and type of the hormones. So we need the mechanisms assessed in experimental research. Our team for the first time compared E2 and EE regarding their potency on proliferation and apoptosis, and we concluded, that the risk using EE might be lower compared to the use of E2. However, breast cancer risk mostly depend on the progestogen component. We found, that progestogens can accelerate proliferation via special cell components detected in patients with breast cancer. Two editorials in the journal 'Menopause' on our research regarding the importance of membrane-bound receptors pointed out, that the results in the WHI-study may be explained by mechanisms caused by those receptors. We found that patients with breast cancer express those receptors in malignant but not in benign breast tissue. Our conclusion is that the type of progestogen and also the dose is important for the risk during MHT as well as during contraception, since the same progestogens are used in both therapeutic areas. Future screening on those receptors may identify the women of risk regarding these mechanisms.

(PS04) Breast cancer risk and hormones – part 2

Preconditions of genotoxic estrogen metabolites to induce breast cancer

Alfred Mueck (DE)
University Women's Hospital of Tuebingen

Besides the main metabolite of estradiol (E2) also catecholestrogens are produced, in healthy women only in low amount. However, under certain preconditions (e.g. high BMI, smokers, certain drug use, diseases) they are produced in higher amounts and can act as precursors for quinones which can act genotoxic if not eliminated by protective mechanisms.The prerequisite of carcinogenicity is unrestricted oxidative cell-stress which makes possible a "radicalic one electrone oxidation". This leads to semiquinone-quinone complexes, very reactive compounds, found in the tissue of patients with breast cancer. They can react with DNA even at low concentrations, destroying DNA and causing mutations, one of the reasons that WHO classified estrogens as "carcinogenic". However, these "electrophilic radicals" can be captured by antioxidative pathways, and even by certain estrogen-metabolites like 2-methoxy-estradiol in case of functioning protective enzymes which, however, in case of genetic polymorphisms and/or oxidative cell stress may not work. Cells are equipped with extensive multifactorial antioxidative defenses. Thus only together with additional noxae detrimental "vicious circle" of follow-up oxidations occur. The essential, ultimative prerequisite of carcinogenesis producing the first cancer cell is the exacerbation of oxidative stress. However, proliferation to the clinical cancer during treatment with estrogen-only is slow, and protective metabolites or other mechanisms can work, can even destroy proliferating cancer cells before producing clinical cancer. This can explain results in the WHI-study estrogen-only arm. In contrast, certain synthetic progestogens (not progesterone) can enhance proliferation, so protection mechanisms may not work. In addition they also can impact negative estradiol metabolism.

Are androgens risk factors or protective for the breast?

Bo Von Schoultz (SE)
Karolinska Hospital

There is increasing interest in the role of androgens in the treatment of women but little is known about their long-term safety. There are also very few studies on testosterone therapy and breast cancer risk. However, some observations support the concept that androgens may counteract the stimulatory effects of estrogen and progestogen in the mammary gland. Mammographic breast density and breast cell proliferation could be regarded as surrogate markers for the risk of breast cancer. Recently the addition of testosterone to a common estrogen/progestogen regimen was found to inhibit the stimulatory effects of hormones on breast cell proliferation. Testosterone alone will not increase density of the postmenopausal breast. Androgens have been proposed to exert two distinct effects on the mammary gland: (1) In the absence of estrogens and after aromatase conversion they elicit an ER mediated stimulation. This effect can be blocked by treatment with an anti-estrogen; (2) In the presence of estrogens, androgens will act as anti estrogens and inhibit the estrogenic stimulation of growth. This effect is mediated via the AR and can be blocked by anti androgen.

(PS05) Metabolic syndrome

The metabolic syndrome after the menopause: pro-inflammation and endothelial dysfunction

Peter Chedraui (EC)
Institute of Biomedicine, Universidad Catolica de Santiago de Guayaquil

The metabolic syndrome (METS) is a cluster of lipid and non-lipid factors that increase cardiovascular risk. Three or more of the following criteria are required to meet diagnosis: abdominal obesity, decreased HDL-C levels and increased serum triglycerides, fasting glucose and/or blood pressure levels. The rate of the METS increases after the menopause as a consequence of an emergence of several features: obesity, atherogenic lipid profiles, diabetes, hyperinsulinism, hypertension and co-morbid conditions, possibly but not totally related to increasing estrogenic

deficiency. The METS is considered a pro-inflammatory state with high secretion of cytokines which subsequently produce endothelial dysfunction and increases cardiovascular morbidity and mortality and the risk of developing diabetes. This presentation will aim at presenting an overview of the METS during the menopause, focusing on inflammation and endothelial dysfunction.

Insulin resistance, PCOS and obesity: integrative treatments that can improve insulin sensitivity

Alessandro Genazzani (IT), Giulia Despini (IT), Camilla Benedetti (IT), Riccardo Bonacini (IT), Alessia Prati (IT)
Gynecological Endocrinology Centre, Department of Obstretics and Gynecology, University of Modena & Reggio Emilia, Italy

PCOS is characterized by chronic anovulation, hyperandrogenism, polycystic ovaries but shows also overweight/obesity and hyperinsulinism or insulin resistance. This last condition can be due to overfeeding as well as by a costitutional predisposition to an abnormal control of glucose metabolism. 40–45% of all PCOS patients are overweight/obese and show an hyperinsulinism in response to the oral glucose tollerance test (OGTT). Such reduced insulin sensitivity can be observed also in 10–15% of the normal weight PCOS, thus confirming that hyperinsulinism can show up not only in relation to obesity or to excess of weight but also as an intrinsic abnormal ability to control glucose metabolism. Insulin sensitivity can be improved using glucose sensitizer drugs, such as metformin, so that to reduce the negative modulation exerted by hyperinsulinemia on the reproductive axis as well as on neuroendocrine control of reproduction with relevent effects also on adrenal function and neurosteroid production. Recently the use of integrative treatment has been proposed using inositol in 2 of the isomers at present available: myo-inositol (MYO) and d-chiro-inositol (DCI). Both compounds are tightly linked one to the other since MYO is transformed by an epimerase in DCI. Both these compounds works as intra cellular second messangers activated by insulin linkage with its own membrane receptor. Recently also alfa lipoic acid (ALA) has been demonstrated to improve insulin sensitivity with specific positive effects in PCOS with familiar diabetes and its combination with MYO seems to improve greatly insulin sensitivity in PCOS patients.

Obesity and metabolic syndrome in adolescents

Faustino Perez-Lopez (ES)
University of Zaragoza

Excessive body weight is a genetic and environment problem whose prevalence if growing all over the world, including children and adolescents. There is a lack of consensus on the definition of adolescent overweight and obesity that poses barriers for comparisons. Waist circumference is a more precise index than body mass index to detect fat accumulation. Obesity is the most frequent cause of insulin resistance in adolescents and is associated with increased risk of metabolic syndrome components, hyperuricemia, and long-term complications. In teenagers, a better physical fitness is associated with lower levels of insulin and lower resistance to it. Serum uric acid has a positive correlation with insulin resistance while physical activity has an inverse correlation with insulin resistance. The recognition of obesity, insulin resistance and metabolic syndrome in adolescents is important because these conditions are associated with increased risks of diabetes, cardiovascular disease and other co-morbid conditions among adults.

(PS09) Pregnancy and progesterone

Progesterone: from ovulation to pregnancy

Luigi Devoto (CL)
Department of Obsterics and Gynecology, Institute for Maternal and Child Research (IDIMI), San Borja Arriarán Hospital, University of Chile, Santiago

The biosynthesis of Progesterone (P) begins early in the ovulatory cycle: theca-granulosa (GC) luteal cells rising higher levels of P in pre-ovulatory follicle and Corpus Luteum (CL) respectively. LH signaling is critical for P secretion and it is a key modulator of ovulation. The physiological effects of P are mediated by the transient expression of PR-A localized in GC of the pre-ovulatory follicle. PKA-PKC and MAPK-ERK 1/2 signaling regulate PR-A expression that governs the spatiotemporal regulation and expression of ADAMTS-1 and Cathepsin-l proteases that mediate follicular rupture. After follicular rupture the oocyte surrounded by the cumulus reach the fallopian tube that could achieve fertilization. The acrosome reaction of mamalian spermatozoa is believed to be essential for gamete fusión. This reaction is mediated by calcium influx promoted by P via a non-genomic cell membrane receptor. Followed by CL formation the pattern of P production throughout the luteal phase determines menstrual cyclicity and endometrial receptivity for successful implantation and maintenance of early pregnancy. At the time of the window of implantation several endometrial protein like avb3 integrin, LIF, Glycodelyn L-selectin regulated by P4 are expressed in the luminal epithelium to facilitate the cross talk between and endometrium and embryo. In addition therapeutic administration of Progesterone plays and fundamental role in IVF cycles and Premature delivery.

(PS11) Neurosteroids: the brain as a target

Allopregnanolone as a regenerative therapeutic for Alzheimer's disease

Roberta Brinton (US)
University of Southern California

Context: Cures for neurodegenerative diseases remain elusive. Regenerative therapeutics hold the promise of self-renewal and repair in neurodegenerative diseases including Alzheimer's.
Objective: To develop allopregnanolone as the first regenerative therapeutic for Alzheimer's disease.
Patient(s): Early and mid-stage Alzheimer's disease.
Intervention(s): Neurosteroid allopregnanolone.
Main Outcome Measure(s): Neurogenesis, regeneration of white matter, reduction in disease pathology, recovery of cognitive function.
Results: Allopregnanolone induced generation and survival of new neurons in the hippocampus of both aged mice and mice with Alzheimer disease which was accompanied by restoration of both learning and memory. In the brain, allopregnanolone reduced amyloid β burden and microglial activation, and increased markers of myelin generation. Allopregnanolone dose and a regenerative treatment regimen of intermittent exposure were determining factors for therapeutic efficacy. Therapeutic windows of efficacy for allopregnanolone were evident. Chronic toxicology analyses are predictive of clinical safety.
Conclusions: Allopregnanolone is currently in Phase 1B/2A clinical development as the first regenerative therapeutic for Alzheimer's disease.
https://clinicaltrials.gov/ct2/show/NCT02221622?term=brinton+allopregnanolone&rank=1
Development of allopregnanolone dosing and treatment regimen for regeneration in Alzheimer's disease is likely to have broad applicability

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for regeneration in other neurodegenerative diseases such as Parkinson's, neuropathies and multiple sclerosis.
Research supported by US NIH National Institute on Aging (U01 AG031115; UF1AG046148) and the Alzheimer Drug Development Foundation.

(PS12) Atherosclerosis in women

Tissue specificity of the membrane vs. nuclear actions of estrogen receptor alpha: from mouse models to optimization of SERMs.

Jean Francois Arnal (FR)
INSERM U1048 – I2MC – Equipe 9

Thanks to unique mouse models, we and others demonstrated that the estrogen receptor alpha (ERa), but not ERb, is absolutely necessary for most of the arterial and metabolic actions of 17b-estradiol (E2). Estrogens also elicit deleterious effects on the uterus and breast (partly via their proliferative effect which increases the risk of cancer) as well as increased risk of venous thromboembolism, which are the two main limitations of classic estrogen therapies. ER contains two independent transactivation functions AF-1 and AF-2, and our team dissected for the first time *in vivo* the roles of functions ERaAF-1 and AF-2, allowing to define the key role of these nuclear actions in several tissues. More recently, we reported the key role of the ERa fraction localized to the plasma membrane which is absolutely necessary for the protective endothelial actions of E2 as well as, more unexpectedly, for female fertility. One mystery of estrogens biology is that selective ER modulators (SERMs, such as tamoxifen, raloxifen) have a highly tissue-specific action, behaving as agonists in some tissues (such as bone) and as antagonist in others (breast). We will report how these mouse models are helpful to decipher: (i) *in vivo* crucial aspects underlying the response to estrogens, emphasizing the tissue-specific roles of either membrane (as in the endothelium) or nuclear (as in the uterus) ERa in the effect of E2; (ii) the characterization of a new natural SERM (Estetrol) currently tested in a phase III clinical trial as a safer oral contraception, as this molecule has less effect than EE on hepatic-derived coagulation factors, and thereby could not increase the venous thrombosis risk. We will report our present understanding of the mechanisms of this ''liver friendly'' estrogen/SERM.

FSH promotes monocyte-endothelial interaction via up-regulation of VCAM-1 protein in vascular endothelial cells.

Xiaodong Fu (CN), Weiyu Chen (CN), Ping Li (CN), Yuhong Cui (CN), Xiaosa Li (CN), Jinzhi Wei (CN)
Guangzhou Medical University

Cardiovascular diseases are the leading cause of death in postmenopausal women, which is partly attributed to estrogen deficiency. However, the role of follicle-stimulating hormone (FSH) in cardiovascular system remains largely unknown. Recent years it has been reported that FSH receptor (FSHR) is expressed in vascular endothelial cells, suggesting additional roles for FSH in vascular functions. In this study, we detected the FSHR gene and protein expression from human umbilical vein endothelial cells (HUVECs). Treatment with different concentrations of FSH for different time increased VCAM-1 protein expression in HUVECs. This effect was inhibited by the phosphatidylinositol-3 kinase (PI3K) inhibitor wortmmanin or the mammalian target of rapamycin (mTOR) inhibitor rapamycin, or the silencing of Akt, suggesting that PI3K-Akt-mTOR signaling plays important role in FSH-enhanced VCAM-1 expression. On the other hand, the over-expression of p85 subunit of PI3K increased VCAM-1 expression in endothelial cells. Moreover, FSH promoted monocyte-endothelial interaction and high dose of FSH inhibited HUVECs proliferation and promoted apoptosis. In addition to this, we found a positive correlation between VCAM-1 and FSH levels in blood samples from 15 premenopausal and 48 postmenopausal women. Our studies reveal a novel role for FSH in vascular function and suggest that the FSH may have an influential role in cardiovascular diseases such as atherosclerosis.

Assessment of cardiovascular risk at the menopause

John Stevenson (GB)
Royal Brompton Hospital

There are a number of established risk factors for cardiovascular disease (CVD). Some are non-modifiable, such as age and ethnicity, whilst others are amenable to manipulation, such as hypercholesterolemia. These risks are applicable to both genders, with the exception of menopause which is a specific risk factor for women. The onset of the menopause is an ideal opportunity for healthcare professionals to conduct a CVD risk assessment. This should include a personal and family history of cardiovascular events or other conditions associated with increased CVD risk. Lifestyle factors are important, so physical exercise should be assessed and smoking cessation advised. Body mass index and waist circumference should be measured, and dietary advice for weight control should be given as necessary. Blood pressure should be recorded, if necessary supine and rested. Measurement of fasting cholesterol, triglycerides, HDL and LDL together with fasting glucose should be undertaken. If insulin resistance is suspected, a fasting insulin level should also be measured and an insulin resistance index calculated. Lifestyle and therapeutic measures can then be introduced to help correct any risks uncovered, and consideration given for HRT use, particularly for the dose, type and route of administration.

(PS13) IVF: from the patients to the clinic

PGS in IVF repeated implantation failure

Pedro Barri (ES), Monica Parriego (ES), Montse Boada (ES), Buenaventura Coroleu (ES)
Instituto Universitario Dexeus

In our Department, IVF repeated implantation failure (RIF) is defined as the absence of an ongoing pregnancy after 3 embryo transfers with good quality embryos or after the transfer of > 5 embryos. There are anatomic abnormalities such as tubal and intrauterine pathology, that can interfere with embryo implantation. Likewise, endometrial receptivity can be altered for the effect of ovarian stimulation, and for some autoimmune disorders. Sperm damage, and inadequate culture conditions can also be responsible in the etiology of RIF. However in this embryo-uterus dialogue, embryo aneuploidy, despite apparently normal morphology, is the most common cause of implantation failure. Nowadays thanks to the use of CGH techniques we are able to identify these euploid embryos that can be replaced with a high implantation potential. We will present our results with the use of Preimplantation genetic screening (PGS) to manage these patients that will benefit of receiving chromosomically normal embryos and we will analyze the results obtained according to the age of the patient, to the etiology of their infertility, and to the timing of embryo biopsy (day 3 vs. blastocyst biopsy).

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(PS14) IVF: The therapies

Clinical and patient experience with a novel rFSH

Bruno Imthurn (CH), Bemfola Study Group (CH)
University Hospital Zurich

Context: Availability of biosimilars will provide access to high quality biologics to more patients. Specific features such as the injection device can be adapted to improve handling and to reduce wastage of medicines.
Objective: To demonstrate resemblance a biosimilar of recombinant follitropin alfa (rFSH) was tested against its original. To investigate the practical use and the amount of hormone wastage, a new pen model was compared to other commercially available rFSH-pens.
Methods and Patients: A randomized, multi-centre, Phase III study in women undergoing ART was executed. Women in the age range of 20–38 years were recruited and randomized to receive daily a fixed dose of either the biosimilar or the original rFSH. The study tested equivalence in the number of retrieved oocytes as primary endpoint and clinical pregnancy rate and side-effects as secondary endpoints. In a parallel study the handling of three different pen devices were assessed by the patients using a visual analogue scale. The drug wastage of three different products occurring for conducted cycles was calculated.
Results: Compared with the original product the treatment with the biosimilar resulted in a equivalent number of retrieved oocytes as well as a similar clinical pregnancy rate in the first and second cycle. No difference in the rate of clinically relevant ovarian hyperstimulation syndrome was observed. The new pen showed largest proportion of preference compared to the other pen-systems and wastage of gonadotrophin was substantially reduced with the new pen device.
Conclusions: The study demonstrated similar clinical efficacy and safety profiles between the biosimilar of rFSH and its original. The new pen system showed positive assessment of easiness and convenience and can reduce drug wastage.

Towards a hyperstimulation free clinic

Bruno Lunenfeld (US)
Bar Ilan University

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication and refers to a combination of ovarian enlargement due to multiple ovarian cysts and an acute fluid shift out of the intravascular space. It is usually only observed in exogenous gonadotropin cycles following ovulation induced by hCG. Potential strategies for minimizing ovarian hyperstimulation risk and preserving an optimal pregnancy rate are: (1) a protocol combining induction of follicular development with FSH, suppression of endogenous LH with a GnRH antagonist, and GnRH agonist as the ovulatory trigger during IVF cycles . The luteal phase should be supported with a low dose bolus of hCG following the ovarian pick up (OPU). An additional low dose bolus of hCG should be administered on day OPU+ 4. (2) Similar to protocol 1 but 125 hCG daily following ovulation induction for a maximum of 16 days with no further support of the luteal phase. (3) Similar to protocol 1 but ovulation induction with 200 μg of intra nasal (IN) buserelin followed by 100 μg IN buserelin three times a day for luteal support] and continued for a maximum of 16 days. (4). Protocol using the GnRH agonist long protocol, inducing ovulation with hCG and cryopreservation of all embryos preventing both early and late OHSS. (5) Combining GnRHa trigger with freezing all embryos in GnRH antagonist cycles preventing also chances of late onset OHSS. The treating physician needs to be acquainted with the benefit/risk factor of each protocol in order to make an optimal decision which protocol to use in each specific cycle.

(PS15) Vitamin D and bone metabolism

New strategies in the treatment of osteoporosis

Santiago Palacios (ES)
Palacios' Institute of Women's Health

Osteoporosis is a chronic disease which may require treatment for many years and requires not only individual management but often sequential or combination treatments. Monotherapy with antiresorptives is usually the first choice. Sometimes, it is necessary to modify this option for therapeutic failure or for the time of use and risk of side-effects. The appearance of the anabolic parathyroid hormone (PTH) agent has opened new possibilities. Anabolic agents are an attractive option due to direct stimulation of bone formation. Postmenopausal women and men with severe and progressive osteoporosis despite antiresorptive treatment (''therapeutic failure'') should be evaluated for treatment with an anabolic option. Moreover, anabolic agents are indicated for 18–24 months in patients at high risk. Another approach would be to add an anabolic treatment to ongoing treatment with antiresorptives. The data also depend on the specific antiresorptive being used. Combination therapies of antiresorptives and anabolic agents have shown a significant increase in bone mineral density compared to monotherapies. However, none of the combinations have been studied for the prevention of fractures. Combination therapy may not be recommended because of the possible increase in cost. The strategy that it is not yet known, it is what to do in cases of severe osteoporosis: we can begin with an antiresorptive and move, if it is necessary to an anabolic, or viceversa, starting with an anabolic treatment and then, to maintain bone mass, we can switch to an antiresorptive drug.

(PS16) Reconstructive surgery

Vulvovaginal congenital anomalies

George Creatsas (GR)
Obstetrics-Gynecology University of Athens, ''Aretaieio'' Hospital

Vulvovaginal Congenital Anomalies
G. Creatsas MD, FACS, FRCOG, FACOG
17th World Congress of Gynecological Endocrinology, Florence, 2–5 March 2016

Mullerian anomalies are usually diagnosed during adolescence. Primary amenorrhea, dysmenorrhea, and occasionally a pelvic inflammatory disease or/and purulent discharge are the prominent symptoms. We have reported 22 cases of Mullerian anomalies with obstruction during adolescence and their reproductive outcome. Patients with this kind of uterine anomalies are oftenly diagnosed during adolescence due to the periodic pelvic pain. Uterine or vaginal masses may be due to hematocolpos or/and hematometra. Primary amenorrhea may also found if the normal vaginal canal is suppressed by a contralateral hematocolpos, in cases of a complete vaginal septum. The clinical history, the gynecological examination and the magnetic resonance imaging as well as the laparoscopy confirm diagnosis. Hysteroscopy may be needed to evaluate the anatomy of the uterine cavity. The urinary tract system should be also checked as there is a coincidence of relative lesions up to 40%. We also present the results of 240 cases with Mayer–Rolitansky–Kustner–Hauser syndrome treated with our technique (Creatsas vaginoplasty) with a mean operation time 28 minutes and a satisfied sexual life up to 94.5%, as well as case reports of congenital uterovaginal anomalies. The management of congenital vulvovaginal anomalies depends on the type of the lesion and includes surgical procedures as: the opening of the genital canal, reconstruction of the genital anomalies and/or the Creatsas vaginoplasty.

When is tubectomy and when ovarectomy indicated in benign gynecological surgery

Liselotte Mettler (DE)
University Hospitals Schleswig-Holstein

Context: With increasing reports on adnexal malignancies after the reproductive age the question whether to leave tubes and ovaries inside at hysterectomies became more and more important.
Objective: Out of 1.014 laparoscopic hysterectomies performed between 2008 and 2015 at the Department of Obstetrics & Gynecology at the University in Kiel, Germany, 378 Subtotal (SLH) and Total Laparoscopic Hysterectomies (TLH), partially performed by conventional laparoscopic and partially by robotic assisted laparoscopic surgery resulted to be in females beyond the age of 50 years.
Methods: In 212 SLH and 166 TLH performed in females after the age of 50 years who were pre-menopausal or after the menopause all fallopian tubes were resected while only in 146 patients bilateral ovarectomy was performed.
Patients and Results: Neither intraoperatively nor in the consecutive 6 years any tubal or ovarian malignancy was detected at a retrospective evaluation of this patient collective.
Conclusion: While bilateral tubectomy at hysterectomy is an accepted fact to prevent adenocarcinomas of tubes and ovaries the question of ovarectomies before the age of 65 is discussable. As ovaries also possess other function than oestrogen and progesterone production their resection has to be considered individually in cases of normally looking ovaries. In our 232 patients were the ovaries remained at hysterectomy – all patients had no family history of cancer – in the whole observation period of six years no genital malignancies occurred.

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(PS17) High-risk pregnancy

FIGO Initiative on gestational diabetes mellitus (GDM): a pragmatic guide for the diagnosis, management and care

Moshe Hod (IL)
Rabin Medical Center

The International Federation of Gynecology and Obstetrics (FIGO) has recently published a pragmatic guide to the diagnosis, management and care of women with GDM. This presentation will deal primarily with issues regarding diagnosis. FIGO recommends that all women should be tested for hyperglycemia during pregnancy and encourages its member associations to develop strategies to achieve this goal, adapted to local conditions. Whilst FIGO has primarily endorsed the WHO (2013) and IADPSG (2010) criteria for GDM based on a one step diagnostic 75 g OGTT, it is recognised that, due to resource constraints, particularly in the developing world, local strategies may vary and should be considered equally acceptable. In this context, the diagnostic approaches promoted by DIPSI for India, the Ministry of Health for China, EBCOG for Europe, Latin American authorities for South America, ADIPS for Australia, NICE for the United Kingdom and local clinical practice in the Middle Eastern countries are specifically documented and acknowledged as representative of evidence or consensus based standards of care relevant to their local health care contexts. Beyond questions of GDM diagnosis, the FIGO document offers a pragmatic approach to major issues in the management of GDM, accompanied by a comprehensive assessment of such strategies using the GRADE framework.

(PS18) Ovarian cancer and androgens secreting

Ovarian carcinoma in BRCA mutation carriers

Peter Kenemans (NL)
Free University VU Medical Center

Cancers of the ovary found in women with a BRCA1 or a BRCA2 germline mutation are of the serous subtype and are often of tubal origin. Ovarian Surface Epithelium cells have commonly been suggested to be the precursor of these ovarian serous carcinomas. However, our studies and those by others support the hypothesis that seeding of cells of the inner Surface Epithelium of the Fallopian Tube onto the ovary (during fimbrial movement over the ovary) is more likely. In addition, a proportion of serous ovarian cancers may derive from the tubal phenotype epithelium lining ovarian inclusion cysts. Our studies on the prevalence of (pre)malignancies in ovaries and Fallopian tubes of BRCA mutation carriers show that these are rare in the ovary, but that over one third of prophylactically removed Fallopian tubes harbor premalignant lesions, with changes in the expression of cell cycle related proteins Ki67, p21 and p27. Clinical implications. The commonly accepted prophylactic regimen for women at hereditary high risk for these serous carcinomas is removal of both ovaries and Fallopian tubes. These women become postmenopausal with flushes, sterility and bone demineralisation. If BRCA related carcinomas do not primarily arise in the ovary but in the Fallopian tube, prophylactic removal of only both Fallopian tubes might be sufficient to achieve a significant reduction in risk of serous intraperitoneal carcinomas.

(PS19) Dysfunctional Uterine Bleeding (DUB) and fibroids

Lessons learned from the preclinical drug discovery of PRMs for non-surgical treatment of uterine fibroids

Takeshi Maruo (JP)
Kobe Children's Hospital

This introduces translational research initiated in 1992 by unexpected comment from a patient with use of levonorgestrel-releasing IUS (Mirena) for contraceptive purpose. The patient informed us that heavy menorrhagia caused by uterine myoma was markedly reduced. Despite the striking reduction in menorrhagia, myoma volume during use of Mirena increased in some instances. Thus, effects of P4 on leiomyoma cell growth were characterized, and it became evident that P4 acts in combination with E2 to promote leiomyoma cell growth. Consequently, effects of progesterone receptor modulators (PRMs) on leiomyoma cell growth were determined *in vitro*. PRM treatment decreased proliferation, increased apoptosis and reduced angiogenic factors and their receptors expression in leiomyoma cells. Furthermore, PRM increased extracellular matrix metalloproteinase inducer and MMP contents, and decreased TIMP contents as well as collagen contents in leiomyoma cells. However, PRM did not affect normal myometrial cells. PRM seems to inhibit leiomyoma cell growth in a cell-type specific manner in the uterus. Actually, clinical trials of PRM in patients with uterine myomas have revealed that administration of ulipristal or asoprisnil reduces myoma volume and improves myoma-associated symptoms. This translational research from bedside to bench and vice versa may open up a new non-surgical treatment of uterine fibroids.

New management for uterine fibroids

John Sciarra (US)
Northwestern University Medical School

New management for uterine fibroids include myomectomy, uterine artery embolization, MRI guided focused ultrasound, and new surgical and medical therapies. Abdominal myomectomy is complicated today by the morcellation issue, but hysteroscopic myomectomy remains very effective. Uterine artery embolization is 80–90% effective in decreasing menorrhagia, and complications are few but occasionally are serious. Follow up of over 2000 patients for 3 years reveals a 9.8% rate of subsequent hysterectomy and a 2.8% rate of subsequent myomectomy. MRI guided focused ultrasound is a new technique for treatment of uterine fibroids that is being used in several countries including China. Transvaginal uterine artery occlusion has been tried with a clinical investigation protocol but has not been introduced into clinical practice. A new surgical technique for fibroid therapy is laparoscopically directed radio frequency ablation, and this technique is now beginning to enter clinical practice. New medical therapies for uterine fibroids include the use of aromatase inhibitors and progesterone receptor modulators, especially Ulipristal Acetate (UPA) that is now available in many countries and is undergoing phase 3 clinical trials in the United States. With the success of UPA for the medical treatment of fibroids, there is considerable interest in the development of new pharmaceuticals for fibroid therapy. Two examples will be presented. In conclusion, while hysterectomy is 100% effective in treating benign uterine pathology, alternative methods are not. Accordingly, when considering alternatives to hysterectomy, the options should be presented to the patient, and the patient should be involved in the decision making process.

(PS20) Clinical trials in menopause

Clinical trials in menopause. HRT and venous thromboembolism – what differences between US and South European treatments?

Marianne Canonico (FR)
INSERM

Despites a significant decrease in hormone therapy (HT) use, million women worldwide remain prescribed this treatment to counteract climacteric symptoms during the menopausal transition. HT always consists of estrogens with or without progestogens but there is several treatment modalities, including different molecules, doses and routes of administration. Since many years, benefit-risk ratio of HT has been evaluated in several randomized controlled trials (RCT). In these trials, estrogens were exclusively administered by oral route and mostly consisted of a synthetic molecule, conjugated equine estrogens. They were used alone or combined most of the time with medroxyprogesterone acetate, a pregnane derivative progestogen with androgenic power and less frequently with norethisterone acetate, a nortestosterone derivative. Results consistently showed a significant increased risk of venous thromboembolism (VTE) among current HT users and this increase was more pronounced for estrogens plus progestogens users than for estrogens alone ones. In South European countries, HT preferentially consist of transdermal 17b-estradiol alone or combined with micronized progesterone. Although the effect of these molecules and route of administration has never been evaluated in RCT, several well-done observational studies consistently showed that these specific treatments might be safe with respect to thrombotic risk. In addition, norpregnane derivatives could be associated with an increased VTE risk. In conclusion, results obtained in RCT cannot be extrapolated to South European treatments that preferentially consist of transdermal 17b-estradiol alone or combined with micronized progesterone and that may be safe with respect to thrombotic risk. Both the route of estrogen administration and the progestogens are thus important determinants of VTE risk among HT users.

An update of studies on HRT since the initial WHI reports

Elizabeth Gurney (US), Margaret Nachtigall (US), Frederick Naftolin (US), Lila Nachtigall (US)

The Women's Health Initiative (WHI) assessed the effects of starting hormone therapy (HT) in postmenopausal women 50–79 years old. This population was, on average more than 12 years post-menopausal at the start of HT. The study was ended early, due to increased risk of coronary heart disease, breast cancer, stroke, and thromboembolic complications. WHI sub-analyses and extended follow-up offer a more complete picture. Starting HT in postmenopausal women less than ten years from last menstrual period has much less risk and there is statistically significant protection against hip fracture, colon cancer, metabolic syndrome/diabetes and cardiovascular risk factors. Estrogen alone is acknowledged protective against invasive breast cancer and colon cancer and cardiovascular events. Cessation of HT is associated with increased cardiovascular events. No adverse relationship to dementia has been shown among women started on HT around the time of menopause. Other studies have appeared that show the same results plus improved mood and quality of life. Studies with non-MPA progestins and novel estrogens/SERMs for endometrial protection are promising. The WHI raised important questions. Ten years later, many have been answered, including confirmation that HT for most newly menopausal women is safe, effective and sufficient. The treatment of the aging woman, including hormone treatment after menopause, should remain one of our highest clinical and research priorities.

The rejoice trial for dyspareunia: a new solubilized estradiol (VAGICAP), implications for labeling

James Pickar (US), Brian Bernick (US), Sebastian Mirkin (US)
Columbia University

The Rejoice Trial is a double-blind, randomized, placebo controlled, multicenter phase 3 trial. It evaluated 3 doses (4, 10 and 25 mcg) of a bio-identical hormone medication, estradiol, in a VagiCap, for reducing the severity of the symptoms of vulvovaginal atrophy [VVA] (a component of the genitourinary syndrome of menopause), particularly dyspareunia, over 12 weeks. The VagiCap is an applicator-free softgel capsule administered vaginally. The study enrolled over 700 post-menopausal women at approximately 100 study sites. Prior pharmacokinetic studies evaluating the 10 and 25 mcg doses had already suggested a new lower Cmax and AUC, indicating little systemic absorption. The Rejoice Trial evaluated the safety and four co-primary efficacy endpoints: the change in vaginal superficial and parabasal cells, pH and the symptom of moderate to severe dyspareunia associated with VVA. A number of secondary endpoints and pharmacokinetic evaluations were also performed. Study results are expected to be analyzed beginning in the fourth quarter of 2015 and initial results will be presented. Additionally, the question as to whether the boxed warning contained in the US class labeling of vaginally applied estrogen products appropriately reflects the data, will be discussed.

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(PS21) Menopause and personal risks

Personalized medicine after menopause: the case of women with profiles of risk

Antonio Cano (ES)
University of Valencia

Context: Hormone deprivation has an impact on health because estrogen receptors are expressed systemically. Bone, cardiovascular tree, and the central nervous system accumulate most of the effect. Hormone therapy is most adequate as a solution, but still limited to treatment of symptoms by guidelines.
Objective: To address the best strategy for risk reduction.
Methods: Two key questions are how to adequately measure personal risk and when that risk is sufficient to introduce pharmacological treatment. The first question is entirely based upon the personalisation tools that, interestingly, have to focus on the risk for final events and not for intermediate endpoints.
Intervention, results and conclusion: Decisions are still based in clinical scales of risk prediction, with genomics advancing dramatically. In postmenopausal osteoporosis there is the debate of whether treating osteopenic women, who accumulate most fractures. Risk scales help in stratifying measures, including the judicious insert of lifestyle. The case of cardiovascular disease entails more difficulty in Europe, with risk scales less discriminative than the Framingham. Furthermore, a useful scale for stroke is still being expected. The absence of faithful tools imposes age or image biomarkers as surrogates. Breast cancer is another area of debate because effective chemoprevention is available. Advances in genomics are providing hope for better discrimination.

(PS22) Hypogonadism and POF

Factors improving fertility rate in women with premature ovarian insufficiency

Svetlana Vujovic (RS)
Faculty of Medicine, Clinic of Endocrinology, Diabetes and Diseases of Metabolism, Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia

More human approach to women with premature ovarian insufficiency (POI) seeking for pregnancy is required and obligatory. In our group of 1200 women with POI 350 wanted pregnancy. Estro-progestagens therapy results in 1–3% pregnancy rate. Can we, clinicians, do anything else in improving fertility rate prior to modern era technologies? Our suggestion would be: (1) Decrease FSH value to 10–15 IU/L by increasing estrogen doses from 3–10. day of the cycle. Oocyte donation can be suggested after six month interval of FSH between 10–15IU/L and no dominant follicle. (2) Perform oral glucose tolerance test (OGTT) with 75 gr of glucose and glycaemia and insulin detection on half hour during 2 hours and calculate area under the curve (AUC). Insulin sensitizing agents has to be included, when necessary, 3–6 month before pregnancy. (3) TSH has to be 1–2.5 mM/L 3 months before pregnancy in women with Hashimoto thyreoiditis. (4) Tests for thrombophyllia (MTHFR, Leyden V, FII, PAI) are less expensive than repeated *in vitro* fertilisations (IVFs). Fraxiparin therapy has to be included according to indications. 4.Treating endometriosis due to regulation of the immune response. (5) Encourage patient explaining that AMH is not the only important hormone for ovarian reserve, relaxing, coming back to the nature minimum 1 hour every day, excluding stressors and night work, and enjoying with the partner. (6) add melatonin and DHEAS, when it is necessary. Following all these instructions we reach, until now, increase of fertility rate to 9%.Endometrial responsivity and endocrine preparing for the pregnancy is a complex mechanism including neuroendocrine system and not only *in vitro* fertilisation technique.

(PS25) Women beyond menopause: problems, objectives, hopes and our responsibility

Progestins and breast cancer: risk highlights from France

Anne Gompel (FR)
Université Paris Descartes

Menopausal Hormone Therapy (MHT) is the most efficient treatment to alleviate the bothersome symptoms of menopause. Following the publication of WHI highly publicized in 2002, a drastic drop in hormone use occurred. This was associated with misperception in the level of risk of breast cancer highlighted by several questionnaires in women whom showed the fear of breast cancer. The exact features are different. In the WHI randomized trial, the combined therapy was associated with a small increase in the risk as 4.5 excess cases/1000 over 5 years (HR, 1.34; 95% CI, 1.03–1.75) in women of 50–59 years old. It is admitted that if the use of MHT is associated with an increase in the risk of breast cancer, this is due to a promoter effect on preexisting tumors. Furthermore, it is likely that progesterone could be associated with a lower risk of breast cancer compared with progestin. The estrogen only trial from the WHI reported even a decrease in breast cancer risk which can be explained by various hypothesis. It thus important to inform the women who wish to use a MHT and to evaluate their risk of breast cancer. In the French cohort study, Mission, it appears that in the ''true life'' where gynecologists selected women according to their risk, no increase in the relative risk of breast cancer was observed. Taken into account individual risk could thus help to decrease the small increase in the risk of breast cancer. The tools for that strategy will be presented.

Usage of compounded HRT throughout the world: current trends and gaps

Sebastian Mirkin (US), Julia Amadio (US), Brian Bernick (US)
Therapeutics MD

The use of HRT decreased worldwide significantly after the publication of the WHI; however, there was a large increase in the use of compounded, non-regulatory approved HRT (CHRT) that has gone largely unrecognized. Quantifying the use of CHRT is difficult since CHRT are not tracked in any systematic manner. To understand the use and attitudes toward CHRT word wide, Medline and PubMed were searched for relevant articles using pertinent key words. Also, surveys and market research studies have been evaluated in an attempt to understand the full scope of CHRT use worldwide. Three different studies quantify the use of CHRT in the US. It is estimated that 20–40 million annual prescriptions of CHRT are utilized by approximately 2–3 million US women. An Australian study determined that CHRT is used by approximately a third of the overall HRT users. Two US studies determined that prescribing practices for CHBT vary between specialties. OB/GYNs and GPs more commonly prescribed regulatory-approved HRT while WMDs were more likely to prescribe CHRT. There is a lack of knowledge regarding the regulatory status and regulations of CHRT by prescribers and MDs. Throughout the world CHRT is promoted in the internet and claims are not evidence based. Several studies evaluated women's perception and knowledge about CHRT. Women appear not to distinguish between CHRT and regulatory-approved products and are unaware of the lack of the medical

evidence supporting CHRT use or reported concerns about the quality and safety of CHRT. Given a significant prescription volume and the risks associated with of CHRT use, providers should educate themselves and consumers about the differences between regulatory-approved and CHRT formulations. Additionally, there is an unmet need for well-studied, regulated, alternative natural regimens that don't currently exist on the market.

(PS27) Contraception: from the past to the future

Obesity and contraceptive choices

Sven Skouby (DK)
University of Copenhagen

The rate of obesity worldwide is at epidemic proportions and currently 30% are overweight (BMI>25) in Europe and 40% obese (BMI>30) in The United States. As an integral part of obesity the metabolic syndrome describes a clustering of metabolic abnormalities that together with obesity increase the cardiovascular and diabetes risk. Consequently, use of safe and effective contraceptive methods is of paramount importance in obese women. However, both obese and diabetic women are less likely to use contraception or to receive preventative health care services as compared to women of normal weight. Although the number of studies is limited current evidence suggests that modern types of hormonal contraceptives are safe and provide important non-contraceptive benefits to obese women, The impact of obesity on drug pharmacokinetics may result in lower blood levels of steroid contraceptives reducing their ability to prevent pregnancy, but the actual change is probably minimal. Of note existing data suggest that long-acting, reversible contraceptives maintain excellent efficacy in obese women. To day, therefore, obese women should be offered the full range of contraceptive options, with counseling that balances the risks and benefits of each method, including unintended pregnancy. Addressing the need for adequate contraception in post-bariatric-surgery patients is more frequently becoming an issue. This is because the initial months following surgery are associated with rapid weight loss, which could potentially cause adverse effects on a pregnancy, although and conversely, some data support the fact that many adverse maternal and neonatal outcomes may be lower after having had bariatric surgery.

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Debates

(DEB04) From vulvo vaginal atrophy to genito-urinary sindrome of menopause

From vulvovaginal atrophy to the genitourinary syndrome of menopause: what's in a name?

Jan Shifren (US)
Massachusetts General Hospital

Genitourinary syndrome of menopause (GSM) is the new preferred term for the signs and symptoms associated with postmenopausal estrogen deficiency involving changes to the labia, vagina, urethra, and bladder. The syndrome may include symptoms of genital dryness, burning, and irritation; sexual symptoms of diminished lubrication and pain; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all of the signs and symptoms, which must be bothersome and should not be better accounted for by another diagnosis. The term GSM was defined at a consensus conference by a group of international experts in gynecology, sexual medicine, and urogynecology co-sponsored by The North American Menopause Society (NAMS) and the International Society for the Study of Women's Sexual Health (ISSWSH). The previously available term for this condition, vulvovaginal atrophy (VVA), describes the appearance of genitalia affected by estrogen deficiency, without providing any information on associated symptoms. In addition, ''atrophy'' has negative connotations and ''vagina'' is not a universally acceptable term in the public media, limiting discussion of this syndrome and effective treatments. GSM is a comprehensive term that includes symptomatic VVA and has recently been accepted by the American College of Obstetricians and Gynecologists. Expanded use of the term GSM throughout the world may result in improved understanding and treatment of this important condition.

(DEB05) Progesterone, progestins and brain tissue repair

Precision medicine and neural regeneneration: why precision matters

Roberta Brinton (US)
University of Southern California

Context: Principles and strategies of precision medicine applied to clinical trials of regenerative neurosteroids.
Objective: To advance and accelerate translational research and clinical trial design predictive of neural regeneration.
Patient(s): Populations at risk for and diagnosed with neurodegenerative diseases.
Intervention(s): Regenerative neurosteroid therapeutics to prevent neurodegenerative disease in populations at risk, delay progression of disease in those affected and restore function in those with neurodegenerative disease.
Main Outcome Measure(s): Advance, accelerate and achieve greater success by applying precision medicine principles and strategies to translational and clinical research for neural regeneration.
Result(s): Regenerative therapeutics for neurological disease will require specific dose and therapeutic regimens. Different etiologies, trajectory of degeneration and the systems biology mechanisms of disease will impact therapeutic efficacy. Biomarkers that align with stage of disease and which are predictive of therapeutic efficacy are critical. Decreased rate of degeneration or increased structural and functional recovery would be indicative of regenerative efficacy. Inducible pluripotent stem cells derived from clinical trial participants could serve as source of neural stem cells for predicting regenerative potential and therapeutic response.
Conclusions: Promoting endogenous regenerative potential will require precision in formulation, dosing regimen, and route of administration. Incorporating gender, genetics, age, and stage of disease progression in both preclinical translational analyses and clinical trials are critical to achieving precision medicine for neural regeneration.

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(DEB08) Transdermal estradiol plus oral micronized progesterone: the safer menopausal hormone therapy?

Diverging effects on the normal breast of percutaneous estradiol/oral micronized progesterone vs. oral conjugated equine estrogens/medroxyprogesterone acetate. Impact on mammographic density, proliferation, and tumor related genes.

Gunnar Söderqvist (SE)
Karolinska Institutet

Context: Effects of different HRTs on breast cancer risk markers.
Objective: To investigate the relations between mammographic breast density (MD),breast cell proliferation and gene activation during natural vs. synthetic HRT.
Patients – Interventions: Seventy-seven healthy postmenopausal women were randomized to sequential hormone therapy with two 28-day cycles of either oral 0.625 mg CEE or 2.5 g 0.06% (1.5 mg E2) percutaneous E2-gel daily, with the addition of 5 mg of oral medroxyprogesterone acetate (MPA), or 200 mg of oral micronized P, daily, respectively, 14/28 days per cycle.
Materials and methods – Main Outcome Measures: MD was assessed by both Bi-Rads score and digitized measurement and immunohistochemistry was done for Ki-67, Bcl-2 and PR B before and after 2 months of treatment as was microarray analysis for 28 556 genes on core needle biopsies from eight consecutive patients. This was subject to Ingenuity Pathways Analysis (IPA) for assessment of up- or down-regulated genes. Rt-PCR on 16 key genes from 30 patients was used for confirmation.
Results: Six/35 women had a digitized MD increase exceeding 15% percentage units in the CEE/MPA group, compared to 0/29 women in the E2/P group. There was a significant positive correlation $R = 0.40$, $p = 0.03$, between the increase in MD and increase in Ki-67 positive cells during treatment, which was associated with a MKi-67 gene activation, $R = 0.62$, $p = 0.04$.
Conclusion: There was a more adverse effect on mammograhic breast density for CEE/MPA than for E2/P. The significant correlation between the increase in breast epithelial proliferation and the increase in MD gives further insights in the debated biologic nature of mammographic breast density induced by HRT.

Scientific Society Symposia

Bone health along the women's life (organized by Romanian Society of Endocrinological Gynecology)

The age of menarche and osteoporosis – when is really important?

Carmen Barbu (RO)
Carol Davila University of Medicine and Pharmacy

Menarche and menopause are milestones of normal reproductive life for women, identifying the beginning and the end of the reproductive life in women. Different studies have linked ages at menarche and menopause in many health consequences for women in later life like osteoporosis, cardiovascular risk, diabetes mellitus. In postmenopausal women, the cumulative exposure to endogenous estrogens, measured as years between menarche and menopause, was showed to be a significant protective factor against the development of postmenopausal osteoporosis. Consequently, early menarche and late menopause were associated with high BMD. Among these, the reproductive period showed the strongest association with BMD. Some studies showed that age at menopause between 40 and 45 years, but not age at menarche, correlated with low bone mineral density in postmenopausal females. Early menarche alone has some relation to high BMD in postmenopausal women but is more relevant in premenopausal women. The age at menarche seems to have the main relevance for the peak bone mass and for premenopausal women and after certain age, any difference in BMD in women experiencing different menarche ages or even menopause has disappeared. With increased recognition of premenopausal osteoporosis due to specific conditions or even as a consequences of previous treatments like cancer treatments in children, it is considered important to prevent risk factors that disturb the beginning of menstruation in adolescent girls as a major to improve the peal bone mass and reducing risk of fracture later in life.

Bone health and type II Diabetes Mellitus in postmenopausal women – what is the link?

Ioana Vartej (GR)
Endocrine Private Center Trikala Greece and University Carol Davila Bucharest Romania

Osteoporosis and type 2 diabetes are major public health problems particularly in postmenopausal women.Recent studies showed increased fracture risk in patients with type 2 diabetes despite an increased BMD, due to reduced bone quality. The reduction of bone strength and increased bone fragility in type 2 diabetes, which is not reflected by BMD, depend on bone quality deterioration rather than bone mass reduction. Thus, surrogate markers are needed to replace BMD in assessing fracture risks of diabetic patients, such as trabecular bone score. Quantitative ultrasound may be a more useful method for fracture risk prediction in postmenopausal women with type 2 diabetes than DXA. Postmenopausal women with type 2 diabetes have higher fracture rates of hip, humerus and foot than non-diabetic women. A larger body size and higher bone mass associate a higher fracture risk. Diabetes could impact bone health through several mechanisms: accumulation of advanced glycation end products (AGEs) in collagen; chronic microvascular complications; reduced bone turnover; increased risk of falls due to hypoglycemia, retinopathy or neuropathy; vitamin D deficiency; renal failure. Also, the skeleton has a regulatory effect on glucose metabolism by osteocalcin that regulates insulin sensitivity. We need to screen diabetic patients for osteoporosis and develop fracture prevention strategies. Due to the ineffectiveness of BMD in assessing fracture risk in type 2 diabetes, the major clinical problems are how to assess the risks and when to start fracture prevention therapy. Postmenopausal women with type 2 diabetes must ensure adequate calcium and vitamin D intake, achieve good glycemic control, avoid glitazones and when criteria are met, treatment should be prescribed. Bisphosphonates appear to be effective in reducing fracture risk in postmenopausal women with type 2 diabetes.

Chilean National Guideline and Organization for Care of Climacteric Women, by levels of complexity (organized by Sociedad Chilena de Endocrinología Ginecológica(SOCHEG))

Definition of levels of care and HTM according to criteria of complexity

Patricio Barriga Pooley (CL)
Universidad Finis Terrae, Universidad San Sebastian

To plan a comprehensive management of menopause, which is massive through networks of health, it is essential to establish criteria that determine the complexity level of the main clinical situations to be handled in the health network, including the prescription of menopausal hormone therapy (MHT). The primary level is the equivalent to General Practitioner clinics. The second level is the specialized care reference center. The Chilean Ministry of Health program for management of the climacteric woman defines the clinical situations that we considered can be handled at the primary level. The program defines, as well, the criteria proposed for deriving patients to the secondary level in the health network. We describe these definitions and also special conditions that merit special guidelines, as major depression or adjustment disorder, which is particularly prevalent in Chilean middle-aged female population. Another group to be derived to the secondary level are women who remain eligible for MHT but require more knowledge by the prescriber for higher-risk situations, such as thrombophilia, hypertension or decompensated or parenchymal damage diabetes and anticonvulsive therapy as in the case of epilepsy.

Installing the national program for care of climacteric women, state of progress

Sergio Brantes Glavic (CL)
Universidad de Chile

The guidelines of the Chilean Ministry of Health for care of the climacteric woman presented in this symposium, were approved by the government recently, in 2014. Coverage targets and impact in the medium and long term were defined by the Ministry of Health. It is being introduced in 1800 outpatient primary care facilities and 200 secondary referral centers, throughout the country. We show the strategy for the implementation of the program. We describe the methods used to train professionals through classroom courses, teleconferences, instructional videos, and joint workshops. We discuss the acceptance and the difficulties encountered during the implementation of the program along the country. It is notable that these management guidelines are fully applicable in any medical office or health care network. The description of this experience in the International Congress of Gynecological Endocrinology has the objective to show this plan of management of climacteric women, looking forward for international consensus discussions for improvement of the standards in the comprehensive care for women in menopause age.

Overview of a national comprehensive care plan for climacteric women

Arnaldo Porcile (CL)
Universidad de Chile

Worldwide, there is a big and growing population of menopausal middle-aged women requiring care in organized health networks. In Chile, according to national population records, to morbidity and mortality statistics and to different national surveys of health needs, these women have shown to have a high prevalence of problems in the physical, psychological, sexual and social spheres. Highlights include: depression (40%), obesity (44%), hypertension (40%), type 2 diabetes mellitus (19%), dyslipidemia (60%), smoking (32%), osteopenia (45%), sedentarism (91%), amongst others. A pilot project in an outpatient clinic of the public health system in Santiago de Chile, demonstrated a positive impact of a holistic management approach of the menopausal woman, improving the quality of life of these women (data will be shown). The need to care on middle-aged women with epidemiological criteria was evidenced, as well as the need to address care in a comprehensive way to cover the full range of problems affecting menopausal women. They need to relieve symptoms, prevent disease and also confront social problems: changing roles related to children or grandchildren, partner relationship, work, eventually helping sick relatives and others. We concluded that the clinical management programs of middle-aged women should identify the hierarchy of problems affecting each individual case and generate algorithms for treatment, including hormone therapies and effective interventions for the current morbidity. We worked together with the national health authorities to create a comprehensive management plan with accurate algorithms for the evaluation and clinical management of major health problems of women, including quality of life. We describe the basis of the program developed for the comprehensive management of menopause.

Addressing morbidity and HTM for each woman, keeping the focus on quality of life.

Paula Vanhauwaert Sudy (CL)
Socheg

The Chilean Ministry of Health program for management of the climacteric woman (OT) have 3 main *Objectives*: improve the quality of life (QoL), detect and treat comorbidities and the prevention of chronic illnesses. To achieve this a structured multidisciplinary program was established. The program begins with a pre-established anamnesis including the Menopause Rating Scale (MRS), a physical examination and laboratory tests. With all this a diagnosis is made and a plan of treatment is designed according the recommendations of the OT. The decisions involving QoL are taken according to the MRS score. The MRS evaluates different symptoms of the menopause syndrome and gives an evaluation of the QoL. The OT stablished a score above which the health professionals must offer a treatment because not doing so would be unethical. The hormonal treatment (HT) is the treatment of choice if no contraindication exist. If HT is excluded other treatments must be offered. The detection of comorbidities is essential for both, prescription of HT and health issues. For metabolic diseases the OT promotes the use of the ATPIII criteria. The evaluation of anthropometric parameters, habits and other psychosocial factors are useful to intervene on healthy life style modifications. The peri and post menopause is also an excellent time window to intervene and prevent the development of other pathologies such as osteoporosis and neoplasia so the screening and strategies to prevent them are also included in the OT. The psychosocial aspects are evaluated and worked out trough group workshops with structured methodologies and specific objectives designed to achieve the transfer of skills in interpersonal relationships, stress management, empowerment and self-esteem. Finally, a global, personalized plan of treatment and follow up is made with the main goal of improve her quality of life.

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Endocrine and other factors in infertility success (Organized by the Mediterranean Society for Reproductive Medicine -MSRM-)

Repeated implantation failure: a new potential treatment option

Antonios Makrygiannakis (GR)
University of Crete

Implantation failure is rather a common event since only 73% of the concepted embryos are implanted into the endometrial cavity, and only 50% of them will end up as live births. The immunology of RIF is complex. Cytokines and uterine Natural Killer cells are definitely involved. Additionally the extracellular matrix is also altered as this is described by MMP alterations. The role of inflammation is also crucial as the prostaglandin profile is also reported to be changed. In the frame of reproductive immunology, our group and others have demonstrated the immunomodulatory role of the CRH peptide during implantation and early pregnancy development. It has been shown that CRH is expressed in the implantation sites, and that CRH facilitates decidualization. Additionally we have shown that CRH facilitates maternal tolerance during implantation by inducing FasL expression upon the trophoblast surface, triggering in turn, Fas-expressing T cell apoptosis. Recently, it has been reported that endometrial injury –as this is performed by a pipelle biopsy – one cycle before an IVF/ET, significantly increased the implantation, pregnancy and live birth rates in women who had one or more IVF failure. More over it has been shown that insertion of autologous peripheral blood monocytes (PBMC) along with HCG to the uterine cavity during the ET, significantly increased clinical pregnancy, implantation and live birth rates in patients with repeated failure of IVF/ET. By combining the knowledge on CRH and its association with a Th2 profile, and the reported effect of the PBMCs on IVF/ET efficacy, we investigated whether the intra-uterine administration of CRH-treated PBMCs during ET could increase IVF/ET in women with RIF. Our results indicate that such intervention significantly improves the clinical pregnancy rate, supporting a new clinical application in the field.

Physiological role of progesterone in the luteal phase and the endometrium

Ioannis Messinis (GR)
University of Thessaly

It is well known that the relationships between the ovaries and the hypothalamic-pituitary system are determined by the feedback mechanisms mediated by the ovarian steroids. During the normal menstrual cycle, the two gonadotrophins play an important role in the selection of the dominant follicle. At midcycle, the positive feedback effect of estradiol is activated and the endogenous LH is displayed. The LH surge is responsible for the induction of luteinization, resumption of oocytes meiosis, rupture of the follicle and formation of the corpus luteam. Following luteinization and the formation of the corpus luteum, serum progesterone levels increase reaching a peak in the mid-luteal phase. Progesterone in the luteal phase plays important physiological roles. This steroid is the main mediator of the negative feedback mechanism on LH and FSH secretion. Progesterone also exerts local luteotrophic actions in the corpus luteum by preventing apoptosis. In addition, it prevents corpus luteum degradation. Progesterone has a major role in the maturation of the endometrium. Specifically, it antagonizes estrogen-induced proliferation in uterine epithelium and differentiates endometrial stromal cells to a decidual phenotype. In the first half of the luteal phase, endometrium is characterized by declining proliferation and secretory differentiation, while in the second half proliferation in epithelial cells is low but there are decidual changes with high proliferation in the stroma. After the onset of luteolysis, progesterone concentrations decline, leading to a cascade of events, which results in proteolytic breakdown of the superficial endometrium, focal bleeding and cell death. All these events are prevented only after conception and implantation via the production of human chorionic gonadotrophin.

Meet Experts of International Academy of Human Reproduction (organized by International Academy of Human Reproduction (IAHR))

Luteal phase disfuntion associated with ovarian stimulation

Luigi Devoto (CL)
Institute for Maternal and Child Research (IDIMI), Department of Obsterics and Gynecology, San Borja Arriarán Hospital, University of Chile, Santiago

The human corpus luteum (CL) is the major source of steroid hormones. The pattern of progesterone (P) production throughout the luteal phase (LP) determines menstrual cyclicity and endometrial receptivity for successful implantation and maintenance of early pregnancy. However, in non-stimulated cycle thre is a lack of a reliable test to diagnose this disorder.CL dysfunction following ovarian hyperstimulation in IVF cycles has bas been established The pathophysiology of gonadotrophin-stimulated cycles dysfunction has been attributed to supra-physiological steroids level resulting a deviation from physiology, in which a simultaneous surge of LH and FSH is responsible for triggering ovulation followed by pulsatile LH and P secretion. The use of GnRHa or antagonist that interfere with LH secretion during the LP, arise that luteal support with P, remains mandatory of IVF protocols. Investigators have advocated several pharmacological strategies to prevent CL endocrine and molecular endometrial dysfunction in stimulated cycles: simple minimal stimulation protocols with a bolus of GnRH agonist for ovulation trigger with or low doses of hCG followed by P and E2 administration to support LP. This treatment provides good quality oocytes presumably associated with the simultaneous surge of LH-FSH and eliminate significantly the risk of OHHS. Finally, new pharmacologic options and molecular assessment of endometrium opened opportunities for a tailored approach to luteal phase support.

Ezrin and estrogen receptor (ER) expression by epidermoid cervical cancer (CXCA)

S-D Choi (US), A. Fadiel (US), T-H Kim (US), Frederick Naftolin (US)

Rationale: The effect of HPV on cervical tissue and development of CXCA is only partly understood, but ER's and ezrin are involved. We tested their relationship during the development and action of CXCA.
Methods: Immunohistochemistry for ERα, ERβ, and ezrin was evaluated using ''H'' testing on sections from 7–10 normal through metastatic CXCA patients. Effects of estradiol was studied in a metastatic CXCA cell line.
Results: ERα, ERβ, and ezrin were expressed in normal cervix epithelium. Abundant koilocytosis (surrogate for HPV) was present in the affected patients. Although ezrin expression increased on a steep linear slope as the disease progressed to metastatic CXCA, ERα and ERβ expression were markedly reduced by the attainment of dysplasia and remained low and flat through invasive CXCA. In metastatic cells,

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estrogen increased the immune-ezrin close to the nucleus and induced a metastatic phenotype.
Conclusions: HPV affected all proteins studied. Ezrin overexpression indicates a role in development of CXCA. The fall of ER was dramatic and sustained but estrogen action could be shown, fitting with reports of temporary response of CXCA to SERM's. These changes are strongly associated with disease progression and metastasis of CXCA.

Menopausal hormone therapy: Endocrine Society guidelines and advances (organized by the Endocrine Society)

Endocrine Society Guidelines for treatment of menopausal symptoms

Anne Gompel (FR)
Université Paris Descartes

A group of 6 experts(Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Pinkerton JO.A, Santen RJ) representing the Endocrine Society, the European Society of Endocrinology, IMS, EMAS, NAMS, established recommendations from the best available scientific evidence. These recommendations are published in the J Clin Endocrinol Metab 100: 3975–4011, 2015. The conclusions are that Menopausal hormone therapy (MHT) is the most effective treatment for vasomotor symptoms and other symptoms of the climacteric. Benefits may exceed risks for the majority of symptomatic postmenopausal women within ten years following the menopause and at an age 50–60y. It is recommended to evaluate the individual risk factors in order to tailor the treatment. In particular, cardiovascular and breast cancer risk should be evaluated in order to prescribe the most appropriate therapy depending on risk/benefit considerations. Non-hormonal options are also available for vasomotor symptoms in case of contraindication to MH. Topical therapy by low-dose vaginal estrogen, vaginal moisturizers and lubricants should be systematically proposed to women for the genitourinary syndrome of menopause; ospemifene can be prescribed, but with some contraindications. In cases of relative contraindications to MHT if the woman is willing to use it, after full information, the treatment can be discussed. In addition, postmenopausal women should be informed on lifestyle measures. The recommendations will be detailed in the presentation.

Modern approaches to the combined treatment of myoma, endometriosis and hyperplastic process of uterus (organized by Russian Society of Obstetricians and Gynecologist, Russian Society of Reproductive Medicine and Surgery, Russian Association of Endometriosis)

Modern trends in combined treatment of genital endometriosis

Maria Yarmolinskaya (RU), Arseny Molotkov (RU), Anna Tsypurdeeva (RU), Elena Durneva (RU), Dmitry Tsitskarava (RU), Elena Suslova (RU)
D. O. Ott Research Institute of Obstetrics, Gynecology and Reproductology

Context: Due to the fact that endometriosis is a chronic progressive and recurrent disease, its combined treatment (surgery and post-operative hormonal therapy) is considered to be the most effective. Objective of the study was the creation of postoperative hormonal therapy algorithm for patients with genital endometriosis (GE) of different stages of severity.
Methods: The study included 1842 patients with laparoscopically verified GE, the average age of women was 34.4±5.8 years. Patients. In 71% of patients we diagnosed GE of III and IV stages. 74% of patients had chronic pelvic pain, 43% dyspareunia, 56% of patients – infertility. In 58% of cases cystectomy was performed, in 49% we made excision of endometriosis of pelvic peritoneum, in 22% – removal of endometriotic infiltrate, in 1.3% – we performed resection of recto-sigmoid part of colon. Within 6 months after surgery 42% of patients received aGnRH, 35% – dienogest 2 mg, 12% – combined contraceptives (CC), 11% women were prescribed aromatase inhibitors in combination with progestagens.
Results: In the group of patients, treated after surgery with CC, in 68% of cases recurrence of endometriosis was found; in 13% of cases after aGnRH treatment, in 12% of cases after treatment with dienogest and in 8% after aromatase inhibitors. It was noted that aromatase inhibitors are the most effective medication in eliminating pelvic pain syndrome.
Conclusions: Thus, for patients with GE of I-II degrees, who do not plan pregnancy now, it is appropriate to appoint anti-recurrence therapy (dienogest or low-dose CC in extended regimen) before pregnancy planning. For patients with GE of III-IV stages with pain syndrome or infertility and preserved ovarian reserve, appointment of aGnRH is recommended, if ovarian reserve is reduced – aromatase inhibitors or dienogest should be prescribed.

New aspects in contraception (Organized by the European Society of Contraception -ESC-)

Contraception in some medical disorders

György Bártfai (HU)
University of Szeged

Hormonal contraception is a frequently used method to avoid unwanted pregnancies. Currently more than 100 million women are using one kind of hormonal contraception all over the world. However, hormonal contraception is always associated with risks and/or benefits of contraceptive or non-contraceptive nature. Furthermore, in some medical disorders the use of contraception could be a relatively or absolutely contraindicated. Therefore, it is paramount of importance to consider the risk and benefits especially in case of medical disorders. The ovarian cancer is the sixth most frequently occurred malignant disease in women. Case-control and cohort studies unanimously proved the beneficial non-contraceptive effects of hormonal contraceptive use ie. already five years hormonal contraceptive use led to low ovarian cancer risk. Therefore the contraceptive benefit and the non- contraceptive ones surpass the risk caused by hormonal contraceptives. However, in some other medical disorders the risk taking hormonal contraceptives is higher than the benefits. Liver tumour or active hepatitis considered as a contraindication to take combined oral hormonal contraceptives (COC) and progestogen only pill (POP) and injecables are also not usually recommended. Unexplained vaginal bleeding is frequently occurs in women in reproductive age. According to the WHO medical eligibility criteria for contraceptive for women with this condition use of copper bearing intra uterine device is contraindicated and neither hormonal implants nor injectables are not recommended. COC and POP are considered for them as a generally used method.

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New aspects in contraception (Organized by the European Society of Contraception -ESC-)

Contraception in women with BRCA 1 or BRCA2 mutation

Kristina Gemzell Danielsson (SE)
Karolinska Institutet

Ovarian steroids, as well as synthetic gestagens and estrogens have a role in breast cell proliferation and the development of breast cancer, the most common cancer among women. Women with BRCA1-and-2 mutations have an increased risk of developing breast cancer, frequently during their reproductive age. An association between combined hormonal contraception (CHC) and breast cancer has been proposed. In women with BRCA1-and-2 mutation limited evidence is available which indicate that the risk of breast cancer among these women is probably not modified by the use of CHC. Since women with BRCA1-and-2 mutations have an increased risk of developing ovarian cancer CHC may actually offer advantages due to its protective effect against ovarian cancer. Future possibilities may include the use of progesterone receptor modulators (PRMs) for contraception. Our preliminary results implicate a possible protective effect of PRMs on the breast epithelium. The ability of PRMs to block breast epithelial cell proliferation may prove beneficial when used by any woman for contraceptive purposes or for other indications.

New aspects in contraception (Organized by the European Society of Contraception -ESC-)

What is a positive family history with regard to VTE risk in women with need for hormonal contraception

Gabriele Merki-Feld (CH)
University Hospital

Venous thromboembolism susceptibility genes are present in 5–10% of the general population and in at least 40% of patients with VTE. The list of genetic factors is growing. A positive family history (FH) for VTE is a strong contraindication for the use of combined hormonal contraceptives. If one first degree relative has experienced a VTE the family history is considered to be positive. However, in gynaecologic counselling we usually consider a FH as positive, if this relative 50 years or younger. In the presentation we will discuss the value of the cutoff of 50 years and the rolle of second and third degree relatives. in a Swedish study a VTE in third degree realtives was associated with an OR of 1.55 for VTE (second degree relatives 2.3). It still has to be determined whether genetic testing provides additional prognostic value once the family history has been determined. A positive family history should be considered as a reason to avoid CHC and rather recommend IUD or POC, if available and acceptable.

Session of International Consortium for Male Contraception (organized by International Consortium for Male Contraception (ICMC))

The condom, inside out.

Jean-Jacques Amy (BE)
Vrije Universiteit Brussel, Brussels, Belgium,

Background and objectives: With very few exceptions, the literature concerning the history of condoms is replete with errors.
Methods: To mention only authenticated facts, primary sources were accessed.
Findings: The origin of 'condom' is still debated. According to one plausible hypothesis the word is derived from the Latin verb 'condĕre' (to sheathe) or the corresponding noun 'condus' (receptacle). Alternatively, it could stem from the Venetian variant 'gondon' of the Italian word 'guantone' (glove). The earliest known mention of this barrier method is in Antoninus Liberalis' fable of Minos and Pasiphae (2nd century AD). Covering the penis with an animal gallbladder for contraception was recommended by the Persian physician Al-Akhawayni (10th century). The oldest extant 'skin' (animal membrane) condoms date back to 1642–1646. Such devices became increasingly popular for avoiding sexually transmitted infections (STIs); in the 18th century their value for birth control was acknowledged. Rubber condoms were obtainable from 1855; since 1930, they are made of latex. The story is illustrated, in parallel, by the salient changes that took place over time in sexual attitudes and behaviours. Reference is made to distinctive figures such as Boswell, Mrs. Philips, Casanova, Marguerite Gourdan, Richard Carlile.
Conclusion: Condoms, when used consistently, protect satisfactorily against unwanted pregnancy and certain STIs, including HIV. The usage of this easily accessible, reversible method is still very much topical.

Session of the Hungarian society of gynecological endocrinology (organized by Hungarian Society of Gynecological Endocrinology)

Hormonal aspects of the iron metabolism during pregnancy

Karoly Hajnaczky (HU)
Peterfy S. Hospital, Budapest,

Erythroid hyperplasia of the maternal bone marrow provides a significant enhancement of circulating red cell mass. The human placental lactogen of placental origin has a pivotal role in this process. The erythropoietin (EPO) produced by kidneyis, glycopeptide containing 165 amino acids, has central role in the regulation of red cell production in both mothers and foetuses. The EPO can not cross the placenta. This fact has a therapeutic consequence, the recombinant EPO-products given to mothers are not able to exert to any effects on foetal blood production. In accordance with the available data, the hepcidin, glycopeptide of 25 amino acids, has a central role in the scope of regulation of iron metabolism. The main site of its synthesis is the liver as some sorts of white blood cells can produce it in a less significant quantity. The role of hepcidin is to form a connection between the innate immunity and iron metabolism. The inflammatory processes affec expectant women. The most frequently occuring ones are the urinary tract infections, enhance the production of hepcidin which results in the disturbances of iron metabolism. As a result of the constantly persisting inflammatory processes, anaemia of

inflammation appears (normocytic normochromic anaemia) in the mothers and the iron transportation via placenta towards the foetus decreases in a significant extent. In case of misdiagnosed primary autoimmune hypothyreoidism (usually mild forms) and underdosed thyroxine replacement therapy can develop normocytic normochromic anaemia in the mothers. Measurement of plasma TSH-value is indispensable in the field of differentiation of anaemic forms during pregnancies.
(Lecture for the Session of the Hungarian Gynecologycal Endocrinology Society)

Sperm biomarkers in male infertility and testicular cancer: genetic, epigenetic and functional examinations

Attila Jakab (HU)[1], Matyas Benyo (HU)[2], Zsuzsa Kassai (HU)[1], Gyongyi Bekesi (HU)[3], Attila Mokánszki (HU)[4], Eva Olah (HU)[5], Zsuzsa Molnar (HU)[4]
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Context: Male infertility and testicular cancer (TC) increases common origin is assumed. Sperm biomarkers have value in fertility prognosis. Aneuploidy and DNA decondensation is related to pregnancy loss, hyaluronic acid (HA) binding reflects genetic integrity and maturity related fertilization potential.
Objective: Relations between sperm concentration, HA binding, aneuploidy and DNA condensation in infertility and TC. *Patients*: 28 TC, 20 infertile oligozoospermic (OS) and 20 normozoospermic (NS) men.
Interventions: Semen assessed as per WHO. HA binding assay (HBA) was the functional test, HBA score calculated. For aneuploidy multicolor FISH for chromosomes X, Y and 17, for nuclear decondensation aniline blue (AB) staining were used.
Outcome: No difference in aneuploidy and AB comparing NS and TC, although the sperm concentration ($p < 0.001$) and HBA score ($p < 0.001$) lower in the TC. Aneuploidy, AB staining higher and HBA score lower in OS than in TC ($p < 0.001$). In non-TC men, strong correlations between sperm concentration and aneuploidy rate ($r = -0.64$), aniline blue staining ($r = -0.88$) and HBA score ($r = 0.84$). In TC, apart from weak relation between sperm concentration and aneuploidy ($R = 0.64$), no other correlations.
Results: Relations exist between sperm count and the examined biomarkers. The lowest HA binding capacity, highest aneuploidy and decondensation were observed in OS infertile men. In contrast, in TC only slightly decreased HA binding and mild elevation of aneuploidy and decondensation was detected and no relation between sperm concentration and HA binding or condensation.
Conclusions: In contrast to infertile men, in TC there are no relations between sperm concentration, genetic integrity and nuclear condensation. Although sperm concentration is low at diagnosis, cryobanking for TC men carry no elevated risk of transmitting genetic abnormalities at ART.

Circulating heat shock protein 70 (HSPA1A) levels in pregestational and gestational diabetes mellitus

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First Department of Obstetrics and Gynecology, Semmelweis University, Budapest, Hungary,

Context: Recent data indicate that serum Hsp70 (HSPA1A) levels are increased in type 1 and type 2 diabetes mellitus. However, there is no report in the literature on circulating Hsp70 levels in gestational diabetes mellitus.
Objective: To determine serum Hsp70 levels in pregnant women with pregestational diabetes, women with gestational diabetes and healthy pregnant women, as well as to examine whether parameters of carbohydrate metabolism are related to circulating Hsp70 levels.
Patients and methods: Eleven pregnant women with pregestational diabetes, 38 women with gestational diabetes and 40 healthy pregnant women with a normal oral glucose tolerance test were involved in our case-control study. Serum Hsp70 levels were measured by ELISA. Plasma glucose levels, serum insulin concentrations, HbA1c values and the Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) index were also determined.
Results: Serum Hsp70 concentrations were significantly higher in women with pregestational and gestational diabetes mellitus than in healthy pregnant women. In addition, pregestational diabetic women had significantly higher Hsp70 levels than those with gestational diabetes. Furthermore, in the group of women with gestational diabetes mellitus, serum Hsp70 levels showed a significant positive correlation with HbA1c values. However, there was no other relationship between clinical features and metabolic parameters of the study subjects and their serum Hsp70 levels in either study group.
Conclusions: We demonstrated for the first time in the literature that serum Hsp70 levels are increased and correlate with HbA1c values in women with gestational diabetes mellitus. Nevertheless, further studies are needed to determine whether circulating Hsp70 plays a causative role in the pathogenesis of gestational diabetes or elevated serum Hsp70 levels are only consequences of the disease.

Development of diagnostic criteria of polycystic ovary syndrome (PCOS) – Hungarian experiences from the view of management

Andras Szilagyi (HU)
University Teaching Hospital of Kaposvar

Although PCOS has been defined clinically, biochemically, and by ultrasound, it is a heterogenous disorder. The most widely used diagnostic criteria of PCOS were established by the first Rotterdam Consensus Workshop on PCOS in 2013. According to the Rotterdam criteria PCOS can be diagnosed if 2 out of 3 criteria (oligo- or anovulation, hyperandrogenism, polycystic ovaries) are present. Using the possible combination of these three criteria, four different phenotypes of PCOS may be identified. The four phenotypes raise several questions that are not fully answered for the time being: prevalence of the phenotypes, degree of severity they represent, short and long-term consequences of PCOS depending on the phenotypes. The Rotterdam criteria and the phenotypes are applied in Hungary as well. Diagnostic criteria are widely used, but the phenotype of a given PCOS patient is rarely identified. The phenotype and especially the degree of hyperandrogenism is used first of all in infertile patients together with the examination of the

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degree of insulin resistance. Insulin sensitizers (metformin and myo-inositol) are widely used in infertile patients who need ovulation induction or IVF in Hungary, but management of long-term consequences of PCOS are rarely managed by life style modifications and/or metformin, inositol or even statins.

Sindrome de Ovario Poliquistico: Desde la etapa prenatal a la senectud (organized by Asociación Latinoamericana de Endocrinología Ginecológica (ALEG))

Reproductive impact of polycystic ovary syndrome (POS)

Raúl Domínguez González (MX)
ALEG

Polycystic ovarian syndrome (POS) endocrinopathy is more common in women of reproductive age (5–7%). *Objective*: With clinical and pathophysiology, find reproductive impact of POS. *Development*: For diagnosis, the Consensus of Rotterdam is used, they must meet at least two criteria: Oligo-ovulation; Menstrual irregularity; Clinical or biochemical signs of hyperandrogenism; Polycystic ovaries by ultrasound. There are three changes: NEUROENDOCRINE (hypersecretion of LH); Metabolic (insulin resistance and hyperinsulinemia); OVARIAN steroidogenesis/Adrenal (alteration in androgen biosynthesis) and folliculogenesis OVARIAN (increased recruitment and reduced choice). Explanation of components of the POS (hyperandrogenism and detention of follicular development) is the increase in androgens intraovarian inhibits the development of follicles that are growing and gives rise to cysts on the periphery. The smaller cysts are more androgenic the developing follicle, because proportionately less secrete estrogen and produce an imbalance between androgens and estrogens. Reproductive impact are at increased risk of dysfunctional metrorrhagia, infertility, abortions, pre-eclampsia, gestational diabetes, premature birth and stillbirth, macrosomia, Small for gestational age. In conclusion, in patients with POS, not only decreased the rate of pregnancy but also an abnormal implantation and an increased incidence of abortion was observed.

Policystic Ovary (PCO): prenatal, childhood starting. . .?

Selva Lima (UY)
Faculty of Medicine Claeh

The policystic ovary syndrome is an endocrine-methabolic disorder, with a high prevalence, and consequences along the life time. Many expert meetings were held to optimise the diagnosis and it is at the beginning of its clinical expression, in adolescence, where difficulties of diagnosis have been presented. In this period of life it is common to begin its presentation with cycle alterations, but many studies have shown that the disorder probably begins at earlier stages (prenatal and childhood), where some risk factors are already outlined for PCO development. Animal models have been used and these investigations suggest that the foetal androgen exposition probably determine a phenotypic expression of PCO and metabolic disorders associated. This is also demonstrated in daughters of PCO mothers. Genetic, environmental or epigenetic risk factors are involved in its development. Low weight at birth is also a strong factor linked with a risk of PCO development, as well as persistent menstrual disorder and hyperandrogenism in adolescents. Knowing all of these aspects predicts the possibility to prevent the consequences.

PCO and menopause

Silvina Witis (AR)
Hospital de Clinicas

PCO, Polycystic ovarian Syndrome, can be diagnosed during early infancy and reproductive periods, however, menopause women are very difficult to identify. The importance of aknowledging these patients are the presence of metabolic and cardiovascular complications, which appear to be higher when compared with controls. Women with PCO during their reproductive years show higher levels of androgens as well as fasting glucose e insulin, hypertension, dyslipemia and a higher risk of diabetes. Therefore, is very important to follow there patients in order to improve the morbidity cause by this syndrome.

Strategies for a healthy menopause (Organized by European Menopause and Andropause Society(EMAS))

Sexual dysfunction in middle aged women

Peter Chedraui (EC)
Institute of Biomedicine, Universidad Catolica de Santiago de Guayaquil

Sexuality during female mid-life is a complex phenomena, as it is affected by many factors such as age, the menopause, partner issues, and also social and cultural factors. In this sense, Latin America has a multiplicity of ethnicities and socio-economical features. Sexual activity during mid-age is an important factor determining dysfunction or not. For instance, one Latin American mid-aged female series found that 25.6% had no sexual activity and 56% had sexual dysfunction (SD), as assessed with the Female Sexual Function Index. In this study, SD correlated to poor vaginal lubrication, lower education and partner SD. Hence, the role of the partner is pivotal. The role of ethnics (i.e indigenous) as a risk factor for SD among mid-aged women has also been reported. This lecture will provide insights of risk factors for SD in mid-aged women, epidemiological aspects and tools used to asses SD.

The true risks of menopausal hormone therapy

John Stevenson (GB)
Royal Brompton Hospital

Many benefits of hormone replacement therapy (HRT) are well established, and some are still emerging. But as with any treatment, benefits have to be weighed against potential risks. The risks of HRT have frequently been overstated, either by reference to flawed studies or by flawed interpretation of existing data. Increased breast cancer risk is a major concern, but there is little evidence that HRT causes breast cancer or increases its mortality. Indeed there is now evidence that certain estrogens may even reduce breast cancer risk. There is no convincing evidence that risk for ovarian cancer or any other cancer is increased by HRT. When HRT is given appropriately with the correct starting dose, risk for stroke is probably not increased and risk for coronary heart disease is actually reduced. A transient increased risk for venous thrombo-embolism is dose dependent and can be avoided by the use of non-oral therapy. There is a small increased risk for gallbladder disease which may be confined to oral HRT use. The fact that all-cause mortality is not increased by HRT, and indeed may be reduced, underlines the overall safety of the therapy even in the long term.

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Symposium of the Chinese Society of Gynecological Endocrinology

Abnormal uterine bleedings – one of the main problems in Chinese women

Alfred Mueck (DE)
University Women's Hospital of Tuebingen

According to the new definition of FIGO ''Abnormal Uterine Bleedings (AUB)'' are any significant deviation from normal frequency, regularity, heaviness and duration of menstrual bleedings. Terms like ''menorrhagia, hypermenorrhoea, metrorhagia'' should no longer be used, severe bleedings should be named as ''Heavy Menstrual Bleedings (HMB)''. That diagnosis should be made by menstrual history, backed up by low serum ferritin and low hemoglobin levels. According to the causes of AUB the PALM-COEIN Classification (FIGO) should be used, classifying as follows: For ''PALM'': P = Polyp; A=Adenomyosis; L=Leiomyoma; M=Malignancy; For ''COEIN'': C=Coagulopathy; O=Ovulatory Dysfunction; E=Endometrial Hyperproliferation; I=Iatrogenic; *N* = Not yet classified (all others). In our Beijing OB/GYN hospital, Capital Medical University, China, there are about 1 Million outpatients/year. More than 20% have bleeding problems, in contrast almost no increased risk of venous thromboembolism have been observed, as we recently have published (Mueck AO, Ruan X. Maturitas 2015; 82:266–270). On the basis of the FIGO definition typical cases will be discussed as we can seen very often in Chinese women, and surgical, hormonal and non-hormonal treatment options to stop the bleedings will be given after interactive discussion.

Menopausal management – China's view

Xiangyan Ruan (CN)
Beijing Obstetrics & Gynecology Hospital, Capital Medical University

About 200 million climacteric women in China. Menopause General Management is very important. due to China menopause society established much more later (established in 2000)than some advanced countries in the world,so this presentation will focuse on my own clinic practice the Requirements of menopause health care: Total Health Promotion; Safe & effective HRT; Individual nutrition; Environment safety; Exercise training; Effective rehabilitation; Living Style; Mental Assistance.

procedures: Medical history-Physical examination-Lab & Others-Analysis diagnosis-Systematic treatment-Public education Complete System:All done in one time; All work completed in 1 and half hour; Diagnose all diseases in the category; Systematic treatment and advice; All data recorded in paper and E form; Print all reports.

Individualization: Individualized examination items; Individualized HRT plan; Individualized HRT adjustment; Individualized nutrition plan; Individualized exercise plan; Individualized living direction.

Follow and Record: Complete follow up procedures; All data are recorded; Data could be analyzed at any time; Data recorded for life time.

Conclusion: The principle of Clinical procedures for postmenopausal woman's health care must be adjusted by individual cases.

Association analysis between HFM1 variation and POI in Chinese women

Jie Wu (CN)
The First Affiliated Hospital of Nanjing Medical University

Primary ovarian insufficiency (POI) is clinically defined as the absence of normal menses for at least 4 months before the age of 40 years, and two serum follicle-stimulating hormone (FSH) concentrations exceeding 30–40 IU/L at least one month apart. HFM1 is a meiosis-specific gene and expressed in germ-line tissues. More recently, evidence has indicated that variations in HFM1 gene could be causative for POI. The aim of the present study was to investigate the association between HFM1 gene variants and sporadic POI in Chinese women. A total of 138 POI patients and 316 healthy controls were recruited in this study. We screened the entire HFM1 coding region by direct sequencing in all subjects and identified six variants of HFM1 gene in POI group. The variation rate of HFM1 in POI group is significantly higher than control group ($p < 0.01$). The p.His414Pro and p.Arg1194Cys were predicted to be probably damaging to the HFM1 protein function, while p.Glu50Lys, p.Phe775Leu and p.Ser1123Pro mutants might not have any deleterious effect on the structure or function of the protein by on-line predictors. Taken together, our data suggested HFM1 gene might be associated with primary ovarian insufficiency in Chinese population.

PCOS management – China view

Wei Zhang (CN)
Ob/Gyn Hospital of Fudan University

Polycystic ovary syndrome (PCOS) is a heterogeneous and complex endocrine disorder characterized by ovulatory dysfunction, hyperandrogenism and morphologically polycystic ovary. The disease can cause infertility and is also associated with an increased risk of other metabolic, cardiovascular, and neoplastic diseases later in life. Great efforts have been made in the last decade by Chinese scholars. According the results of studies in China, the phenotype of Chinese women with PCOS is different from other nationality, so the guidelines of diagnosis and treatment of PCOS was established by the Chinese Society of Gynecology Endocrinology based on data from Chinese population. The diagnosis criteria reflect the phenotypic heterogeneity of the syndrome in Han nationality, and treatment choices were set up according to the phenotype of Chinese women and individual patient's needs. The features and characteristics of Chinese PCOS will be introduced, and China perspective on the diagnosis and management of PCOS will be presented introduced in this view.

Sponsored Symposia

Acido alfa-lipoico a supporto della durata fisiologica della gravidanza: evidenze e prospettive (sponsorizzato da LO.LI Pharma)

Acido alfa-lipoico vs. progesterone nella minaccia di aborto: quali evidenze?

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Premessa: L'instaurarsi di una gravidanza è un processo molto delicato in quanto è noto che il 70% dei concepimenti va in realtà incontro a fallimento. Gli specifici meccanismi molecolari e cellulari che sottintendono il buon esito di una normale gravidanza sono ancora relativamente noti e la minaccia d'aborto rappresenta una delle complicanze più temute e che maggiormente si possono riscontrare fino alla 22a settimana di gestazione, anche se la maggior frequenza la riscontriamo nel primo trimestre. Non è facile inquadrare le cause che possono portare alla minaccia d'aborto. La gravidanza è fortemente influenzata da aspetti immunitari e si inserisce nella complessa

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fisiopatologia dell'organismo materno, delineando un fondamentale capitolo da studiare per evidenziare eventuali problematiche che possano permettere il trattamento terapeutico. I meccanismi immunologici ed endocrini coinvolti nel primo trimestre di gravidanza potrebbero ricondursi ad una relazione tra il trofoblasto umano e i linfociti della decidua: le cellule Th-2 della decidua producono citochine Th-2 che inducono il rilascio di gonadotropina corionica (hCG) dal trofoblasto. L'hCG stimola la produzione di progesterone da parte del corpo luteo, e poi un aumento della secrezione delle citochine Th-2 e una riduzione delle citochine Th-1. In questo quadro complesso, l'uso del progesterone per contrastare la minaccia d'aborto è prescritto da protocolli terapeutici, sebbene esistono poche evidenze concrete a supporto della sua efficacia e la reale portata della sua efficacia è ancora oggi dibattuta. L'acido alfa lipoico (ALA) è una molecola naturale e sicura con riconosciute proprietà antiossidanti, antinfiammatorie e immunomodulanti. È in grado di normalizzare diverse anomalie patologiche causate da uno squilibrio del complesso network di citochine, chemochine e fattori di crescita. Su tali basi, oggi sta acquisendo sempre più interesse l'indagine clinica atta a verificare l'efficacia di tale molecola nell'ambito della gestione della minaccia di aborto. Su tali basi, è stato condotto un primo studio pilota (RCT) con l'obiettivo di confrontare l'effetto della somministrazione vaginale con ALA vs. il progesterone, in casi di minaccia di aborto con evidenza ecografica di ematoma subcoriale. Metodi: Cinquantaquattro donne in gravidanza nel primo trimestre di gravidanza con minaccia di aborto (dolore addominale in presenza o meno di perdite vaginali) e ematoma subcoriale sono state incluse nello studio. Il gruppo controllo ha ricevuto ogni giorno 400 mg di progesterone vaginale, mentre le pazienti incluse nel gruppo di indagine sono state trattate con ALA vaginale una volta al giorno (DAV® capsule vaginali, Lo.Li. Pharma srl, Italia). I trattamenti sono stati somministrati fino alla risoluzione completa del quadro clinico. Risultati: Nel gruppo trattato con ALA vaginale si è osservato un processo di riassorbimento dell'ematoma significativamente più rapido rispetto alla progressione rilevata nel gruppo progesterone ($p < 0.05$). Inoltre, sebbene gli altri parametri controllati (dolore pelvico e sanguinamento vaginale) non-hanno mostrato differenze significative tra i due gruppi, un minor numero di aborti è stato registrato nel gruppo ALA rispetto al gruppo di Progesterone. Conclusioni: I nostri dati forniscono un'iniziale prova sull'efficacia dell'ALA vaginale nel processo di risoluzione della minaccia di aborto. I risultati ottenuti da questo prima studio pilota, sono stati arricchiti da maggiori evidenze cliniche in seguito ad un secondo studio mirato ad evidenziare l'efficacia dell'ALA vaginale vs. progesterone in una coorte più ampia di pazienti.

Meccanismi infiammatori nel parto pretermine: effetti dell'acido alfa-lipoico vaginale

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Premessa: Il parto pretermine (PPT) viene definito come la nascita prima della 37 settimana compiuta di gestazione; nei paesi sviluppati si verifica nel 6–8% di tutte le gravidanze, ed è associato ad elevata morbilità e mortalità neonatale. Vista l'importanza dei numerosi risvolti non-solo clinici ma anche socio-economici, gli studi rivolti a comprendere i fattori di rischio e i meccanismi fisiopatologici coinvolti nel PPT sono numerosi. In particolare, negli ultimi 20 anni è stato approfondito il ruolo delle interleuchine infiammatorie quali fattori inducenti il raccorciamento cervicale, espressione del meccanismo di ''infiammazione'' che sottende al PPT. Sulla base di tali studi, sono in corso ricerche che hanno l'obiettivo di individuare nuove strategie per la riduzione del numero di PPT in donne a rischio. In particolare, l'attenzione è stata recentemente posta sul potenziale ruolo dell'acido alfa-lipoico considerato che studi *in vitro* hanno evidenziato le sue capacità di inibire alcune citochine pro-infiammatorie, quali TNFα e IL-1β, implicate nei processi di rottura pretermine delle membrane (pPROM) e di raccorciamento cervicale. Inoltre, studi *in vivo* hanno dimostrato le capacità immunomodulanti di tale molecola. Considerato le limitazioni legate alla scarsa biodisponibilità orale dell'acido lipoico, oggetto del nostro studio è stato quello di valutare l'efficacia di una sua somministrazione locale (vaginale) nel contrastare sia i cambiamenti morfologici del collo dell'utero che il rilascio di citochine pro- e anti-infiammatorie. Pertanto, in uno studio clinico a doppio cieco, sono state arruolate primigravide con lunghezza cervicale compresa tra 30mm e 15mm riscontrata tra le 24 e le 30 settimane di gestazione per valutare l'efficacia della somministrazione di acido lipoico per via vaginale (DAV® capsule vaginali, LoLiPharma srl) confrontandola con placebo. Metodi: Le donne arruolate sono state randomizzate in 2 gruppi: un gruppo ha ricevuto capsule vaginali contenenti acido lipoico, l'altro invece placebo. I trattamenti sono stati somministrati per 30 giorni. Le visite sono state effettuate all'arruolamento (T0) e dopo 15 e 30, con esecuzione della cervicometria e tampone vaginale per il dosaggio delle citochine. Risultati e Conclusioni: L'interim analisi coi dati preliminari ottenuti da questo studio pilota verranno presentati e discussi.

Ematomi sottocoriali nel primo trimestre: cause, trattamenti e approcci terapeutici

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Premessa: La minaccia d'aborto, associata o meno alla formazione di ematoma sottocoriale, rappresenta un capitolo importante di patologia ostetrica considerato che nel primo trimestre di gravidanza avvengono processi fondamentali affinché la gravidanza si impianti regolarmente e la sua evoluzione non-sia gravata da complicanze. L'ecografia è oggi l'indagine di riferimento nella minaccia d'aborto, poiché permette di effettuare una precisa diagnosi e rilevare eventuali fattori prognostici. In tale contesto, un dato importante da analizzare ecograficamente è l'eventuale presenza di ematoma subcoriale che appare come una zona anecogena di dimensioni variabili posizionata tra l'amnios e corion. La localizzazione dell'ematoma a livello del fondo ha sicuramente una prognosi peggiore rispetto a quando si localizza in sede sopracervicale. Inoltre, quanto maggiore è il distacco tanto più la gravidanza si considera a rischio, ed è quindi necessario mettere in atto tutte le misure terapeutiche atte a favorire il riassorbimento dell'ematoma al fine di ottenere una evoluzione positiva della gravidanza. Ad oggi gli approcci terapeutici utilizzati per favorire il riassorbimento degli ematomi sono scarsi e non-sufficientemente valutati tramite studi clinici. Il ''bed rest'' e l'uso del progesterone sono sicuramente tra gli approcci più utilizzati nella pratica clinica sebbene studi clinici ne mettano in dubbio una reale efficacia. In questo contesto, l'acido alfa-lipoico, avendo importanti proprietà antiinfiammatorie ed immunomodulanti, potrebbe rappresentare una valida alternativa la cui efficacia merita di essere indagata tramite studi clinici. Il nostro obiettivo è stato quello di ottenere delle valutazioni preliminari in tal senso, tramite uno studio clinico pilota. Metodi: Sono state arruolate donne con minaccia d'aborto di età compresa tra 20 e 38 anni, tra la 6a e la 13a settimana di gestazione, con evidenza ecografica di ematoma sottocoriale e sintomatologia clinica caratterizzata da perdite ematiche vaginali e contrazioni uterine spontanee. Lo studio ha previsto la randomizzazione delle pazienti in due gruppi: uno in cui alla somministrazione orale di acido lipoico (300 mg, 2 volte al giorno) è stato associato progesterone endovaginale (200 mg, 2 volte al giorno) e l'altro in cui le pazienti sono state trattate esclusivamente con lo stesso dosaggio di progesterone endovaginale, fino alla risoluzione del quadro clinico-ecografico. Risultati: Relativamente alla risoluzione dell'ematoma, il miglioramento è stato generale, ma con diversi tempi di guarigione, che sono risultati significativamente più veloci nei pazienti trattati con acido lipoico associato a progesterone. Inoltre, differenze evidenti, ma non-statisticamente significative, si sono registrate anche per la scomparsa del dolore addominale, delle contrazioni uterine e del sanguinamento vaginale. I trattamenti non-hanno causato alcun effetto negativo sulla madre o sul feto. Conclusioni: I risultati indicano che le pazienti trattate con acido lipoico più progesterone hanno avuto una migliore e più

rapida evoluzione dei segni clinici e dei sintomi relativi alla minaccia di aborto. Questi dati preliminari aprono nuove possibilità per ridurre notevolmente le complicazioni legate alla minaccia di aborto e migliorare l'esito della gravidanza, utilizzando, durante il primo trimestre di gestazione, una molecola naturale e sicura.

Oral Presentations

(OP01) From congenital to adolescent disorders

Peculiarities of sexual development and reproductive function in underweight and overweight young women with childhood onset weight problems

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Context: Extremes of body mass adversely affects reproductive function, but evidence is inconsistent especially in relation to effect of age of body weight changes.
Objective: Detection of peculiarities of sexual development, prevalence of different reproductive disorders and correlations of respective hormonal changes with BMI in young females with childhood onset weight problems.
Methods: BMI, waist-to-hip ratio, age of body weight changes, assessment of hirsutism, acne, stretch marks and hyperpigmentation, menstrual disturbances or fertility problems were recorded. Gynecological ultrasound was performed. FSH, LH, E2, TT, FT, PRL, SHBG, DHEA-S, 17α-OHP, COR, HOMA-IR were measured. In 4 cases karyotype was detected.
Patients: 48 underweight and 55 overweight/obese young females with different reproductive problems.
Results: Most patients with high BMI had upper body fat distribution, whilst low BMI patients had equal or lower body fat distribution ($p = 0.000$). Age of menarche and types of menstrual disorders did not differ between study groups. PCOS and metabolic syndrome predominated in overweight patients, whilst NCAH and ovarian dysfunction prevailed in underweight patients ($p < 0.05$). Infertility was mostly observed in patients with high BMI ($p < 0.05$). Hypogonadotropic hypogonadism was not found in lean females since childhood. Correlation was established between onset of menstrual disruption and progression of BMI changes ($R = 0.448$, $p = 0.005$). BMI negatively correlated with FSH and SHBG and positively correlated with FT and TT ($p < 0.05$).
Conclusions: Peculiarities of menstrual function and hormonal changes in young women with childhood onset weight problems are related to types of reproductive disorders and their childhood BMI. BMI correction should be the first goal of efficient therapy.

Phenotypically Female 46XY DSD adolescents: does hormone replacement therapy (HRT) improve biochemical and ultrasound markers of endothelial function

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Context: Estrogens in healthy premenopausal females play a cardio-protective role, whereas gonadal decline leads to an increase of cardiovascular risk. Due to the rarity of DSD (Disorders of Sex Development),cardiovascular risk in this population,is not widely studied in the literature.
Objective:The aim of the present study was to evaluate the impact of Hormone Replacement Therapy (HRT) on ultrasound and biochemical markers of endothelial function of phenotypically female 46XY DSD patients.
Methods and Patients: Twenty DSD adolescents, (7 with Swyer Syndrome and 13 with Complete Androgen Insensitivity Syndrome),were included in this study. We examined Flow Mediated Dilatation (FMD) and Arterial Intima Media Thickness (IMT) and ran a novel biochemical panel for endothelial function; including VE-Cadherin, (associated with atherosclerotic plaque inflammation), E-selectin, (associated with coronary disease), as well as von Willebrand factor and sThrombomodulin, which are markers of endothelial damage.
Intervention: HRT, consisting of 2mg 17β-estradiol/1mg norethisterone p.o., for six months.
Main Outcome and Results: A statistically significant decrease of VE-Cadherin (from 4.05ng/ml to 2.20ng/ml, $p = 0.002$) and E-selectin (from 73.98ng/ml to 56.73ng/ml, $p = 0.004$) was documented. No statistically significant change was indicated regarding Thrombomodulin and vWf. FMD was significantly improved (from 5.4% to 8.15%, $p = 0.003$), while carotid IMT was decreased (0.065 cm vs. 0.060 cm, $p = 0.018$).
Conclusions: The administration of 6-month HRT improved endothelial function (FMD and VE-Cadherin) and restrained atherosclerosis progression, as demonstrated by the improvement of IMT and E-selectin. Further research is needed in order to confirm the results observed in this rare population during this study, by using both different hormonal regimens and different methods of administration of HRT.

Reproductive outcome in women with congenital adrenal hyperplasia – a population-based cohort study

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Context: Congenital adrenal hyperplasia (CAH) is a genetic disease that leads to hyperandrogenism, hypocortisolism and hypoaldosteronism. The phenotype varies between mild forms to severe, potentially lethal, salt wasting (SW) forms.
Objectve: To investigate the reproductive outcome in women with CAH.
Methods: Population-based registry study using the Swedish Medical Birth Registry and the Swedish Total Population Registry.
Patients: Three-hundred thirty-five women with CAH were identified and 33 500 controls were selected matched by age and place of birth. The median age was 25.3 (IQR 15.8–37.8).

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Main Outcome Measure: The proportion of women that had given birth.
Results: Of the 335 women with CAH included, 69 gave birth to at least one child (21%), this was lower than in controls 12 395/33 500 (37%), $p < 0.001$. Women with CAH had fewer children than controls, mean 0.37 vs. 0.77, $p < 0.01$. They were slightly older at the birth of their first child, 27.9 ± 5.1 vs. 26.4 ± 5.0 years, $p < 0.01$. Women with SW CAH had fewer children than women with less severe forms, $p < 0.001$. Despite a similar weight gain in pregnancy (13.3 kg in CAH and 14.8 in controls, $p = 0.3$), more women with CAH were diagnosed with gestational diabetes than controls, 5.6% vs. 0.7%, $p < 0.001$. The incidence of preeclampsia was similar between women with CAH and controls. More women with CAH than controls were delivered through caesarean section (mostly planned), 23.0% vs. 5.2%, $p < 0.001$, but there was no difference in instrumental vaginal delivery. There was no difference in Apgar score at 5 minutes or frequency of small-for-gestational age.
Conclusions: We found the parity rate to be lower in women with CAH. The low parity rate also in controls is explained by the low median age of the cohort. The pregnancy outcome in women with CAH was generally good but gestational diabetes and caesarean sections were more common.

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Correlation between single nucleotide polymorphisms of genes encoding estrogen receptor alpha (ESR1), estradiol circulating levels and lumbar spine bone mineral density (LBMD) in adolescents with anorexia nervosa (AN)

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Context – Objective: To assess the correlation between the analyzed single nucleotide polymorphisms of genes encoding estrogen receptor alpha (ESR1) and Body Mass Index (BMI), cycling status, estradiol circulating levels and Lumbar spine Bone Mineral Density (LBMD) in girls with Anorexia Nervosa (AN).
Methods – Patient(s) – Intervention(s): Case-control study of 40 adolescent girls with AN (according to DSM-V) and 10 age-matched controls. Genes encoding estrogen receptor alpha (ESR1), BMI, cycling status, estradiol circulating levels and LBMD were assessed in all participants.
Main Outcome Measure(s) – Result(s): Distribution of ESR1-XbaI genotypes did not differ between groups, but the AA genotype was associated with decreased LBMD Z-score (≤ -1). Considering the relationship between serum concentrations of estradiol (E2) and LBMD Z-score, in patients girls with AN, separately per allele for ESR1-XbaI polymorphism, we observed that patients carrying the G allele, who have current circulating estradiol concentrations equal to or greater than 30pg/mL are in less risk to have decreased LBMD Z-score (≤ -1) ($p = 0.037$). Conversely, carriers of the (A) allele were more likely to have decreased LBMD Z-score regardless of E2 serum concentrations ($p = 0.999$).
Conclusions: In conclusion, AN carriers of the A allele of ESR-XbaI are in greater risk for decreased BMD in relation to those with the mutated gene, while carriers of the G allele are more likely to have a reduced risk of decreased LBMD-Z score, which depends on the levels of circulating estradiol. Prompt recognition of each patient subgroup may contribute to the prevention of adverse sequel on bone metabolism through early administration of the proper therapeutic treatment.

The impact of sex hormones to cardiovascular development in Turner patients

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Context: A complete Estrogen (E) deficient, caused by gonadal dysgenesis is one of the main symptoms in Turner syndrome (TS). The impact of E use in TS remains controversial.
Objective: to assess the impact of sex hormones to cardiovascular development in TS.
Methods: 42 patients with TS ≥18 years (yrs) were enrolled in the prospective study and divided into 2 groups: E initiation (I) < 15 yrs (1G), or ≥15 yrs (2G). The effect of natural (NE) or synthetic E (SE) to cardiovascular state and the impact of age, congenital cardiovascular disorders (CCD), karyotype, heart ratio (HR), blood pressure (BP), carbohydrates and lipids levels to aortic diameter (AD) were analyzed. AD (adjusted for body surface area (BSA)) using cardioechoscopy was evaluated.
Main Outcome Measures: Aortic dilation was defined as AD > 2.0 cm/m^2 and presented as the main outcome.
Results: E <15 yrs were started in 55% ($n = 23$), ≥15 yrs in 45% ($n = 19$) patients. 54% ($n = 23$) of TS were on NE, 14% ($n = 6$) on SE, 32% ($n = 14$) did not receive any treatment. Mean age was different between groups (1 G 27.6±6 yrs, 2 G 33.8±5.8 yrs, $p = 0.002$). BP, fasting glucose, total cholesterol (Tch), Estradiol (E2), Testosterone (T) levels were not significant between groups. The ascending AD was larger in 1 G (20.2±3.9 cm compared with 18.11±2.45 cm in 2G, $p = 0.02$). HR was higher in 1 G (88±6.8 compared with 82±11 in 2 G, $p = 0.014$). E2 and T levels were different between NE and SE groups (E2 – 515±240 in NE compared with 286±66 in SE, $p = 0.005$; T – 2.1±1.2 in NE, 1.0 ±0.34 in SE, $p = 0.016$), but E2 levels did not correlate to AD. AD did not correlate to karyotype, CCD or age. The root AD had a significant negative correlation to EI age ($r = (-)0.342$, $p = 0.027$). Ascending AD negative correlated to T levels ($r = (-)3.29$, $p = 0.036$).
Conclusion: Early EI in TS might negative effect the ascending AD. T might have the influence to AD also.

Clinical and sexual peculiarities of patients with male kariotype and female phenotype

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Objective: Revealing of clinical and sexual peculiarities of patients with 46,XY kariotype and female phenotype.
Methods and Patients: Clinical, ultrasound (US), cytogenetic, hormonal examinations (HE) were done for all 39 patients (14–41yy), as well as analysis of psychosexual orientation and sexual life. Laparoscopy, gonadectomy and gonad's hystomorphological investigation (HI) were performed in 35 patients.
Results: According to the results of investigation diagnosis of CAIS was defined in 30 patients, Swayer syndrome (SS) – in 6 patients, ovotesticular disorder (OTD) – in 3 patients. All patients had female psychosexual orientation. Patients with SS had clinical and hormonal characteristics of hypergonadotropic hypogonadism. US revealed streak uterus and gonads. In all cases after Gonadectomy, HI of gonads revealed structure of connective tissue and only in one case – testicular elements. Research of libido revealed normal female sexual drive in all mentioned patients. All patients with CAIS and OTD hadn't clitoromegaly, vagina was blind and short, uterus was absent. HE revealed normal male level in all patients with CAIS and OTD. In 26

patient with CAIS and 3 patients with OTD gonadectomy was performed. HI revealed testicular tissue in patients with CAIS and testicular tissue on one side and ovotesticular tissue on another side in patients with OTD. Sexually active patients with CAIS and OTD had no problems with coitus. In all 18 sexually active and 12 sexually inactive patients with CAIS libido was not increased. 3 patients with OTD had increased libido.
Conclusions: Patients with 46,XY kariotype and female phenotype need timely diagnosis and gonadectomy of intra-abdominal located gonads for prevention of malignisation. These patients have female psycho-sexual orientation and possibility of having normal sexual contacts as a females.

Digit ratio (2D:4D ratio) in female Olympic athletes in relation to urinary steroid profile

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Context: The second to fourth digit ratio (2D:4D) is suggested as an indirect measurement of prenatal androgen exposure and has been related to enhanced physical performance in mainly male athletes, especially in power sports.
Objective: The purpose of the present investigation was to examine the 2D:4D ratio for female Olympic athletes and untrained controls and for the female Olympic athletes the 2D:4D ratio in association with the urinary steroid profile and genetic variations in androgen metabolizing enzymes.
Methods: One hundred four female Swedish Olympic athletes and 128 inactive controls participated in the study. Direct digit measurements were performed and digit ratio calculated in all subjects. The urinary steroid profile was analysed using GC-MSMS and androgen metabolizing enzymes were genotyped for copy number variations in UGT2B17 and SNPs in UGT2B7, CYP17, UGT2B15.
Results: Female Olympic athletes demonstrated a significantly lower 2D:4D ratio ($p = 0.027$) compared to the female controls. No significant correlation was seen between digit ratio and urinary steroid profile or for the UGT2B17 genotype or SNPs in UGT2B7, UGT2B15 och CYP17.
Conclusion: Female Olympic athletes demonstrate a lower digit ratio than controls. The digit ratio was however not correlated to urinary steroid profile or genetic variations in androgen metabolizing enzymes. We suggest that digit ratio right hand might be one of several indicators to predict physical performance and sporting success in female athletes although not due to effects on the androgen metabolism.

mRNA expression of genes responsible for female hypogonadotrophic hypogonadism

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Nowadays several tens of genes involved in the functioning of the reproductive axis are known. Their damage can lead to a syndrome called hypogonadotropic hypogonadism (HH). However DNA lesions can be found just in 5–15% of such cases. So we decided to measure mRNA expression of several genes which can be found in leukocytes of peripheral blood namely GNRHR and GNRH1 (are necessary for adequate biological effect of GnRH); PROK2 and CHD7 (are responsible for the migration of GnRH neurons), WDR11 and DUSP6 (are involved in normal sexual development). A quantitative determination of mRNA expression of these particular genes were comlpeted in the fresh peripheral blood sample by PCR in real time. Examined *Patients*: 9 women with hypogonadotropic hypogonadism (age from 18 to 28 yrs); duration of the disease from 2 to 15 years; 3 of them – amenorrhea I and 6 – amenorrhea II. Reasons of amenorrhea II were: stress, excessive exercises, rapid body weight loss, past use of oral contraceptives. The control group: 19 healthy women; age from 19 to 37 y.o.; with regular ovalutory menstrual cycle, some of them have children. mRNA expression of examined genes differed from normal patterns in each case of hypogonadotropic hypogonadism. Changes in GNRHR, GNRH1 and DUSP6 mRNA expression were found in most of cases. However variations of mRNA expression were multidirectional in each case and there was no similarity among expression profiles of patients according to amenorrhea type or anamnestic factors. According to our preliminary results, in women with hypogonadotropic hypogonadism the functional activity damage of ''reproductive-responsible'' genes could be found in each case. Probably mRNA expression measuring could be a perspective method for proving hypothalamo-pituitary level of reproductive disorders and may help to determine which genes should be tested for DNA impairment.

Peculiarities of nonclassical congenital adrenal hyperplasia in adolescent girls

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Context: Nonclassical congenital adrenal hyperplasia,most common autosomal recessive disorder,caused by incomplete deficiency of enzymes, appears later in life. Clinical manifestations vary from severe to mildsymptoms of hyperandrogenism. Acurate diagnosis is essential for correction of disorders.
Objective: To define peculiarities of NAH in adolescent girls.
Methods: 53 girls, aged 13–18, with clinical signs of hyperandrogenism were involved in case- control study. Inclusion criteria- high serum 17OHP and/or DHEAS levels. 15 same aged healthy volunteers served as a control. The results were analyzed statistically by ANOVA.
Results: 84.9% had hirsutism, 66% seborrhea, 83% acne,18.8% slight enlargement of clitoris, 41.5% oligomenorrhea, 9.4% amenorrhea, 35.8% monophasic cycle, 13.2% short lutheal phase. Polycystic changes of the ovaries were detected in 52.8%. Average serum concentrations of 17OHP, DHEAS, T were significantly higher compare to control.There was no difference regarding average concentrations of PRL, Cortisol, LH. Average level of FSH was significantly lower and average LH/FSH ratio significantly higher compare to control. In PCO patients average levels of LH and T were significantly higher compare to normal ovary patients.
Conclusions: Nonclassical congenital adrenal hyperplasia, manifested in adolescent girls, is characterized by clinical signs of hyperandrogenism: hirsutism, acne, seborrhea. Virilization is not characteristic feature of mild forms of the disease. Obesity is not typical as well. Majority of patients show irregular menses that leads to polycystic changes in the ovaries. Hormonal profile includes icreased secretion of 17OHP, DHEAS and Testosteron. Typical are low FSH level, with high LH/FSH ratio. For patients with polycystic ovaries,specific indicators are increased LH and Testosterone secretion.

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Double genetic defect in a case of congenital hypogonadotropic hypogonadism

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Context: Congenital hypogonadotropic hypogonadism (CHH) is a rare cause of delayed puberty and impaired fertility in both male and female patients. Significant progress in the discovery of the genetic basis for this condition has been made recently. Of particular interest is the concept of oligogenicity, the occurrence in the same patient of mutations in several genes that are involved in CHH.
Objective: We report a case of CHH in a young girl with mutations in two genes involved in gonadotrope function.
Patient and method: The patient, aged 17, was addressed in gynecology for the exploration of primary amenorrhea. Clinically, the patient had normal height (1.65m) and normal weight (67kg) with B3 Tanner stage. The patient reportedly had normal olfaction. In her family, however, her father had a history of delayed puberty treated with androgens for a certain time. Afterwards, he spontaneously fathered 3 children. Her older brother was also treated by androgens for a delayed puberty. Her paternal aunt had delayed puberty and primary amenorrhea, never treated.
Intervention(s): A biological, imaging and genetic exploration was performed.
Result(s): The biology confirmed hypogonadotropic hypogonadism in the patient. The rest of the hormonal evaluation was normal. Pituitary MRI was normal. Pelvic MRI revealed a hypoplastic uterus. A heterozygous splice-site mutation in the FGFR1 gene and a heterozygous substitution in the GNRHR gene were found in the patient and her father. Her brother only had the FGFR1 mutation.
Conclusions: The reported case illustrates the concept of oligogenicity in CHH, supporting the need for a complete genetic analysis of the panel of genes involved. The case also underlines the variability of expression of these mutations. Further research needs to be conducted in order to improve our understanding of the variable expressivity in CHH.

(OP02) Uterine myoma and other diseases

Prolactin and prolactin receptor expression on the adrenal of hyperprolactinemic mice treated with estrogen and progesterone

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Objective: To evaluate the effects of metoclopramide-induced hyperprolactinemia on prolactin and prolactin receptor expression by Immunohistochemistry.
Methods: A total of 12 animals with intact ovaries were allocated to two groups: G1 (saline solution) and G2 (metoclopramide). A total of 30 oophorectomized animals was randomized to five subgroups: G3 (saline solution), G4 (metoclopramide), G5 (metoclopramide+17β-estradiol), G6 (metoclopramide+micronized progesterone), and G7 (metoclopramide+17β-estradiol+micronized progesterone). The drugs and the vehicle were administered subcutaneously using a volume of 100μL per solution. After 50 days, semi-quantitative immunohistochemical analysis of the adrenal gland was performed using the expression index (EI) calculation method.
Results: All groups expressed prolactin and prolactin receptor; however, both the intensity and the frequency of labeled cells were heterogeneous. With respect to prolactin receptor, the area fraction of labeled cells varied from 1 (0–10%) to 3 (> 50%). Based on the mean immunostaining intensity, G2 and G4 showed strong expression; G6 and G7 presented a mild reaction; and G1, G3, and G5 exhibited a weak reaction. Concerning prolactin, the area fraction of labeled cells varied from 1 (0–10%) to 3 (> 50%), and groups G6 and G7 showed a strong reaction; G2, G4, and G5 showed a mild reaction; and G1 and G3 exhibited a weak reaction.
Conclusion: Our data suggest that metoclopramide-induced hyperprolactinemia may increase prolactin receptor expression in the adrenal gland of mice. Furthermore, hyperprolactinemic animals treated with progesterone alone or in association with estrogen may have an increased prolactin expression.

GLI transcription factors involvement in leiomyoma genesis

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Introduction: Uterine leiomyoma are the most common gynecologic benign tumors affecting women of reproductive age. The pathophysiology of leiomyoma origin and growth is not clear. Recently it was demonstrated that activation of GLI family of transcription factors are related to the development of several tumors.
Objective: To evaluate the expression profile of transcription factors GLI in leiomyoma samples comparing to normal myometrium.
Methods: We evaluated 100 samples (20 myometrium and 80 leiomyomas) obtained from Obstetrics and Gynecology Department from Hospital das Clínicas da Faculdade de Medicina da Universidade de Sao Paulo (Sao Paulo/Brazil). Gli 1, 2 and 3 gene and miRNAs expression was assessed by quantitative Real Time PCR and the percentage of DNA methylation of GLI1 and GLI3 genes were investigated using Methyl-Profiler DNA Methylation qPCR Assays (Qiagen). All molecular results were submitted to statistical analyses.
Results: GLI1–2 showed higher expression and GLI3 lower expression in leiomyomas, comparing to myometrium. miR-125b-5p, a GLI1 positive regulator, had similar expression profile of its target gene. Both miR-31–5p and miR-26b-5p act as regulators of GLI2. miR-31–5p had direct correlation with GLI-2 gene expression, while miR-26b-5p showed an inverse correlation, in the leiomyomas. miR-93–5p is described as GLI3 regulator and its expression was inversed to that gene profile. The DNA methylation assessment exhibit GLI1 ($p = 0.034$) and GLI3 ($p = 0.001$) genes with higher methylation percentage in their promoter region in leiomyoma than myometrium samples.
Conclusion: Our results showed that GLIs differential gene expression profile between leiomyoma and myometrium may occur due promoter methylation. A role of regulatory miR-31–5p, miR-26b-5 and miR-93–5p miRNAs may explain the differential protein expression described in the literature.

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The preoperative treatment of women with myoma of the uterus using ulipristal acetate

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Context: The prevalence of fibroids in Belarus is ~25% in reproductive age.
Objective: To assess the effectiveness of the selective progesterone receptor modulator (ulipristal acetate) in pre-surgical treatment of patients with uterine myomas.
Methods: Routine clinical and immunohistochemical: estrogen and progesterone receptors; Ki-67, vascular endothelial growth factor (VEGF).
Patients: Twenty-six patients aged 37–42 years with uterine myomas.
Interventions: The treated group ($n = 16$) received ulipristal acetate 5 mg/day for 3 months as a pre-surgical treatment, a control group ($n = 10$) was without treatment. Myomas removed surgically and underwent histological examination.
Main Outcome Measures: Size of the uterine myomas and the dominant myoma, the occurrence of amenorrhea.
Results: After a 3-month course of ulipristal acetate therapy in the treated group the mean sizes of the uterine myomas decreased from 15.2±1.1 to 12.1±0.7 cm, the size of the dominant myoma was reduced by 3±0.6 cm in diameter, amenorrhea defined as absence of menstruation was reported in 16(100%) of patients. No significant adverse effects were noted. The women were impressed with the convenience the drug. A morphological examination showed low-active perivascular growth areas; large sites of dystrophic changes of leiomyocytes; sclerosis of the pseudocapsule, single mitotic figures, and marked apoptosis. Ki-67 was presented single cells; VEGF had a weak-to-moderate expression, expression of progesterone was 78–87%.
Conclusion: The mechanism of the regressive effect of ulipristal acetate on uterine myoma has been shown to be a selective tissue-specific receptor protein modulator, inhibiting the transcription of progesterone in cells of uterine myomas.

Clinical and histological features of follicular ovarian cysts

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Background: It is known that the small sizes of ovarian formation are often mistaken for tumor formation and subjected to conservative anti-inflammatory therapy. The final diagnosis of the nature of the ovarian formation is established by histological examination of a remote capsule. The aim of the study was to investigate the clinical manifestations and morphological features of follicular ovarian cysts for timely decision on the necessity of their surgical treatment.
Material and methods: We have studied the clinical course of benign tumors of the ovaries in 50 patients admitted to the gynecology department of maternity complex No. 9. Preoperative examination included ultrasound with color Doppler blood vessels of the ovary and the determination of blood tumor marker CA-125. Interpretation of the results of determining the value of tumor marker CA-125 was conducted in accordance with the results of histological examination.
Results: Feature of follicular cysts in our patients was the presence of ultrasound thin-walled capsules, no papillae on the inside of the capsule. At color Doppler mapping were impaired vascularization of the capsule, the capsule in the vessels of the cyst revealed elevated resistance index values up to 0.8, in the uterine and ovarian blood flow vessels characterized by low speed. Determination of tumor marker CA-125 in patients with follicular ovarian cysts conducted before surgery showed that, the average number does not exceed the acceptance rate of 35 units/ml. Follicular cysts are often presented as a unilateral walled with a smooth inner wall. Histologically, connective wall was lined with multi-row follicular epithelium, under which the cells are arranged theca interna.
Conclusions: Nonspecific clinical symptoms of benign ovarian and diversity of their histological forms indicate a need for careful preoperative examination.

Dienogest's action on endometrial pattern before hysteroscopic surgery for submucous myomas: prelimary results of an off-label, prospective, randomized study

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Context: Although several drugs were used to achieve hypotrophy/atrophy of the endometrium before hysteroscopic surgery, currently there is no clear consensus about this procedure.
Objective: The aim of this single-center, prospective, randomized, parallel-group study was to compare Dienogest and Danazol as endometrial preparation in patients who have to undergo hysteroscopic surgery for submucous myomas.
Methods: Pre- and post-treatment characterization of endometrium was performed by hysteroscopic visual observation and histologic confirmation.
Patient(s): We enrolled 80 consecutive eligible patients, in reproductive age, affected by submucous myomas.
Intervention(s): The enrolled patients were randomly assigned to two groups: 40 were treated with 2 mg of Dienogest/die, 40 with 100 mg of danazol/die, both orally for 5 weeks, starting on day 1 of menstruation.
Main Outcome Measure(s): Pre- and post-treament evalutation of endometrial patterns; cervical dilatation time, total operative time, the infusion volume and severity of the bleeding during the operative hysteroscopy; side effects.
Result(s): Post treatment comparison of endometrial patterns showed a significant more marked effect of Dienogest, respect to Danazol, in atrophying endometrium (''normotrophic non-responders'' vs. ''hypotrophic'' – ''atrophic'', $p = 0.028$). Intraoperative data showed no significant difference between the two groups for cervical dilatation time ($p = 0.326$), while in the Dienogest group we found a significant reduction of operative time ($p = 0.001$), infusion volume ($p = 0.001$), severity of bleeding ($p = 0.042$). Moreover, Dienogest caused less side effects ($p = 0.008$).
Conclusions: According to our data analysis, Dienogest, respect to Danazol, is more effective for the preparation of the endometrium in patients who have to undergo hysteroscopic surgery for submucous myomas, and causes less side effects.

3-Month versus 6-month treatment with ulipristal acetate prior to laparoscopic hysterectomy of large myomatous uteri

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Context: Large myomas may be difficult to be excised by laparoscopy and the repair of the uterine wall defects may be challenging for surgeons with limited experience in laparoscopic suturing. Different hormonal therapies have been proposed to decrease uterine volume and fibroid size before surgery.

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Objectives: The primary objective was to compare the perioperative outcomes of patients treated with ulipristal acetate (UPA) for either 3 or 6 months before laparoscopic hysterectomy of large myomatous uteri. The secondary outcome was to compare the changes in uterine volume (UV) between the two study groups.
Patients: Premenopausal women with symptomatic uterine fibroids and estimated uterine volume $\geq 500\,cm^3$ requiring hysterectomy.
Methods: Uterine volume was assessed by ultrasonography. All patients received 3-month treatment with UPA 5 mg/day. At the end of the treatment, patients choose to undergo surgery (group A) or to receive a second cycle of 3-month UPA treatment (group B). Patients underwent total laparoscopic hysterectomy. Data were analyzed according to intention to treat.
Main outcomes: 18 patients were included in group A and 13 in group B. After 3-month treatment, the percentage decrease in UV was similar in the two groups (24.0% in group A and 27.2% in group B, $p = 0.215$). In group B, the percentage decrease in UV was higher after 6-month treatment (35.4%) than after 3-month treatment ($p < 0.001$). Prior to surgery, uterine volume was lower in group B than in group A ($p = 0.001$). No patient required conversion to laparotomy. The operative time was lower in group B than in group A ($p = 0.012$).
Conclusions: 6-month treatment with UPA decreases the operative time compared with 3-month treatment but it does not affect the intraoperative blood loss, the length of hospitalization and the incidence of complications.

Ulipristal acetate prior to high complexity hysteroscopic myomectomy: prospective comparative pilot study.

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Context: Hysteroscopic myomectomy is the surgical procedure of choice for the treatment of submucosal myomas because it is minimally invasive and has the advantage of preserving the integrity of the uterine wall. Limited data is available on the use of ulipristal acetate prior to hysteroscopic myomectomy.
Objectives: To evaluate the efficacy of preoperative treatment with ulipristal acetate (UPA) in patients undergoing high complexity hysteroscopic myomectomy.
Patients: Patients of reproductive age requiring hysteroscopic myomectomy with STEPW score = 5 or 6.
Methods: Patients included in the study either underwent direct surgery (group S) or received a 3-month preoperative treatment with UPA (group UPA). Based on a power calculation, 25 patients were included in each study group.
Main outcomes: The characteristics of myomas were similar in the two study groups. The 3-month UPA treatment caused a 21.9% ($\pm$ 10.3%) mean ($\pm$ SD) percentage decrease in myoma volume. The number of complete resections (primary outcome of the study) was higher in group UPA (92.0%) than in group S (68.0%; $p = 0.034$). The operative time was lower in group UPA than in group S ($p = 0.048$), while there was no significant difference in fluid balance between the two study groups ($p = 0.256$). The incidence of complications was similar in the two groups ($p = 0.609$). Patient satisfaction at 3 months from surgery was higher in group UPA than in group S ($p = 0.041$).
Conclusions: A 3-month preoperative treatment with UPA increases the possibility of complete resection in high complexity hysteroscopic myomectomy; it decreases the operative time and improves patient satisfaction at three months from surgery.

Is dynamic tsh evaluation necessary to diagnose subclinical hypothyroidism in luteal deficiency?

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INTRODUCTION:It is known that thyroid disorders can influence menstrual cycle, but subclinical hypothyroidism(SH), as cause of ovulation disorders and luteal deficiency (LD) in particular, is underestimated. Monitoring women's cycles according to the Billings Ovulation Method BOM), can allow a precise timing for hormonal evaluation and diagnose LD. Usually, a basal TSH value of 2.5 ug/ml is considered as cut-off for a good luteal function, but alone cannot identify all cases of SH. In order to verify the sensitivity of TSH dynamics, we have performed TRH test (200 ug iv) in patients with LD, stratifying women according to different ranges of basal TSH values. *METHODS*: We enrolled 35 women, 20–45 ys, consulting our Centre for learning the BOM for achieving or spacing pregnancy.22 exhibited an history of infertility. LD was diagnosed by a shortened post-Peak phase length (<11 days) and low progesterone (P) levels on the 6th o r7th days after the ''mucus peak''.At TRH test SH was diagnosed with TSH peak >15 mcU/ml (normal basal TSH range:0.4–3.2 ug/ml,by ECLIA). *RESULTS*: According to basal TSH levels,patients were divided in 3 groups: group A ($n = 7$.0.8–1.4 ug/ml), group B ($n = 8$.1.5–2.4), group C ($n = 20$. 2.5–6.5). An increased TSH response was observed in 3/7 patients of group A,5/8 of group B, all patients of group C. In the overall group, the evidence of thyroid autoantibodies was 17% and therefore we escluded auto-immune mechanism as cause of ovarian dysfunction. Mean progesterone levels were in the low-normal range in all groups (mean$\pm$SEM:9.15$\pm$0.7 in groupA, 9.5$\pm$2.0 in groupB, 8.5$\pm$0.4 in groupC). *CONCLUSION*: These data suggest that SH has an important impact on luteal function; BOM can be effective for screening these situations and give rise a useful tool in diagnostic and therapeutic options in subfertile couples. Dynamic TSH evaluation can allow to diagnose SH, even in presence of normal TSH basal levels.

Features of surgical treatment in women of reproductive age after previously performed uterine artery embolization and MRgFUS ablation of fibroids

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Context: Uterine fibroids is the most common disease among women of reproductive age and consist of 10 to 30% of all gynecological diseases. Nowadays there are different methods of treatment of uterine fibroids, one of them is the uterine artery embolization and MRgFUS ablation of fibroids, but these methods are not radical, and their effectiveness depends on the patient's age and clinical manifestation, size, localization of uterine fibroids.
Objective: assessment of the efficiency of uterine artery embolization and MRgFUS ablation of fibroids in women of reproductive age with uterine myoma by MRI and intraoperative visualization.
Materials and methods: We have examined a group of 32 patients previously underwent UAE. And a group 26 patients previously performed MRgFUS ablation of fibroids. Age of the women ranged from 22 to 40 years. The main complaints were menorrhagia (80.2%), pelvic pain in the abdomen (70%), absence of pregnancy (95%).
Results: Intraoperatively, in the group after UAE in 40% of patients with uterine body was represented by conglomerates of multiple fibroids with pronounced signs of secondary changes, compared to 26% in the

group after MRgFUS ablation, where were only secondary changes in the nodes. 23% of patients in the group after UAE and 65% of patients after MRgFUS -revealed multiple uterine fibroids, 15.6% – the number of fibroids exceed 20 in group after UAE. Increased diffuse bleeding tissue was observed in 46.0% of patients and main part of operations were carried out in a reinfusion.
Conclusions: This study demonstrate necessary of further research, including the development of clear indications for embolization and MRgFUS ablation in patients with uterine myoma in the reproductive age. And to clarify the effect of the above methods is the condition of the endometrium, myometrium and ovarian function.

Preoperative treatment of uterine fibroids, accompanied by menorrhagia and anemia

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Introduction: Uterine fibroids are the most common benign tumors, originating from smooth muscle cells of the cervix or uterine. Menorrhagia is the most severe symptom of uterine leiomyomas. Heavy bleedings can result in anemia, decreased quality of life. The main goal of conservative treatment is to stopping excessive bleeding. A new opportunity for management of symptomatic fibroids is using Ulipristal acetate (SPRM).
Objective: To Study the efficacy of UA use before laparoscopic myomectomy in patients with symptomatic fibroids.
Patients: 55 women with symptomatic fibroids, from November to July 2014. The average age was 37.4±4.2.
Intervention: 30 patients underwent LM after 3 month UA treatment (group I) and 25 patients underwent LM only (group II).
Measurements: Fibroids were diagnosed by US. PBAC was used to assess menstrual bleeding. Anemia was assessed by the Hb levels. Efficacy of UA was evaluated by: stopping bleeding, decreasing in fibroid volume, increase of Hb, complaints. Also evaluated the following operative parameters: operative time, blood loss, Hb levels, hyperthermia, hospital stay.
Results: Excessive bleeding stopped after 4–7 days from start of treat in all patients. Mean PBAC was significantly decreased, Hb-increased. US revealed decrease in fibroid size. The operative time and blood loss in gr I was significantly lower then in gr II. On the second postoperative day Hb was significantly higher in grI. There was no statistical differences in hospital stay, duration of hyperthermia in two groups.
Conclusion: Preoperative treatment by UA before LM is effective for women with uterine fibroids, accompanied by menorrhagia and anemia. This treatment is useful in sustained increasing of Hb, decreasing fibroids and uterine volume befor surgery, as well in decreasing operative time and blood loss.

Effect of royal jelly on premenstrual syndrome: a randomized, triple-blind, placebo controlled trial

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Premenstrual syndrome (PMS), which characterized by a range of cyclical physical and psychological symptoms, may have negative effects on family relationship, social and work behavior. PMS sometimes need therapeutic non-pharmacological management.
Objectives: To assess the effect of oral consumption of 1000 mg Royal Jelly capsule on PMS.
Method: In this randomized, triple-blind, placebo-controlled trial, 110 volunteer students of female dormitories of Tehran University of Medical Sciences, were randomly assigned to intervention and control group. Each participant in the intervention group took 1000 mg Royal Jelly capsule orally per day, starting on the first day of menstruation and continued the same treatment daily throughout two consecutive menstrual cycles, while participants in the intervention group took placebo capsules as same method. The outcome measure in this study was PMS score as obtained through the Premenstrual Profile 2005. All ethical points were considered and approved by Research Committee of University.
Results: Average of age in Intervention group was 23.34 ± 3.46, and in placebo group were 22.45 ± 4.37. Equality of personal characteristics and baseline level of the premenstrual score was checked before intervention. After two consecutive months PMS score had decreased from 23.17 ± 17.43 to 11.42 ± 14.58 (Mean change: 11.75; 95% confidence interval [CI]: 8.31 to 15.19) in intervention group and in Placebo group, PMS score changed from 21.48 ± 16.39 to 20.27 ± 15.76 (Mean change: 1.20; 95% CI: -1.69 to 4.10). There was significant difference between mean changes. (Mean difference: 10.54; 95% CI: 6.10 to 14.98).
Conclusions: The results of the study have demonstrated that two months consumption of Royal Jelly was effective in reducing PMS.
Acknowledgments: This study received grants from Tehran University of Medical Sciences (Year 101–2013)

(OP03) From placenta to preeclampsia: from biology to clinical practice

Progesterone support following assisted reproductive technique (ART) reduces the risk of pre-eclampsia

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Context: Pre-eclampsia (PE) contributes to poor maternal morbidity and mortality. Progesterone is hypothesized to reduce risk of PE.
Objective: To determine the effect of progestogen supplementation during ART in reducing the incidence of PE.
Method: A retrospective comparative analysis among 1140 pregnancies between January 2006 and March 2015 conducted in a tertiary centre. A total of 570 pregnancies who conceived following ART with progesterone supplementation (progesterone group) and an age-matched spontaneous pregnancies, without progesterone supplementation (controls, $n = 570$) were included in the analysis. Progesterone group received progesterone support following ART/IUI until 14–16 weeks gestation either with dydrogesterone or in combination with hydroxyprogesterone.
Results: The rate of PE was significantly lower in the study group compared to controls (8.4% vs. 14.2%, $p < 0.05$). Women supplemented with dydrogesterone only group showed a lower PE incidence, however it was not statistically significant (19 cases out of a total of 276; 6.9%; $p = 0.2$).
Conclusions: Dydrogesterone, either given singly or in combination with hydroxyprogesterone was found to have significantly lower incidence of PE compared to those not receiving progesterone support.

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The effect of steroidogenesis changes during pregnancy in the pathogenesis of postpartum depression

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Introduction: Postpartum mental disorders present a serious health risk to both mother and child, and dealing with the consequences burdens health and social systems often on a long-term basis. There is no currently generally accepted theory about the causes and mechanisms of postpartum mental disorders.
Methods: We performed three samples of maternal blood. The first sampling was 4 weeks prior to term; the second sampling was after the onset of uterine contractions (the beginning of spontaneous labour); the third sampling was during the third stage of labour (immediately after childbirth). Additionally, we collected mixed umbilical cord blood. The almost complete steroid metabolome was analysed by gas chromatography – mass spectrometry followed by RIA for some steroids. Mental changes in women in the peripartum period were observed using the Hamilton Depression Rating Scale. The local Ethics Committee approved the study.
Results: We found already the changes in androgens levels correlating with postpartum mood disorders four weeks prior to childbirth. The strongest correlations between steroid and postpartum mood change were found in samples of venous blood samples collected from mothers after childbirth and from umbilical cord blood. The main role played testosterone, possibly of maternal origin and estrogens originating from the fetal compartment.
Conclusion: These results suggest that changes in both maternal and fetal steroidogenesis are involved in the development of mental changes in the postpartum period. Descriptions of changes in steroidogenesis in relation to postpartum depression could help clarify the causes of this disease, and changes in some steroid hormones are a promising marker of mental changes in the postpartum period.
Supported by the project MZCR for conceptual development of research organization 00023761 Institute of Endocrinology.

Effects of polysaccharide nanoparticles on an in-vitro placental model

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Polysaccharide nanoparticles show good security and biocompatibility and have broad prospects in drug delivery field, but whether polysaccharide nanoparticles can cross the placental barrier and the mechanism of translocation are still unclear. The purposes of the study were to prepare polysaccharide nanoparticles and to evaluate their potential for translocation in human placental barrier. BeWo b30 cell line was used to build the in-vitro human placental model, which originated from a human choriocarcinoma. Mono-layer of BeWo cells was ensured by measuring the transepithelial electrical resistance (TEER) and tight junction staining. Cells were seeded in transwell inserts and nanoparticles were added in the apical chamber of the inserts and collect samples from the basal chamber. The methods to investigate the characteristics involves particle size and distribution, zeta potential and morphology of nanoparticles using dynamic light scattering (DLS) and transmission electron microscopy. The prepared polysaccharide oxide nanometer particles have the even diameter distribution (478.4 $\pm$ 3.1nm) and may across the in-vitro human placental model. The findings of the study may help to understand the effects of polysaccharide nanoparticles on human placenta barrier during the translocation and provide applications in obstetrics field of drug use during pregnancy.

Keywords

Polysaccharide nanoparticles; placental barrier; BeWo cells; barrier transport; pregnancy

Pravastatin improves placental perfusion and decreases umbilical artery vascular resistance in patients with ischemic placental disease

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Ischemic placental diseases, characterized by abnormal placental blood flow, such as preeclampsia and intrauterine growth restriction are major causes of maternal and fetal morbidity and mortality worldwide.
Objective: Analysis of therapeutic effects of pravastatin on improvement of placental perfusion and decrease of umbilical artery vascular resistance in patients with ischemic placental disease.
Methods: *In this study 6 Patients, where isolated increased umbilical vascular resistance with normal uterine artery doppler findings, were included. pravastatin was administered to all Patients between 21–25th week, when umbilical artery pulsatility index was above limits for gestational age. Patients were scanned in 2–4 week interval to follow up changes in vascular resistance in umbilical artery.*
Results: Two patients had dichorionic twin pregnancy where ischemic placental disease occurred in one fetus. Other four patients has singleton pregnancy. In patients with twin pregnancy Pravastatin therapy was introduced when AEDV appeared in umbilical artery. Blood flow improved and we managed to extend pregnancies until 34 weeks. Cardiotocographic findings were normal in both fetuses without signs of asphyxia until delivery. In another 4 patients Pravastatin was introduced when PI values were above normal limits for gestational age. Umbilical artery PI values were decreased up to normal range and remained normal until term delivery. .All neonates were born without signs of intrauterine asphyxia.
Conclusion: In patients with isolated ischemic placental disease, with normal uterine artery vascular resistance, increased placental perfusion and decreased vascular resistance in umbilical arteries was achieved after administration of Pravastatin. Administration of Pravastatin reduced the incidence of early premature delivery due to fetal asphyxia.

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Placental Syncytin-2 bearing exosomes promote immune-tolerance against fetus during pregnancy

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Pregnancy is a unique event in which a foreign fetus survives to full term without apparent rejection by the mother's immune system. Syncytin-2 is a protein derived from human endogenous retrovirus sequences and is an important player in the formation of the placenta. Syncytin-2 is incorporared on the surface of extracellular microvesicles, known as exosomes, which are released from the placenta. Previous studies have suggested that placenta exosomes had the intricate capacity to modulate function of various immune cell types, such as DCs and macrophages. In light of our recent results, we will determine if exosome-associated Syncytin-2 act upon immune cell function and if variation in their levels changes the immunosuppressive function of placenta-derived exosomes. Using Jurkat T cell, we demonstrated that synthetic peptide homologous to the sequence of syncytin-2 ISD dimer induced MAP kinases ERK1 and ERK 2 phosphorylation and inhibits TNF-α production after PMA- Ionomycin stimulation. We also showed that (Sync-2-ISD)2 consistently suppressed IL-2, IL-5, IL-6, IFN-γ and TNF-α production in PBMC supernatant following stimulation with anti-CD3/CD28 or PMA- Ionomycin after incubation with (Sync-2-ISD)2. We further demonstrated that placental Syncytin-2 bearing exosomes down-regulate TNF-α expression in Jurkat T cell and Th1 cytokines in PBMC. To confirm the involvement of Syncytin-2 in immune-regulation during pregnancy, we down regulated Syncytin-2 expression using small interfering RNA. Syncytin-2-depleted trophoblast exosomes were next incubated with PBMC and we demonstrated that syncytin 2 depletion prevent down-modulation of Th1 cytokines. In conclusion, our data suggested that syncytin-2 contributes greatly to prevent fetal allo-rejection by creating a ''tolerant'' microenvironment characterised by lowering Th1 cytokines.

High-fidelity simulation in a post-partum hemorrhage scenario

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Introduction: Simulation in obstetric has been demonstrated to be a unique tool to train practitioner to face rare but potentially severe obstetric emergencies and it enhances the basic and complex technical skill, communication skill, multidisciplinary and team working. In particular, it has been shown to be very useful in a post-partum hemorrhage (PPH) scenario in which quick identification and response to the emergency is necessary in preventing maternal morbidity and mortality.
Objective: The aim of the study is to determine whether the use of high-fidelity simulation based-training (SimMom, Laerdal) in a post-partum hemorrhage scenario would improve the performance of obstetric practitioners and the team working.
Study Design: Twenty-six residents in Obstetrics and Gynecology, 10 residents in Anesthesiology and 20 professional nurses are randomized in two groups. All of them filled a pre-assessment test. After that, they have been divided into two groups, each one is formed by thirteen Ob/Gyn residents, five Anesthesiology residents and ten professional nurses. The first group is involved in an educational debriefing session and a subsequent post-partum hemorrhage simulation. The other group participates in an unanticipated simulated post-partum hemorrhage scenario. This module was repeated 3 weeks later. Each simulation is scored, based on standardized checklists, which focused on 15 technical action and 10 communication tasks, by an external physician observer.
Results: Both Residents and nurses show significant improvement in mean maneuver skill and communication scores after simulation training and debriefing session in comparison to naïve group. After 3 weeks, the first group still presents better score even if also the naive group improves technical and communicating skills.
Conclusion: High-fidelity simulation improves professional's performance in facing PPH. Simulation and team training significantly improves postpartum hemorrhage management since it develops both technical and communicating skills in participants.

Cabergoline treatment for recurrent Cushing's disease during pregnancy

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Introduction: Cushing's disease during pregnancy is associated with an increased risk for maternal and fetal complications. In recurrent Cushing's disease following transsphenoidal surgery, and when reoperation is not feasible, medical treatment is usually considered. Cabergoline was found to be effective in reducing hypercortisolism in Cushing's disease. Evolving data concerning the safety of cabergoline use during pregnancy show no significant increase in the rate of complications during pregnancy or postnatal period.
Case report: We report a 29-year-old woman with recurrent Cushing's disease, three years after transsphenoidal resection of pituitary ACTH-secreting macroadenoma. The patient presented with a 6 month history of weight gain, legs swelling, hirsutism, and irregular menses. Laboratory evaluation revealed: 24-h urinary free cortisol concentration of 131 mcg/24h (RR:20–90 mcg/24h), ACTH concentration of 22 pmol/L (RR:1.11–10 pmol/L),& serum cortisol, measured at 8:00 A.M. after 1 mg dexamethasone administration at 23:00 PM, of 6.2 mcg/dL. Repeated MRI revealed empty sella, with a small gadolinium-enhancing lesion, suspected to be an adenoma remnant on the medial wall of the right cavernous sinus. As the patient was not willing to undergo repeat surgical intervention, treatment with cabergoline was initiated, with a gradual dose titration up to 3.5 mg/week. Clinical improvement ensued & 4 months later, she conceived spontaneously. Cabergoline treatment at a dose of 2 mg/week was continued throughout pregnancy, during which the patient showed complete clinical remission. Consecutive tests of 24-h urinary free cortisol concentration were not found to be elevated. Pregnancy and delivery were uneventful.
Conclusion: This case report demonstrates that cabergoline may be an effective & safe therapeutic option for the treatment of Cushing's disease during pregnancy.

D2-Thr92Ala polymorphism and its role on preeclampsia as well on thyroid hormone levels

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Context: Type 2 iodothyronine deiodinase (D2) is an enzyme implicated in the transformation of thyroxine (T4) into 3.5,3-triiodothyronine (T3).
Objective: To determine the effect of the D2-Thr92Ala polymorphism on the severity of preeclampsia and also on the thyroid hormone levels.

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Methods: Patients- Main Outcome Measure 126 preeclamptic women and 131 normal pregnant women were genotyped using PCR-RFLP analysis. TSH, FT4 and FT3 levels were determined using ELISA methods.
Results: The risk to develop preeclampsia in association with the homozygous D2-Ala92/Ala92 genotype was 4.04 ($p < 0.001$). Higher risk for mild (OR 4.19, $p < 0.001$) and severe preeclampsia (OR3.77, $p = 0.003$) in carriers of the homozygous D2-Ala92/Ala92 genotype was observed. Preeclamptic women carriers the D2-Ala92 allele had higher TSH levels as compared to preeclamptic women negative for this genetic variation (μU/ml, 3.91±2.52 vs. 2.19±1.46, $p < 0.001$). Preeclamptic women carriers of this genetic variation had significantly higher FT4 levels (ng/dl, 2.32±0.89 vs. 1.02±0.33, $p = 0.003$) and significantly lower FT3 levels (pg/ml, 1.33±0.65 vs. 3.03±0.47, $p < 0.001$) than preeclamptic women negative for D2-Ala92 allele. Significantly higher FT4 levels was observed in women with PIH (ng/dl, 1.26±0.54 vs. 0.94±0.34, $p = 0.038$) and severe preeclampsia (ng/dl, 1.71±0.82 vs. 1.11±0.24, $p = 0.02$) carriers of the D2-Ala92 allele as compared with non-carriers. Significanlty lower FT3 levels was observed in PIH (pg/ml, 2.53±0.61 vs. 3.04±0.53, $p = 0.014$) mild (pg/ml, 2.4±0.79 vs. 3.04±0.09, $p < 0.001$) and severe preeclampsia (pg/ml, 1.96±1.17 vs. 3.09±2.06, $p = 0.009$) carriers of the D2-Ala92 allele as compared to non-carriers.
Conclusion: The results obtained confirmed the influence of the D2-Thr92Ala on the severity of preeclampsia and also on thyroid hormone status and its possible role in future determination of hypothyroidism.

Association of first-trimester angiogenic factors with placental histological findings in late preeclampsia

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Context: Early identification of late preeclampsia.
Objective: To explore in women with late PE the association between maternal levels of angiogenic/antiangiogenic factors at first trimester of pregnancy and histological findings attributable to placental underperfusion (PUP).
Methods, patients, interventions, measures: A nested case-control cohort study was conducted of 73 pregnancies complicated by late PE (>34 weeks at delivery) matched with controls. First trimester uterine artery Doppler (UtA); and maternal levels of placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) were retrieved. Placentas were histologically evaluated using a hierarchical and standardized classification system.
Results: In 54 (74%) placentas, 89 placental histological findings qualifying for PUP were found. There was a significant trend towards lower levels of PlGF across study groups (MoM values: 1.53, 1.41 and 1.37; $p < 0.001$) and higher uterine artery Doppler pulsatility (MoM values: 1, 1.26 and 1.32; $p < 0.001$), sFlt-1 levels (MoM values: 3.11, 3.11 and 3.22; $p = 0.002$) and sFlt-1/PlGF ratio (MoM values: 2.3, 2.3 and 2.44; $p < 0.001$). There was also a significant trend towards worst perinatal outcomes across the study groups in terms of gestational age at delivery, cesarean section for not reassuring fetal status, birth weight and neonatal acidosis.
Discussion: In late-onset PE an imbalance of circulating angiogenic and anti-angiogenic factors already present at first trimester is associated to histological findings reflecting placental insufficiency. First trimester screening by angiogenic factors might help to identify among late PE cases those with a placental involvement.
Conclusion: In late-onset preeclampsia, first trimester uterine Doppler and circulating levels of angiogenic/antiangiogenic factors are associated to placental underperfusion.

(OP04) IVF/ICSI: patients and their problems

Reaching for paternity: A phenomenological interview study on trans men's desire to have children after undergoing fertility preservation

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Context: Assisted reproduction has extended beyond the normative heterosexual family, and lesbian, gay and bisexual's rights to have children have been recognized. Since 2013 (in Sweden), this right also includes transgender people. However, research in the area is still sparse and no studies have investigated trans men's (female-to-male transsexuals) desire to have children in connection with fertility preservation (FP).
Objective: To investigate how trans men experience life after undergoing FP with focus on their desire to build a family.
Methods: Prospective study, inclusion started May 2014 and is still ongoing. Face-to-face qualitative interviews with a phenomenological approach.
Patients: Fifteen trans men (age 19–33).
Intervention: After diagnosed with transsexualism (ICD-10), patients received fertility counseling and underwent fertility preservation by egg freezing.
Main Outcome Measure: The interviews focused on plans of having children and motives behind undergoing FP.
Results: Trans men who had undergone FP experienced their desire to build a family as highly limited by biological, psychological, societal and legal boundaries. This caused distress and bitterness, especially when political decisions hindered them to reach life goals. The experience of FP was overall positive, and gave them respite while waiting for societal changes that could open additional possibilities to reach paternity.
Conclusions: Our preliminary results indicate that trans men who undergo FP have a strong desire to have children. However, these patients experience limited possibilities to achieve paternity. There is a need to offer specifically developed reproductive counselling directed to trans men in order to discuss reproductive possibilities that might be accessible to them.

Ovarian reserve tests for prediction of poor ovarian response and in vitro fertilization outcome

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Context: The success of assisted reproductive technology largely depends on adequate ovarian response. Poor response to ovarian stimulation affects a significant portion of women undergoing *in vitro* fertilization (IVF).
Objective: To evaluate the value of recently used ovarian reserve tests: age, follicle stimulating hormone (FSH), anti-Mullerian hormone (AMH) and Antral Follicle Count (AFC) for prediction of the outcome of IVF and to determine the more reliable markers for prediction of poor ovarian response after ovulation induction.

Patients: The prospective study included 111 infertile women, who underwent IVF with or without ICSI. Patients with an oocyte count ≤ 3 were considered as poor responders.
Interventions: Determination of AFC, levels of FSH and AMH on the cycle day 2- 3.
Main Outcome Measures: Number of oocytes retrieved and clinical pregnancy.
Results: The correlation between AMH and number of oocytes was the strongest ($r = 0.6$), as well as between AFC and number of oocytes ($r = 0.6$). There were significant differences between poor and good responders in all parameters (age, FSH, AMH, AFC, number of oocytes and embryos) ($p < 0.05$). According to Binary Regression Analysis for Poor Ovarian Response AFC was the only factor which significantly predicted poor response after ovulation induction. The cut-off value of AFC was 5 (ROCAUC=0.816; sensitivity 90%, specificity 65%). The Binary Logistic Regression analysis for clinical pregnancy shows, that age is the only factor, which significantly predicts the likelihood of clinical pregnancy (B=0.14; $p = 0.005$). The cut-off value of age – 33.5 (ROCAUC=0.733; sensitivity 79%, specificity 50%).
Conclusions: AMH and AFC are good predictors of ovarian response. AFC is the most reliable factor for prediction of poor response after ovulation induction. Age is the best factor for prediction of clinical pregnancy during IVF.

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Comparison of metabolomics profiling and morphological assessment for evaluation of embryo quality and reproductive potential

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Context and *Objective*: The purpose of the current study was to determine if the metabolomics profiling of spent embryo culture media could predict embryo quality and embryonic reproductive potential.
Methods: All patients had regular ovulatory cycle, normal hormone levels, normal semen analysis in their partner. All patients received GnRH agonist protocol as ovulation stimulation protocol and had a day 3 embryo transfer.
Patients: All women under 39 years of age with primary or secondary unexplained infertility of at least 1.5 years duration undergoing IVF/ICSI treatment were included.
Interventons: The spent embryo culture medial were analyzed by Raman spectroscopy. The means of the spectra from all samples were determined and subtracted from all of the samples obtained at the respective site.
Main Outcome Measures: embryo grading, clinical pregnancy
Results: Sixty-four spent embryo culture medias from 39 patients were evaluated with Raman Spectroscopy. According to the conventional morphological assessment 26 of them belong Grade-1 embryos while 38 of them belong Grade-2 embryos. According to Raman Spectroscopy 25 of them were Grade 1 embryos, while 39 of them were Grade 2 embryos. Band component analysis was applied on 64 preprocessed spectra, individually. The most interesting fit results were found in 815–1065 and 1140–1500 cm^{-1} region. The clinical pregnancy rate between morphologically graded and Raman spectroscopy evaluated embryos were similar ($p > 0.05$).
Conclusions: Morphological assessment approach heavily relies on the visual information obtained by the embryologist. Hence, it is subject to interobserver variance. In this study, our findings suggest that Raman spectroscopy can predict embryo quality and reproductive outcome in a more objective manner by metabolomics profiling of spent embryo culture media as efficiently as the morphological assessment.

Utilization of all fresh and frozen embryos after single embryo transfer for IVF/ICSI: the effect of ovarian response on cumulative live birth rates

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Context: Few studies have addressed the issue of the optimal number of oocytes retrieved in conventional ovarian stimulation. While the before-mentioned studies focused on the number of embryos transferred, the ongoing pregnancy rates and the live birth rates associated to the oocytes yield, cumulative live birth rate is the most meaningful outcome for the infertile patient.
Objective: The current retrospective cohort study was undertaken to further investigate the potential relation between the degree of ovarian response and the cumulative live birth rate following the first IVF cycle in a fixed GnRH-antagonist protocol with elective single embryo transfer (eSET). The rationale of our study is the analysis of cumulative live birth rates (LBR), taking into account fresh and frozen embryo transfers.
Methods: Retrospective cohort study . Eligible women were those who underwent (i) their first IVF cycle and (ii) had eSET in the fresh cycle from 2009 to 2013. All patients had (iii) normal menstrual cycles, (iv) and (v) stimulated with a fixed antagonist protocol (vi) with 150–225 IU dose of recombinant FSH (rFSH). Vitrification was used as method of cryopreservetion.
Main outcome: Cumulative LBR belong categories of ovarian response
Results: With patients divided to four groups according to oocytes yield no sig the cumulative LBR presented a significant upward trend, with the maximum value obtained in the >15 oocytes category. In particular the cumulative LBR of the >15 oocytes category (61.47%) was significantly higher ($p = 0.004$) than that of the 10–15 oocytes category (50.46%). In multivariate analysis ovarian response remained an independent predictor.
Conclusions: While the ovarian response doesn't seem to significantly influence LBR in fresh cycles, the results change dramatically when frozen cycles are analyzed.

The case for comprehensive genetic testing of gamete donors

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Donor Sibling Registry

Context: The Donor Sibling Registry (DSR) is a worldwide charity organization dedicated to educating, connecting and supporting donors, recipients and offspring. With 48.000 members, the DSR has connected 12.800 genetic first-degree relatives.
Methods: The DSR also shines light on serious genetic concerns about gamete donation, frequently counseling recipients whose children have inherited undisclosed genetic disorders, or who've discovered their donor was dishonest regarding health, or who learn that the sperm bank didn't notify them about reported illness.
Patients: The number and severity of these health matters is discomfiting. Since donors can father many offspring (one DSR donor has more than 200 known offspring) donors can transmit disease to scores of children around the world.
Intervention: Some sperm banks refuse to update donor/offspring medical information. Some make the process of reporting so complex

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or expensive that donors and recipients simply cannot comply or afford it.
Main Outcome: Most sperm banks obtain a written personal/family medical history. Some conduct basic laboratory testing, to detect specific mutations of specific genes or test donors for carrier status of the most common genetic conditions, such as CF or SMA. Without full genome sequencing, it is impossible to know about the thousands of genetic conditions that have been discovered.
Intervention: Full sequencing of a gene takes longer, is more extensive, and is much more expensive. But a negative result would then reduce the likelihood of carrier status much more than targeted mutation analysis.
Conclusion: Large US and Danish sperm banks ship sperm to clinics in more than 40 countries worldwide. To protect donors, recipients, and offspring, the implementation of regulation by an independent authority, mandating compulsory full genome sequencing is necessary.

Outcomes of oocyte donation in female cancer survivors with and without history of radiotherapy

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Context: Oocyte donation (OD) is indicated in female cancer survivors that have a reproductive wish but have developed ovarian failure as consequence of their cancer treatment. Women who have received radiotherapy (RT) may in addition suffer from a uterine infertility factor. Data concerning possible effects of RT on uterine physiology are limited and controversial.
Objective: to study if the history of RT influences the outcomes of OD in women cured of cancer.
Methods: comparison of OD outcomes in cancer survivors with vs. without history of RT.
Patient(s): Between 2003 and 2015, 31 women with infertility related to the side effects of cancer treatment had OD cycles in our clinic. 102 embryo transfers with either fresh (52) or frozen (50) embryos were performed. Fifteen women had history of either total body irradiation or pelvic radiation (case group). The control group of 16 patients had been treated with combination of chemotherapy (CT) and surgery or surgery alone.
Intervention(s): Retrospective chart review at Academic Reproductive Medicine Clinic
Main Outcome Measure(s): Pregnancy, live birth.
Result(s): In the case group, 47 cycles resulted in 11 pregnancies (23%) and 9 live births (19%). In the control group, 55 cycles resulted in 20 pregnancies (36.4%) and 16 live births (29.1%).
Conclusions: Among cancer survivors, the OD outcomes after RT seem to be worse than outcomes after CT or combination of surgery and CT. Logistic regression analysis of OD outcomes including perinatal outcomes in cancer survivors with and without history of RT in comparison to the group of patients without previous malignancies will follow.

Serum stem cell factor assay in elderly poor responder patients undergoing IVF: a new biomarker to customize follicle aspiration cycle by cycle

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Context: Padua University-Assisted Reproduction Unit
Objective: To evaluate if serum concentration of SCF(stem cell factor) at ovulation-induction may represent a new tool to establish if perform or not follicle aspiration in elderly poor-responder(POR) patients.
Methods: Observational cohort study
Patient(s): Thirty-seven elderly infertile patients(43–50 years-old) estimated POR (Bologna-Criteria)
Intervention(s): Patients were first treated by standard-long-agonist protocol (sCOS) with only recombinant-FSH(rFSH) and, in case of treatment failure, were secondly treated by LH-protocol (LHCOH) different from sCOH only for the rLH supplementation (150 UI daily from the 4th day of rFSH). On pick up day, we measured (ELISA-Kit) the follicular and the serum levels SCF (fSCF and sSCF).
Main Outcome Measure(s): We evaluated if different protocols of stimulation may significantly influence fSCF and if these levels can reflect sSCF concentrations. We evaluate whether sSCF at ovulation induction might be associated with the number and the quality of oocytes and embryos obtained. Finally we indicate a cutoff value to proceed with oocyte retrieval.
Result(s): sCOH and LHCOH protocols did not show statistical differences in term of fSCF and sSCF concentrations. On the contrary fSCF and sSCF levels showed a strong linear correlation.[$p < 0.001$] Estimating the chance of collecting MII-oocytes we found that at least 3 MII-oocytes was collected with sSCF>800pg/mL, 2 MII-oocytes with sSCF>600pg/mL, 1 MII-oocytes with sSCF>400 pg/mL. MII-oocytes was not recovered with s-SCF<400pg/mL. We found that all the 5 obtained pregnancies occurred in patients with s-SCF values>1000pg/mL at pick-up.
Conclusions: The capability of sSCF to predict MII oocyte retrieved lead us to speculate regarding the potential application of this biomarker for the improvement of IVF treatments efficiency in elderly POR patients.

Endometrial receptivity genetic expression and histological analysis in women with repeated implantation failure

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Context: Successful implantation requires quality and functional embryos synchronized with a receptive endometrium. The probability of successful embryo implantation is approximately 30%. Repeated implantation failure is a challenging clinical entity in human reproduction.

Objective: To evaluate and compare the results of two different methods used to determine the endometrial receptivity status in patients with repeated implantation failure.
Methods: Prospective nonrandomized observational study performed at Hospital Angeles del Pedregal, México City.
Patients: Eleven patients with infertility and repeated implantation failure diagnosis.
Interventions: Endometrial biopsies for receptivity genetic expression and histological analysis.
Main outcome measure: Endometrial receptivity status according to genetic expression using the Endometrial Receptivity Array and histological analysis.
Results: Eleven patients were analyzed (mean age 41.5 years), with regular menstrual cycle patterns. Seven patients underwent surgery for uterine factors. A total of 14 fresh and 18 frozen cycles with 30 and 32 embryos transferred among all patients. Endometrial receptivity genetic expression reported: 3 pre-receptive, 6 receptive and 2 post-receptive endometrium. Histological endometrial analysis reported 1 proliferative, 7 initial secretory and 3 late secretory endometrium. After adjusting endometrial window of implantation we achieved pregnancies in 3 patients, no pregnancy in 2 patients and 6 patients with no embryo transfer performed yet.
Conclusions: Endometrial receptivity remains as a critical challenge among patients with repeated implantation failure, as well the embryo quality. Endometrial genetic expression and window of implantation adjustment could represent a very useful tool for human reproduction techniques when performing personalized embryo transfers.

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Analysis using intracytoplasmic sperm injection obtained by fresh and thawed testicular sperm extraction in in vitro fertilization

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Objective: Intracytoplasmic sperm injection (ICSI) has grown to become the first choice of treatment for severe male factor infertility. Testicular Sperm Extraction (TESE) can get sperm 60% of the time, even in the most difficult cases. Sperm taken directly from the testicles never reaches a normal function because maturation occurs in the epididymis. Testicular sperm is usually immobile immediately after biopsy and especially after thawing of testicular samples. The aim of this study is to analyze the result of successful *in vitro* fertilization cycles after using sperm obtained from testicular and epididymal biopsy, both fresh and thawed.
Methods: Retrospective study analyzing 17 cycles of *in vitro* fertilization in which testicular and epididymal sperm extraction aspiration was performed. Intracytoplasmic sperm injection was used in all cases as a method of oocyte insemination. Development of fertilized embryos was recorded and the best were selected for embryo transfer.
Results: A total of 17 cycles were performed. 10 were conducted with thawed samples and 7 with fresh samples. The average age of patients was 43 years, and the average age for women was 35 years. 79 out of 131 inseminated oocytes fertilized. Only 58 embryos survived until day 3 and only 14 reached the blastocyst stage. 28 embryos were transferred, with 8 confirmed pregnancies and a pregnancy rate of 47%
Conclusions: The development of testicular sperm extraction and intracytoplasmic sperm injection has provided many men with obstructive and nonobstructive azoospermia the opportunity to conceive. This study shows that one can get embryonic development, fertilization and acceptable pregnancy rates using sperm extracted from testicular biopsies, both fresh and thawed.

Uropathogenic microorganisms and female infertility: An in vivo study

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Context: The role of bacterial infections in infertility is controversial. Although clinical significance of sexually transmitted microorganisms viz.Chlamydia trachomatis, Neisseria gonorrhoeae, Treponemapallidum have been implicated in infertility but,infertility due to other microorganisms is still debatable.
Objective: Evaluation of fertility outcome after intravaginal inoculation with various uropathogenic microorganisms
Methods: The sperm impairing Escherichia coli, Staphylococcus aureus, Serratiamarcescens, Candida albicanswere intravaginally inoculated into female Balb/c mice at different doses (104, 106.108 cfu/20 ml) for 10 consecutive days. Following mating on day 12, the mice were kept under observation for fertility outcome studies. Moreover, to study the underlying mechanisms histopathological studies, protein profiling of vaginal lavages, cytokine analysis as well as lipid peroxidation was carried out.
Main Outcome Measure(s): Fertility outcome
Result(s): Vaginal cultures revealed that these strains could efficiently colonize mouse vagina. Mating on day 12 with breeder males led to 100% decrease in fertility as compared to control receiving PBS. Further, no histopathological changes were observed in any of the reproductive organs. Cytokine assay showed no detectable changes in TNF-α whereas in case of IL-10 an increase was seen on day 2 and 3 which then returned to normal.
Conclusions: Sperm impairing microorganisms can asymptomatically colonize female genital tract and mightplay a pivotal role in causing infertility.

(OP05) Gynecological cancers

Serous tubal intraepithelial carcinoma and tubal-peritoneal tranzition zone – new aspects in high-grade serous carcinoma pathogenesis

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Context: Because 'tubal' theory of high-grade serous carcinoma pathogenesis was proved, we should accurately search for the exact zone to be a source for tumor cells in the fallopian tube (FT).
Objective: Tubal-peritoneal transition zone (TPTZ) was supposed to be predisposed for neoplastic changes and was investigated intensively.
Methods: Histology, immunohistochemistry (PgR, E-cadherin, Ki-67, p53), statistics (Student test with Bonferroni correction)
Patients: One hundred fifty patients (195 FTs) with extraovarian pathology ($n = 30$) and ovarian tumors ($n = 120$) were recruited. All fimbrial parts of FTs were investigated. Two-staged algorithm for tubal intraepithelial lesion assessment were used (morphological and immunohistochemical).
Results: Three-hundred seventy-eight TPTZ were assessed. 40.6% TPTZ involved plicae of endosalpinx, from which 43.6% TPTZ localized on

the top of plica, 25.6% – on the side of plica, 30.8% – between plicae. Histological outline of TPTZ was flat (52.1%) convex (40.6%), concave (7.3%). Lymphatic and blood vessels dilatation was diagnosed in most TPTZ (very closed to the basal membrane of FT). Transition metaplasia was revealed in 33%, Walthard nests – in 25%. ''Ovarian'' stroma was diagnosed adjunct to TPTZ in 2%, being out of TPTZ – in 20%. Inflammation infiltration was reveled in patients with tubal pregnancy, chronic salpingitis and hydrosalpinx more frequently ($p < 0.05$). Serous tubal intraepithelial carcinoma (STIC) was diagnosed only in patients with serous carcinoma (in 30%). In 53.3% of patients STIC was revealed adjunct to TPTZ, in 33.3% – in the fimbrial part of FT (out of TPTZ), in 13.3% – out of fimbrial part (differences was statistically significant, $p < 0.05$).

Conclusion: TPTZ is supposed to be an analogue of the transition zones in other organs. Its proximity to STIC in most cases proved the hypothesis about TPTZ to be a ''hot spot'' for serous ovarian carcinogenesis.

Intraepithelial lesions of fallopian tube: improved diagnostic panel and innovative precursor role in ovarian carcinoma pathogenesis

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Context: It is supposed that tubal intraepithelial lesions (TILs) are the most probable precursors of high-grade serous carcinoma (HGSC).Thus, TILs should be diagnose accurately for adequate treatment development.

Objective: We evaluated the incidence of TILs (serous tubal intraepithelial carcinoma (STIC),serous tubal intraepithelial lesion (STIL), p53-signature, secretory cells outgrowth (SCOUT)) in patients with epithelial ovarian tumors and supposed TILs role in serous ovarian carcinogenesis.

Methods: Histology, immunohistochemistry (p53, Ki-67, PAX 2), statistics (Mann–Whitney and $\chi 2$ tests).

Patients: $n = 136$ (HGSC ($n = 20$),serous borderline ovarian tumors (SBOT) ($n = 66$), serous cystadenoma ($n = 30$),non-serous ovarian tumors ($n = 20$).

Interventions: Hysterectomy,salpingo-ovariectomy.

Main Outcome Measure and Results: Histologically unequivocal for STIC lesions were identified in 14.7%,suspicious for STIC–in 25.7%,not suspicious for STIC–in 59.6%. With p53 and Ki-67 expression assessment (due to R. Vang et al. algorithm) STIC were diagnosed in 10% (only in HGSC), STIL in 13.3%, p53-signature in 11.7%, normal/reactive epithelium in 65%. Frequency of TILs and serous tumors malignant potential were associated significantly ($p < 0.05$). Frequency of TILs and histologic types of ovarian carcinoma were correlated significantly ($p < 0.05$). PAX2-negative SCOUT was identified in 75% of HGSC, in 60% of SBOT, in 40% of serous cystadenomas,in 15% of non-serous carcinomas. Frequency of PAX2-negative SCOUT and serous tumors malignant potential were associated significantly ($p < 0.05$). Frequency of PAX2-negative SCOUT and histologic types of ovarian carcinoma were correlated significantly ($p < 0.05$).

Conclusion: Used immunohistochemical algorithm can improve TILs diagnostics. Our data prove the hypothesis that TILs play a significant role in HGSC pathogenesis and SCOUT can be the very early pathogenic event.

Increased 17beta-hydroxysteroid dehydrogenase type 1 mRNA level is correlated with poorer prognosis in endometrial cancer

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Context: Recently, we have shown that the local level of the enzyme 17beta-hydroxysteroid dehydrogenase type 1 (HSD17B1), responsible for the generation of 17beta-estradiol, is elevated in type 1 endometrial cancers (EC) compared with controls and is involved in EC development (Cornel et al 2012, JCEM). Multiple additional enzymes can contribute to the local generation of 17beta-estradiol: aromatase (CYP19) and sulfatase (STS) generate 17beta-estradiol, whereas sulfotransferase (SULT1E1) and 17beta-hydroxysteroid dehydrogenase type 2 (HSD17B2) inactivate it.

Objective: To evaluate if there is a relation between EC patients prognosis and 17beta-estradiol generating enzyme levels.

Patients: Tumour tissue collected directly after hysterectomy of 175 EC patients was included; 141 endometrioid (49 Grade I, 53 Grade II and 39 Grade III) and 34 non-endometrioid tumour types.

Method: The mRNA levels of CYP19, SULT1E1, STS, HSD17B1 and HSD17B2 were measured using micro-array analyses as described before (Krakstad et al 2012 BrJ cancer). Patients were clustered according the mRNA enzyme levels using quartiles. High levels for the 17beta-estradiol generating enzymes (HSD17B1 and STS) were defined as the 4th quartile, whereas low levels were defined as the 1st, 2nd and 3rd quartiles together. For 17beta-estradiol degrading enzymes (HSD17B2 and SULTE1) the lowest quartile was defined as the 1st quartile only, whereas high level was defined as the 2nd, 3rd and 4th quartiles together.

Results: Patients with high HSD17B1 mRNA levels have a significantly poorer prognosis compared to patients with low HSD17B1 levels ($p = 0.007$). There is no significant correlation between high or low HSD17B2, STS, SUL1TE1, and CYP19 mRNA levels and patients prognosis.

Conclusion: High HSD17B1 mRNA level is correlated with poor prognosis in EC patients. Hence, HSD17B1 is a potential prognostic marker.

Genetic risk modifiers of Lynch Syndrome endometrial cancer

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MUMC

Context: The risk to develop endometrial cancers among subjects testing positive for a pathogenic Lynch syndrome mutation varies, making the risk prediction difficult. Genetic risk modifiers alter the risk conferred by inherited Lynch syndrome mutations, and their identification can improve genetic counseling.

Objective: We aimed at identifying rare genetic modifiers of the risk of Lynch syndrome endometrial cancer.

Methods: A family-based approach was used to assess the presence of genetic risk modifiers among 35 Lynch syndrome mutation carriers having either a poor clinical phenotype (early age of endometrial

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cancer diagnosis or multiple cancers) or a neutral clinical phenotype. Putative genetic risk modifiers were identified by Next Generation Sequencing among a panel of 154 genes involved in endometrial physiology and carcinogenesis.
Results: A simple pipeline, based on an allele frequency lower than 0.001 and on predicted non-conservative amino-acid substitutions returned 54 variants that were considered putative risk modifiers. The presence of two or more risk modifying variants in women carrying a pathogenic Lynch syndrome mutation was associated with a poor clinical phenotype.
Conclusion: A gene-panel is proposed that comprehends genes that can carry variants with putative modifying effects on the risk of Lynch syndrome endometrial cancer. Validation in further studies is warranted before considering the possible use of this tool in genetic counseling.

Endometriosis and cancer

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In the last 10 years several epidemiological and basic research studies have been performed to demonstrate a relation between endometriosis and cancer. Numerous histological and molecular/genetic studies have also indicated that endometriosis may transform into cancer. This review of the literature would to be an up-date on the studies available and the knowledge regarding the relation between endometriosis and cancer, by examining recent data available in the literature concerning the risk of cancer in women with endometriosis. Regarding ovarian cancer, at now the available studies have shown that that endometriosis was associated with higher risk of certain histology subtypes of ovarian cancer, including clear-cell carcinoma, endometrioid carcinoma, and low-grade serous carcinoma. More recent studies have demonstrated that the ovarian carcinomas, contrary to what their name suggests, could not originate in the ovaries. Instead, the fallopian tube seems to be the main contributor to these ovarian endometriod and clear cell cancers. The possible tubal origin of endometriosis and then clear cell and endometrioid carcinomas must be confirmed and clarify by further investigations. Regarding endometrial cancer, the studies available demonstrate an association of endometriosis with endometrial cancer. The pathogenesis in endometriosis and endometrial cancer is complicated and the etiopathogenesis of both disorders is multifactorial. Data available on the association between endometriosis and other cancers i.e. breast cancer, melanoma, non-Hodgkin's lymphoma and pancreatic cancer and are not conclusive and further studies are necessary to definitively clarify these association. Women with endometriosis showed overall a better prognosis after a malignancy diagnosis, compared to women without endometriosis.

Clear cell ovarian cancer and endometriosis – is there a relationship? original study

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Context and Objectives: Ovarian clear cell carcinoma is a rare type of ovarian cancer. In recent years, issues of the common genetic origin of endometriosis and ovarian clear cell carcinoma have been raised. The aim of this study was to evaluate the prevalence of this type of cancer, risk factors, prognosis and its potential aetiological association with endometriosis.
Methods: In a retrospective study, we analysed histopathological data of patients operated in the Department due to ovarian cancer from the years 2004–2014. Among the 394 patients operated on for ovarian cancer, clear cell carcinoma was found in 0.02% (9/394).
Interventions: Menstrual history, parity, comorbidities, data from physical examination, operational protocols and histopathological diagnoses were analysed. Follow-up was obtained from 77.8% patients. Statistical analysis was performed using Microsoft Excel 2013.
Results: The mean age of patients at diagnosis was 57.6 years; BMI in the study group was 27.2; the majority of patients were multiparous (77.8%). Clear cell carcinoma was detected mostly at stage Ia ($n = 4$). The concentration of Ca-125 in the study group was: mean average 142.75 U/ml; median 69.3 U/ml. In none of the patients, the coexistence of endometriosis could be clinically or histologically confirmed. The most common comorbidity in the study group was hypertension.
Conclusions: In our clinical material, ovarian clear cell carcinoma is a rare histopathological unit with prognosis comparable to that of serous ovarian cancer. The cause-and-effect relationship between this histopathological subtype and endometriosis can only be proved based on statistical studies of the entire population.

(OP06) IVF/ICSI: the treatments and their possibilities

Effects of low doses of mifepristone on human embryo implantation process in a three-dimensional human endometrial in vitro co-culture system

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Context: The antiprogestin mifepristone has been extensively studied in different doses, duration and periods in the menstrual cycle for use in fertility control and other gynecological indications. In clinical trials, a dose of 200 mg during the early luteal phase prevents pregnancy and it has been demonstrated that exposure to 10 μM in a human endometrial in-vitro co-culture model inhibits embryo implantation.
Objective: To explore the effects of two low doses of mifepristone on human embryo implantation process, using a well-established 3D *in vitro* cell culture model.
Methods: Endometrial biopsies from healthy, fertile women were obtained on cycle day LH+4. Epithelial and stromal cells were isolated and a 3D endometrial cell culture model constructed. The two treatment groups received mifepristone in a concentration of 0.5 μM and 0.05 μM respectively and the control group vehicle only. Human viable embryos were placed on all cultures and after five days of co-culture, the cultures were tested for embryo attachment. The 3D endometrial construct was thereafter analyzed for endometrial receptivity markers by qRT-PCR
Results: None of the embryos in 0.5 μM of mifepristone ($n = 8$) attached to the endometrial construct in *vitro* ($p = 0.004$), whereas four out of ten in 0.05 μM and seven out of ten embryos in the control group attached to the cultures ($p = 0.369$). We also studied the expression of sixteen reported endometrial receptivity markers in the endometrial construct, using qRT-PCR, and found that most of the studied markers were significantly altered after mifepristone exposure. We observed a dose-dependent effect of mifepristone on endometrial receptivity at the molecular as well as at the functional level.
Conclusions: Exposure to a low dose (0.5 μM) of mifepristone during the receptive period successfully inhibits human embryo implantation *in vitro*.

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Recombinant LH supplementation during IVF cycles with a GnRH-antagonist in estimated poor responders: a cross-matched pilot investigation of the optimal daily dose and timing

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Context: Padua University-Assisted Reproduction Unit
Objective: To detect the best timing and daily-dose of rLH administration in estimated poor responders (EPRs) undergone IVF-cycle in order to achieve the greatest number of MII oocytes, the best fertilization-rate and embryos quality, the most appropriate endometrial-thickness at embryo-transfer and the highest pregnancy-rate.
Methods: Prospective-randomized-cross-matched study.
Patient(s): Forty EPRs undergoing two fresh IVF cycles treated by GnRH-antagonist-protocols.
Intervention(s): Patients were assigned to Group-A(rLH-75UI/die) or Group-B(rLH-150UI/die) and further divided in subGroup-A1/subGroup-B1 (rLH started with rFSH) and subGroup-A2/subGroup-B2(rLH started at GnRH-ant administration). Patients who didn't conceive in the first cycle(35-cases) were admitted to second attempt after being cross-matched for Groups/SubGroups.
Main Outcome Measure(s):Follicular growth, number and quality of oocytes retrieved/embryos obtained, endometrial thickness at retrieval, pregnancy rate.
Result(s): Patients treated with 150UI of rLH beginning with GnRH-ant administration showed significantly better outcomes in terms of total number of follicles >10mm, follicles >16mm and 17β-estradiol at ovulation-induction, total number of oocytes and MII-oocytes, total number of embryos, number of grade-I embryos and pregnancy rate. The worst results were observed in patients treated with 75UI of r-LH starting from the GnRH-ant. Considering all subGroups, endometrial-thickness showed a significant linear correlation with the total dose of r-LH independently from the timing of administration.
Conclusions: The most appropriate window for rLH administration seems to be the mid-to-late follicular phase(miming the physiological LH increase). When administered in early-follicular phase, rLH may further improve endometrial thickness and morphology.

Which luteal phase support is better for each IVF stimulation protocol to achieve the highest pregnancy rate? A superiority randomized clinical trial

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Context: Padua University-Assisted Reproduction Unit
Objective: To determine the best luteal phase support (LPS) after IVF cycles.
Methods: Observational prospective study on women undergoing their first fresh non-donor IVF cycle. We analysed IVF outcome according to different LPS strategies.
Patient(s): Three-hundred sixty idiopathic infertile women.
Intervention(s): Patients were divided in three groups according to stimulation protocols: GroupA ($n = 180$), long-agonist; GroupB ($n = 90$), short-agonist; GroupC ($n = 90$), short-antagonist. Each patient was randomly assigned to one of three different subgroups in relation to LPS protocol: Subgroup1 (PG[progesterone] 2 vaginal capsule 200mg/day), Subgroup2 (PG 3 vaginal capsule 200mg plus PG 100mg intramuscular/day), Subgroup3 (PG 3 vaginal capsule 200mg plus PG 100mg intramuscular plus estradiol-valerate 2 vaginal tablets/day).
Main Outcome Measure(s): Clinical pregnancy rate (CPR), ongoing pregnancy rate (OPR).
Result(s): Considering CPR: among GroupA, subgroupA2 showed higher CPR rate than A1[$p < 0.01$] and lower than A3[$p < 0.05$]; among GroupB, subgroupB2 showed higher CPR than B1[$p < 0.01$], no differences between subgroupsB2 and B3 were reported; among GroupC: subgroupC2 showed higher CPR than C1[$p < 0.01$] but lower than C3[$p < 0.01$]. Considering OPR: among GroupA, subgroupA2 showed higher OPR than A1[$p < 0.05$] and no differences were recorded between A3 and A2; in GroupB, subgroupB2 showed higher OPR than B1 as well as B3 in comparison to B2[both $p < 0.05$]; in GroupC, subgroupC3 had higher OPR compared to C1 and C2[$p < 0.01$], while no differences were observed between subgroups C1 and C2.
Conclusions: High-dose PG seems better than low dose to increase both CPR and OPR. E2 supplementation seems mandatory in case of short-GnRH antagonist protocol.

The potential role of GnRH-agonists and antagonists in inducing thyroid physiopathological changes during IVF

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Context: Padua University-Assisted Reproduction Unit
Objective: To evaluate if GnRH(gonadotropin-releasing hormone)agonists and antagonists may differently impact on thyroid function in women undergoing COS(controlled ovarian stimulation).
Methods: Observational study on a cohort of euthyroid women(TSH range: 0.2–4.0mIU/L;T4-values: 9–22pmol/L) treated with long GnRH-agonist protocol or flexible GnRH-antagonist protocol. We dosed 17-β-estradiol(E2) and TSH values before stimulation(T-0) and every 2 days until T-ov-ind(ovulation induction day). In case of TSH levels above the cutoff, patients were screened for T4(thyroxin) and thyroid autoantibodies.
Patient(s): One hundred fifty-six infertile women scheduled for fresh non-donor IVF cycles.
Intervention(s): Seventy patients in GroupA(GnRH-agonist protocol) and 86 in GroupB(GnRH-antagonist protocol). Groups were divided in 4 Subgroups: A1($n = 46$) and B1($n = 61$) for women with a baseline

TSH value <2.5 mIU/L, A2($n = 24$) and B2($n = 25$) if baseline value ≥2.5 mIU/L.
Main Outcome Measure(s): Serum values of TSH, E2, T4, pregnancy rate.
Result(s): In GroupA, E2 at T-ov-ind was increased in comparison to GroupB ($p < 0.01$), whereas TSH values had an opposite trend (increased only in GroupB; $p < 0.001$). 64 women showed TSH values above the cut-off during COS: 7 in GroupA and 57 in GroupB. 5 patients of the Group A(71.4%, 4 with positive antibodies) and 6 of the GroupB (10.5%, 2 with positive antibodies; $p < 0.001$) displayed hypothyroidism. No pregnancy occurred in case of hypothyroidism, whereas in the 53 women with ''isolated TSH increase'' (normal T4, negative antibodies) we recorded 20.7% of clinical pregnancy rate and 54.5% of ongoing pregnancy rate.
Conclusions: Drugs used for gaining hypothalamic control during COS seem to differently interfere with the regulation of thyroid axis.

The Effect of Dehydroepiandrosterone Supplementation on IVF Outcomes in Diminished Ovarian Reserve Women

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Context: Diminished ovarian reserve (DOR) is an ovarian malfunction disease with less number and/or poor quality oocytes and elevated gonadotropin levels in women under the age of 40. Dehydroepiandrosterone (DHEA) supplementation may increase serum basal testosterone and affect follicular recruit, whether DHEA supplementation improve *in vitro* fertilization-embryo transfer(IVF-ET) outcomes in DOR patients remain unclear.
Objective: To evaluate whether DHEA supplementation for 8 weeks improves ovarian response and IVF outcomes in the DOR women.
Method(s): A randomized, prospective study.
Patient(s): Forty-six women with anticipated diminished ovarian reserve.
Intervention(s): Randomization into DHEA group treated with DHEA (25 mg three times a day) or control group treated with placebo for 8 weeks and a subsequent IVF cycle.
Main Outcome Measure(s):Measurement of testosterone(T), serum antimullerian hormone (AMH), inhibin B, DHEA-S, antral follicle count (AFC) and Clinical pregnancy rate.
Results: The DHEA supplementation resulted in significantly higher in serum T (32.50±18.69 vs. 20.53±15.10 ng/ml) and DHEA-S level (1.99±1.62 vs. 1.59±1.41ng/ml). Although serum FSH, AMH, inhibin B levels and clinical pregnancy rate were slightly increased in DHEA group, there was no statistically difference after DHEA treatment.
Conclusion: No significant change in serum FSH, AMH, inhibin B levels and clinical pregnancy rate after DHEA supplementation.

Influence of preovulatory progesterone rise during ovarian stimulation on ivf outcome

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Context: Despite the wide use of GnRH analogues for pituitary down-regulation, serum progesterone (P) level rise is often reported in the late follicullar phase during ovarian stimulation for *in vitro* fertilisation. The incidence of preovulatory P rise has been reported between 5% and 35% of stimulated cycles in women treated with GnRH agonists and between 20% and 38% of cycles when the GnRH antagonist protocol was used. The most likely factors for elevation of serum P concentration are an excess number of follicles and proliferating granulosa cells within these follicles as well as increased activity of follicle stimulating hormone (FSH)-stimulated granulosa cells and LH-stimulated theca cells. It was found that increased serum estradiol concentration is associated with a high risk of premature P rise.
Objective: Prolongation of the follicular phase by delaying human chorionic gonadotrophin administration by 2 days after the presence of ≥3 follicles ≥17mm in recombinant(r)-FSH/GnRH antagonist cycles, resulted in raised concentrations of P. The increased LH receptor sensitivity in the granulosa cells due to higher cumulative exposure to estradiol which, in conjunction with FSH, could be one of the mechanisms to account for the premature elevations in serum P concentrations.
Results: The influence of the preovulatory P rise on IVF outcome remains controversial, because several authors have failed to demonstrate any negative impact, while others reported a detrimental effect associated with the rise of P. Although there is no consensus on the cut-off level to define increased P concentration, it seems that P rise (> or = 1.5 ng/ml or 4.77 nmol/l) may have deleterious effects on endometrial receptivity. The most appropriate choice to avoid the negative effects of P rise is to cancel fresh embryo transfer and freeze all embryos with transfer in the natural cycle.

Effects of recombinant-LH supplementation on the proteomic profile of follicular fluid from poor responder Patients: focus on follicular growth factors and oocyte maturity markers

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Context: Padua University-Assisted Reproduction Unit
Objective: To evaluate if recombinat-LH(rLH) supplementation during COS(controlled ovarian stimulation) in poor-ovarian-responders(POR) may influence the post-receptor signaling involved in follicular growth and oocyte maturity and to determine if these factors could explain the clinical advantages observed with r-LH in POR.
Methods: Observational cohort study
Patient(s): Forty infertile women>40 years (POR according to BolognaCriteria)
Intervention(s): Eligible patients underwent first COS by standard-long-agonist protocol(sCOS) using recombinant-FSH(rFSH) and, in case of no pregnancy, they performed a repeated cycle with an LH-protocol(LHCOS). LHCOS differed from sCOS only in rLH supplementation of 150IU daily (from the 4th day of rFSH). On pick up day, we measured (ELISA-Kit) the follicular levels of EGF,Erk1/2,Akt1/2 and their phosphorylated isoforms (pErk1/2,pAkt1/2)
Main Outcome Measure(s): In the two protocols: different levels of EGF, ERK1/2, pERK1/2, AKT1/2, pAKT1/2 in FF (follicular fluid); the association between intra FF levels of these biomarkers with MII oocyte and first degree embryos.
Result(s): sCOS and LHCOS showed significant differences in terms of EGF, ERK1/2, pERK1/2, AKT1/2, pAKT1/2. Significant correlation was observed between the number of MII oocytes and the levels of all biomarkers. Considering the association with 1st degree embryos: FF levels of pERK1/2 showed a high correlation [r2:0.973; $p < 0.0001$], FF

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levels of p-AKT1/2 showed an acceptable correlation [r2:0.624; $p < 0.05$].
Conclusions: EGF signaling and its downstream PI(3)K-AKT1/2-mTOR and cAMP-PKA-ERK1/2 cascades are enhanced by rLH. Since these pathways have a fundamental role for the acquisition of oocyte competence and probably for embryos quality, the rLH supplementation could represent a strategy to improve the cost-efficacy of IVF in POR.

Hormone therapy prior to ovarian hyperstimolation cycle in women with premature ovarian insufficency: a retrospective analysis

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Premature ovarian failure (POF) is a disorder characterised by the cessation of ovarian function before the age of 40,with amenorrhoea, hypergonadotropinism and hypoestrogenism. It affects1–3%women of reproductive age. Several aetiologies have been postulated but most of the cases are idiopathic. Actually no treatment has been conclusively resulted in enhancement of fertility,thus the use of donor eggs is often the only possibility. Several studies showed, also,that FSH level for a good ovarian response could be10mUI/mL. Hormone replacement therapy in POF could correct the endocrine defect and may be a possibility to improve fertility. The aim of this study is to evaluate if a pre-treatment hormone therapy in patients with hypergonadotropic hypogonadism just prior to their ovarian hyperstimolation cycle can decrease FSH basal level, improve number and quality of retrieved oocytes and finally increase pregnancy rate. This is a retrospective study conduct in our Assisted Reproductive Centre of University of Pisa. Patients with premature ovarian insufficency were enrolled. This diagnosis was based on their history, gonadotropins levels (FSH>15mIU/ml) and ultrasound picture. All the routine infertil analysis should be normal,with the impression of unexplained infertility. Forty-seven subfertile subjects were made part of the study. They were divided into two groups: 25 women started their ovarian hyperstimolation therapy without any pre-treatment and 22 received hormone therapy for3months and then a FSH control every month until FSH level <12mUI/mL; prior to their oocyte cycle. Hormone therapy was administered in the form of Estradiol Valerate 2mg/day for cycle, days 3–26 and of Dydrogesterone 10mg/day orally from cycle, days 16–26.
Conclusion: Pretreatment hormon therapy can decrease FSH level,increase number and quality of retrieved oocytes, of embryos and finally the pregancy rate.

Title clinical study of letrozole combined low-dose highly purified HMG (Hp-HMG) in patients with clomiphene citrate-resistant polycystic ovary syndrome-related infertility

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Objective: To evaluate the effectiveness and safety of letrozole combined Hp-HMG protocol in induction of ovulation for CC-resistant PCOS women.
Methods: Monitoring follicular development with transvaginal ultrasounography and testing blood level of estradiol and LH. On the day of GnRH antagonist(GnRHa) trigger, endometrial thickness was assessed. Patients 200 infertile women of PCOS who had previously diagnosed CC resistance. Intervention A dose of 5 mg of letrozole was given orally for 5 days starting from the third day of a spontaneous or progesterone-induced withdrawal bleeding, and following by sequential low dose Hp-HMG (75IU∼150IU) administration. GnRHa trigger was obtained when the dominant follicle was ≥18mm in diameter or two or more follicle diameters were≥16mm. Luteal support was given after ovulation. All including 395 cycles. Main Outcome Measure(s) The ovulation rate, the clinical pregnancy rate and related parameters. The incidence of adverse events (moderate or severe ovarian hyperstimulation syndrome and multiple pregnancy).
Results: The rate of ovulation was 97.84%, cancellation rate was 1.4%. The periodic single pregnancy rate was 35.35% and cumulative clinical pregnancy rate was 68%.Total of 4 twin gestations and 3 ectopic pregnancies. No severe OHSS and local or systemic side effects were seen. Serum concentration of estradiol on the day of GnRHa trigger was 434.77±237.75pg/ml and endometrial thickness was 9.5±2.1mm.
Conclusion: Letrozole combined low dose Hp-HMG protocol maybe is an effective and safe choice in inducing ovulation for infertile patients with CC-resistant PCOS.

Antimüllerian hormone (AMH) and basal estradiol (E2) as predictors for the outcome of gonadotropin releasing-hormone antagonist stimulated ICSIcyles

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Context: Serum AMH levels across different menstrual cycles are nearly constant and reflect the number of antral and pre-antral follicles present in the ovaries. It is a relevant marker of ovarian reserve and thought to be a predictor of ovarian response after stimulation.
Objective: To test if AMH and basal E2 levels are predictive markers of ovarian response and the treatment outcome in patients undergoing ICSI cycles.
Methods: Analyses of GnRH antagonist cycles over a period of 24 month in a single-center retrospective study. AMH levels were measured at the time of initial presentation. Basal E2 level were measured within the first 10 days of menstrual cycle. The number of mature/immature oocytes (MII/GV/MI) was determined after denudation and pronucleus (PN) formation was assessed between 16 – 20 hours after insemination.
Patient(s): 249 women with a mean age of 34.06 years undergoing antagonist cycle for ICSI treatment in our clinic were included.
Intervention: none
Main Outcome Measure(s): AMH and basal E2 levels, number of immature oocytes, PN formation, fertilization rate and pregnancy rate.
Result(s): AMH level was strongly correlated to the number of follicles ($r = 0.39$, $p < 0.001$), isolated oocytes ($r = 0.70$, $p < 0.001$), immature oocytes ($r = 0.27$, $p < 0.001$) multiple PN fomation ($r = 0.27$, $p < 0.001$). It also correlates with the pregnancy rates ($r = 0.21$, $p < 0.05$). Linear regression between AMH, basal E2 level and pregnancy rate revealed no stronger correlation. No correlation could be found between AMH level and fertilization rate.
Conclusions: AMH measurement predicts response to patients undergoing ovarian hyperstimulation for assisted reproduction in an antagonist protocol. Further a higher AMH level is also associated with a positive treatment outcome and is also related to other dynamic parameters determined during stimulation and embryo culture.

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Blastocyst vitrification and single embryo transfer: comparison study between day 5 and day 6

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Context: Vitrification is a highly efficient technique for the cryopreservation of human blastocysts; recently has almost replaced the slow freezing technique in IVF laboratory.
Objective: This study aims to test the utility of the Rapid-I closed system for blastocyst vitrification and assess the implantation and pregnancy rate following single blastocyst transfer (SBT) of warmed day5/day6 blastocysts.
Methods: The survival, pregnancy and implantation rate was compared for blastocysts vitrified on day 5/day 6 in 503 frozen SBT cycles. All good quality blastocyst were vitrified on day 5 or day 6 using Irvine Vitrification medium and Rapid-I (Vitrolife). After warming blastocysts were cultured for 2 hours before the transfer.
Patient(s): A three-year retrospective study was carried out.
Intervention(s): No differences between day5/day6 protocols.
Main Outcome Measure(s): High survival rates after warming were achieved for both day 5 and day 6 blastocyst. There was no significant difference in outcome following SBT of day5 vs. day 6 vitrified blastocyst.
Results: There was no significant difference in survival between the two groups: 92.2% (309/335) and 90.5% (152/168) respectively. 461 surviving blastocysts were transferred in 461 patients (all SBT). The implantation rate (fetal sac: IPR) and clinical pregnancy rate (fetal heart at 7 weeks: CPR) were 47.5% (219/461) and 37.5% (173/461) respectively. A higher IPR and CPR were achieved following transfer of day5 vs. day6 blastocysts: IPR 50.7% (170/335) vs. 41.6% (70/168) respectively and CPR 39.4% (132/335) vs. 31.5% (53/168) day5/day6. These differences were not statistically significant. *Conclusion(s)*: This study shows that vitrification and warming using a closed system (Rapid-I) followed by a single blastocyst transfer on day5 give similar outcome (IPR and CPR), compared to those transfer on day 6.

(OP07) Gynecological surgery: new options and possibilities

Analysis of ovarian cortex transplantation

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Context: More and more importance is given to the consequences of cancer, its treatment and quality of life after cancer. Radiation and certain chemotherapeutic agents have been shown to increase the risk of infertility in women. The gonadotoxicity is directly related to age, the therapeutic agent and the dose administered. In girls and women, strategies for fertility preservation (FP) include cryopreservation of ovarian tissue. This technique provides not only the preservation of fertility but also hormonal ovarian function.
Objective: Analyse the recovery of ovarian function after cortex transplantation.
Methods: Serum hormone levels (FSH, LH, estradiol, Anti-Müllerian hormone and inhibin B) were analyzed before and after the transplantation. We report an extensive ultrasound study of the ovarian cortex. We introduce the 3D ultrasound (US), Doppler, SonoAVC and HDlive technique to extend the assessment of ovarian function using techniques of advanced image reconstruction.
Patients: We have studied patients after ovarian cortex transplantation.
Intervention: An important follow up of the ovaries has been made using advanced ultrasound and hormone levels.
Main outcome measure: Ovulatory cycles were determined by vaginal ultrasound and serum hormone levels.
Results: With the information extracted from the ultrasound and hormone levels we have obtained important functional data of the ovarian cortex. The high-resolution images with the Doppler and calculation of volumes may add important information to the control of transplantation.
Conclusions: It seems that hormonal determinations are not sufficient to analyse ovarian tissue transplantation. The advanced ultrasound technology can help us to evaluate ovarian cortex transplantation. The hormone determination with advanced ultrasound technique could help to understand the physiology of the ovary.

Robotic-assisted apical lateral suspension for advanced pelvic organ prolapse: surgical technique and peri-operative outcomes

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Context: Abdominal sacral hystero/cervicopexy (ASC) is the gold standard for the treatment of apical prolapse, but requires advanced laparoscopic skills and exposes to potentially life-threatening complications. Lateral apical suspension to the abdominal wall with mesh is a feasible alternative di ASC where robotic assistance may offer specific advantages.
Objective: We here describe the surgical technique and the short-term outcomes of robotic-assisted lateral apical suspension (R-ALS) with the use of a titan-covered T-shaped mesh.
Methods: Patient(s): 40 consecutive patients with IIIrd or IVth stage symptomatic anterior and apical pelvic organ prolapse underwent R-ALS between September 2014 and September 2015.
Main Outcome Measure(s) and Result(s): R-ALS was completed without complications in all cases with a mean operative time of 117 $\pm$ 26 min. From a technical standpoint, robotic assistance allowed for an extremely reproducible technique, with a swift learning curve and consistent length of the surgical steps. The procedure was extremely well tolerated, and resulted in complete resolution of POP-associated symptoms and in improvements of POP- and incontinence-related quality of life scores (PQOL and IIQ7) at 1 month from surgery.
Conclusions: R-ALS is feasible, safe, well-tolerated and effective at a short-term follow-up. R-ALS may represent an effective and simple alternative to abdominal sacral hystero-cervicopexy for the treatment of high-grade apical and anterior POP, avoiding the challenges of sacral mesh fixation. Robotic assistance helps achieving optimally tailored anatomic reconstruction, allowing seamless deep pelvic dissection and suturing.

AMH reduction following ovarian cyst surgery does not seem to reduce fecundity in women

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Context: Ovarian cyst surgery is associated with a postoperative decrease of serum Anti- Müllerian Hormone (AMH) levels.
Objective: To investigate the impact of postoperative AMH decrease following ovarian cyst surgery on the chances to achieve pregnancy and live birth.

Methods: Prospective cohort study with two-year follow up. Serum AMH concentrations were determined pre- and postsurgery (6- and 24 months). Information regarding pregnancy wish and attempts to conceive were obtained by a questionnaire.
Patients: Sixty women of reproductive age (mean 31.8 years) undergoing ovarian surgery for benign cysts.
Intervention: Women had ovarian surgery by cystenucleation ($n = 50$), ovarian resection ($n = 3$) or fenestration/punction ($n = 7$). The cysts were dermoids ($n = 25$), endometriotic ($n = 20$) or follicle cysts/cystadenomas ($n = 15$).
Main Outcome Measure(s): Serum AMH concentrations and changes over time. Association of these changes with pregnancy rate and live birth rate.
Results: Baseline AMH levels decreased significantly in the whole group at six months, and further reduced at two years (2.7 μg/L to 2.0 μg/L to 1.1 μg/L, $p < 0.008$), percentage reduction 42.9%). Baseline AMH was correlated to female age ($p = 0.002$). Following surgery, 18 out of 36 women with a desire of children achieved pregnancy (50%) and live birth rate was 33%. The percentage change in AMH did not differ significantly between the groups (women who conceived vs. those who did not) at two years ($p = 0.117$).
Conclusion: Data reported herein indicate that the AMH decline after ovarian cyst surgery is still maintained two years after surgery. The data do not support that the postoperative AMH decrease following conservative ovarian cyst surgery may reduce the chances to achieve pregnancy.

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Reproductive surgery of uterovaginal anomalies

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Context: Primary infertility diagnosed in 16%, secondary infertility in 27%, pregnancy loss in 41%, abdominal pain in 37% patients with uterovaginal anomalies.
Objective: To optimize the surgical correction and reproductive outcomes for females with genital malformations.
Methods: Clinical investigations included general examination, karyotyping, ultrasonography, MRI, hormonal investigation.
Patients: 2025 females operated since 1992 to 2015: 1854 with uterovaginal anomalies; 171 – with disorders of sexual development.
Interventions: Surgical correction performed by laparoscopy and hysteroscopy, following hystological investigation.
Main Outcome Measures: Creation of neovagyna performed by laparoscopic perytoneal colpopoesis in 352 patients with utero-vaginal aplasia; laparoscopic removing of rudimentary horn in 245 cases; vagynoplasty in 240 adolescents with partial vaginal aplasia; hysteroscopic dissection of intrauterine septum in 445 patients. Cervicovaginal aplasia had 64 patients – hysterectomy of rudimental uterus performed in 45 cases, for 19 patients successfully created the neocervical canal with intrauterine stentation.
Results: More than 52% patients had concomitant infertile factors: tubal and peritoneal adhesions (34%), intrauterine synechia (7%), polycystic ovary and anovulation (19%), ovarian hypofunction (8%). The extra-genital endometriosis removed in 56%, deep infiltrative endometriosis in 23%, ovarian endometriosis in 6%, adenomyosis in 8%, recurrent endometriosis revealed in 12% cases.
Conclusion: The endometriosis was still the major cause of pain and infertility in 56% patients. The reconstructive surgical correction, assisted reproduction methods and pathogenetic rehabilitation appears to improve reproductive outcomes in 57% patients.

Robotic-assisted surgical repair of advanced female pelvic organ prolaspe (POP): long-term anatomical and functional outcomes

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Aim: To assess the long-term anatomical and functional outcomes of different robotic-assisted procedures in the management of advanced pelvic organ prolapse (POP): robotic-assisted abdominal sacrocolpopexy (RASC) for vaginal vault prolapse, supracervical robotic-assisted laparoscopic sacrocolpopexy (SRALS) and robotic-assisted lateral suspension (R-ALS).
Methods: A total of 78 women with symptomatic stages III and IV POP were evaluated from september 2013. 41 patients, with advanced anterior and apical prolapse, underwent R-ALS and 37 patients, with stages III or IV POP involving the apical, anterior and posterior defect, underwent RASC or SRALS (17 vaginal vault prolapse and 20 advanced uterus prolapse). The outcomes of interest of each type of surgical procedure included total operative duration, estimated blood loss, surgical length of stay POP-Q score change, quality of life questionnaire in pelvic floor distress and female sexual function index (FSFI). Follow-up were scheduled at 6 and 12 months.
Results: Complications were few and recurrences rare in short and medium-term follow-up. In R-ASC group complications were limited to mild port-site haematoma in 1 patient, which resolved spontaneously. In R-ALS group we did not have complications. In R-ASC group at 12 months follow-up only 3 women had evidence of a grade 2–3 cystocele recurrence and 1 patient had a grade 4 for vaginal vault prolapse recurrence. In R-ALS group only 1 patient had a grade 3–4 for apical prolapse recurrence and required reoperation. Almost all patients reported satisfactory functional results in the questionnaire.
Conclusions: Application of robotic assistance in the treatment of urogynaecological disorders continues to develop. RASC and R-ALS are safe and effective procedures for the treatment of advanced pelvic organ prolapse.

(OP08) Endometrium, dysfunctional uterine bleeding and contraception

Optimization of the treatment of adolescent girls with relapses of abnormal uterine bleeding

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Background: Abnormal uterine bleeding (AUB) among adolescents make up 10–37% of the children's gynecological morbidity in Russia. Relapse of AUB is a symptom of endometrial hyperplasia, which is caused by a progressive decrease in the ability of cells to apoptosis. Caspase-8 (Casp8) is an objective indicator to assess the activity of the effector phase of apoptosis. Reduced level of Casp8 is an evidence of a defect of apoptosis.
Objectives: Development of the forecast method of AUB relapses in adolescent and determination of further treatment strategy.
Materials and methods: Serum levels of caspase-8 were investigated by ELISA in 60 patients with AUB relapse and 20 healthy adolescents with regular menstrual cycles (control). In order to prevent a relapse of AUB and assess the impact of the Dienogest/Estradiol valerate (DNG/E2V) on the dynamics of serum levels of Casp8, we conducted a

comparative analysis of the effectiveness of the treatment of adolescents with AUB in 1, 3 and 6 months.
Results: Averages of Casp8 in patients with AUB were 3-fold lower ($p < 0.05$) than in healthy girls. This indicated a weak initiation of the effector phase of apoptosis. To predict relapse of AUB, we developed a method based on the determination of the level of Casp8 in the blood. Using the model «Classification and Regression Tree», we have found that with regular menstrual cycle, the level of Casp8 corresponds to values of>0.21 ng/mL. With a projected relapse of AUB this index is $\leq$0.21 ng/ml. An increase of serum Casp8 was indicated in 1 month of the DNG/E2V reception, but this index remained below the cutoff. The level of Casp8 was the higher cutoff in 3 months at 60% patients and in 6 months at 91% patients.
Conclusion: The results allow us to recommend the adolescent girls with AUB anti-relapse DNG/E2V therapy for 6 months at the level of Casp8$\leq$0.21 ng/ml.

Drospirenone-only oral contraceptive: results from a multicenter non-comparative trial of efficacy, safety and tolerability

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Context: POPs do not increase the risk of VTE, stroke, and myocardial infarction. POPs have been associated with poor cycle control and stringent missed pill rules.A novel Drospirenone (DRSP) only pill, was developed to improve tolerability and compliance.
Objective: This study was performed to assess the overall Pearl Index (PI) as the primary endpoint. PI after correction for additional contraception for sexual activity status, and cumulative pregnancy rate were secondary efficacy parameters. The study also provided information regarding its safety and cycle-control profile.
Methods:A prospective, multicenter, non-comparative study was conducted in healthy women at risk of pregnancy, aged 18 to 45 years. The study medication was DRSP 4.0 mg daily for 24 days followed by a placebo for 4 days for 13 28-day treatment cycles.
Intervention(s): Serum or urine pregnancy tests, assessment of vital signs and of general safety laboratory parameters, review of adverse events were performed during follow-up visits. Also, the subjects were asked to fill in an electronic diary starting at the screening visit. Evaluation of bleeding and spotting was based on the subject's daily diary. Acceptability was assessed by the subject and by the investigator
Result(s): A total of 713 participants with 7638 DRSP treatment cycles were analysed. The overall PI was 0.51 [95% CI 0.1053 – 1.4922]. The proportion of participants with any bleeding decreased from Cycle 1 to Cycle 13. Unscheduled bleeding decreased from Cycle 1 to Cycle 13. There were no reports of deep vein thrombosis, pulmonary embolism or hyperkalemia. Study drug acceptability was considered as ''excellent/good'' by over 82% of subjects
Conclusions: This new DRSP only oral contraceptive provides clinical contraceptive efficacy similar to that of the currently marketed COCs, with a good safety profile, and favorable cycle control.

Effect of long-term SPRM treatment on endometrium

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Context: Therapeutic strategies for uterine myomas includes treatment with selective progesterone receptor modulator (SPRM). Modulation of progesterone receptors in myoma leads to volume reduction. Chronic treatment with SPRM causes specific alteration in endometrial morphology. Mechanisms of SPRM effect on endometrium are still unclear.
Objective: The aim of the study is to examine an impact of chronic treatment with SPRM on expression of selected genes involved in the regulation of physiology of endometrium.
Methods: Endometrial gene expression was assessed on mRNA level by Real-Time PCR.
Patient(s): Endometrial samples were collected from 21 patients suffering from uterine fibroids that have been treated with SPRM for 3 months. Control endometrium was collected from 5 women in follicular phase of natural cycles.
Intervention(s): SPRM treatment was administered daily for 3 month. Samples of endometrium were obtained during minihysteroscopy.
Main Outcome Measure(s): Expression level of estrogen receptors (ESR1, ESR2), receptors for growth factors (VEGFR, TGFBR2, FLT1), enzymes responsible for hormone metabolism (HSD17B2), proteins responsible for the regulation of the tissue remodeling (TIMP2, RECK) and selected microRNAs (miR-182, miR-200b, miR-210).
Result(s): Endometrium derived from SPRM treated patients demonstrated statistically significant alteration in the level of HSD17B2.
Conclusions: Reduced expression of HSD17B2 seems to be important for the physiology of the endometrium. Expression alteration may affect local level of estradiol that is essential for phenotype of endometrial cells. Due to involvement of estradiol stimulation in pathophysiology of many gynecological diseases, the obtained results may be clinically relevant. Therefore, the mechanism of 17beta-hydroxysteroid dehydrogenase 2 activity dysregulation requires further explanation.

Women's preferences about menstrual bleeding frequency: results from the ISY 2 (Inconvenience due to women'S monthlY bleeding) Study

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Objectives: For many women, monthly bleeding is painful, inconvenient and affecting everyday life. To assess the level of inconvenience associated with monthly bleeding, determine how many women would prefer less frequent bleeding, and what would motivate this choice.
Method: From August 28th to September 29th 2015, a 15-minute quantitative online survey was conducted among 2.845 women from 18 to 45 years old in six European countries (Czech Republic, Germany, Hungary, Latvia, the Netherlands, and Portugal). Among the participants, 1.420 used a combined hormonal contraceptive (Group A) and 1.425 a non-hormonal contraceptive (excluding copper intrauterine devices) or no contraceptive (Group B). The relationship between the participant's profile, the contraceptive used, the menstrual period

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pattern and the preferred bleeding frequency was investigated. Each participant gave written informed consent.
Results: Age, education, and number of previous pregnancies were the only significant differences between the two groups. The menstrual period was significantly longer (5.1 days vs. 4.6 days), heavier (14% heavy menstrual flow vs. 7%), and with more symptoms (5.7 vs. 5.0) in Group B than in Group A ($p < 0.005$). Pelvic pain, mood swing, and irritability were reported in more than half of the women in each group. Given the choice, 66% of women in Group A and 60% in Group B would opt for longer intervals between periods. Lifestyle reasons, such as sexuality, social life, work and sporting activities, were key factors for this decision.
Conclusions: This survey showed that the majority of women want less than once monthly menstrual periods, with a frequency ranging from once every three months to no periods at all. This can be explained by the desire to avoiding the unpleasant aspects of menstruation and its negative impact on private and professional life.

Myofibroblasts as a key component in the basal endometrium of adenomyosis and superficial endometriosis

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Context: Ectopic endometrial glands and stromal cells characterize the diagnosis of endometriosis (EM) and adenomyosis (AM). Stromal cells in EM express markers of smooth muscles (SMCs) which point to their transformation into myofibroblasts/EM-associated SMCs. Myofibroblasts are transformed fibroblasts acquiring contractile phenotype to be mobile and play a role during tissue repair.
Objective: Are myofibroblasts an integral component of AM-uteri and EM lesions?
Methods: Immunohistochemistry, immunofluroscence for ASMA, Desmin, Viementin, Collagen I and Calponin and Transmission electron microscopy (TEM).
Patients: AM- and control-uteri ($n = 18/14$), superficial peritoneal EM (SPEM) and healthy peritoneum ($n = 23/10$), Rectus abdominis EM and primary culture of endometrial stromal cells.
Main Outcome Measures: Immunoreactive score, TEM analysis, immunofluroscence reaction
Results: Stromal cells in Junctional zone (JZ)-AM expressed ASMA and collagen I while Desmin and Calponin lacked. Stromal cells in control group lacked ASMA, Desmin and Calponin expression. Stromal cells of SPEM glands expressed more ASMA and Calponin centrally than at the periphery and the reverse was true for collagen I with few expressing Desmin. Healthy peritoneum lacked ASMA, Calponin and Desmin expression with lower collagen I expression than in SPEM. Stromal cells in Rectus abdominis EM expressed ASMA and collagen. Myofibroblasts ultrastructure was seen by TEM in SPEM and in stromal cells of JZ-AM. Stromal cells in-vitro expressed Vimentin while only 5–8% expressed ASMA and collagen I. Desmin expression lacked.
Conclusion: Myofibroblasts in the JZ of AM-uteri supports microtrauma at JZ. Their arrangement in SPEM supports two phenotypes; contractile at the center and secretory at the periphery. And this might necessitate the inclusion of myofibroblasts in the diagnosis of EM lesions.

Do progestogens outweigh combined oral contraceptive pills in the management of dysfunctional uterine bleeding during adolescence? A 10-year old experience of a Pediatric-Adolescent Gynecology Division

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Context–Objective: The aim of this study is to assess the effectiveness between progestogens (P) and Combined Oral Contraceptives (COCs) in the management of adolescents with Dysfunctional Uterine Bleeding (DUB) due to anovulation.
Methods–Patient(s)–Intervention(s): Retrospective study of girls, presented between 3/2004 and 3/2014, due to DUB. Medical history was taken, clinical examination, laboratory investigations and ultrasound scan of uterus-ovaries were performed in all adolescents. All girls were treated either with cyclical P or COCs and followed up every 6 months until the end of treatment.
Main Outcome Measure(s)–Result(s): 112 adolescents diagnosed with DUB included in our study. Mean age at menarche, at first attendance and mean Body Mass Index were 12.04 ± 1.63 years, 13.46 ± 3.07 years and 20.65 ± 5.74 kg/m^2 respectively. In 13 adolescents hospitalization was needed. These girls had tried unsuccessfully P for 11 days in their menstrual cycle and finally needed to receive COCs every 6 hours until bleeding stopped, gradually decreased to 1 daily for at least 6 months (mean treatment interval 1.24 years). Among the rest 99, in 37 with mild increase of menstruation ($\leq$10 days) and Hb$>$12 g/dl, P for 11 days in every menstrual cycle settled DUB in all girls. In the rest 62 with moderate increase of menstruation followed by metrorrhagia and/or Hb$<$10 g/dl, only in 24 cyclical P settled the menstrual cycle. In the rest, COCs were needed twice daily until bleeding stopped, gradually decreased to 1 daily for at least 6 months (mean treatment interval 1.57 years).
Conclusions: COCs outweigh cyclical P ($p < 0.01$) in girls with severe DUB, who need hospitalization and in those with moderate increase of menstruation followed by metrorrhagia ($p < 0.05$). On the other hand, cyclical P outweigh COCs in adolescents with DUB and mild increase of menstruation and Hb$>$12 g/dl ($p < 0.05$).

Why endometrial bleeding disorders should be expected in progestin only contraceptive users

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Context–Objective: Understand physiopathology of bleeding disorders to take reasonable therapeutically actions avoiding withdrawals
Methods: Review of the literature.
Patient(s): Progestin only contraceptive (POC) users.
Main Outcome Measure(s): Laboratory test results
Result(s): Cervical mucus blockage and ovulation inhibition are the main mechanisms of action of POCs. Follicle development is not completely avoided. Ovarian estrogen is erratically secreted. Permanent liberation of the hormones from the devices or daily intake will not allow for the orderly action over the endometrium. Daily plasmatic level of the progestin is variable, within and between users. This variability alters the growth and development of normal

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structures, including blood vessel formation. Balance between vascular and nonvascular elements is lost due to the differential effect of the progestins over endothelial growth factors (VEGF). Vascular function is altered (changes in permeability and dilatation). Changes in the vascular structural integrity (strong spiral arteries are absent) result in the development of a vascular plexus of fragile, dilated, leaking vessels. Normal inflammatory cells and mediators are modified, as well as proteolytic enzymes (MMP) and their tissue inhibitors (TIMPs), influencing the strength of the stroma. The presence of leukocyte types and immune cells, a range of different inflammatory mediators, proteolytic enzymes, eicosanoids, and growing factors (tissue and vascular), all altered under the effect of the contraceptive regime.
Conclusions: incomplete blockage of ovarian activity by the exogenous progestin will allow erratic follicular development and hormonal secretion. No sequential order of the natural ovarian sex hormones will alter the normal growth of the endometrial stroma, epithelium and endothelium, resulting in a fragile, leaking vasculature.

Taking charge of dysmenorrhea

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Dysmenorrhea is a pelvic pain starting at the same time as, the menses, also known as menorrhagia. A Dysmenorrhea can be essential, or organic. It is frequently qualified as Primary ie. beginning in adolescence with the onset of the ovulatory cycle, or Secondary, if associated with pelvic pathologies, usually beginning after 20 years of age. The physiopathology based on the prostaglandins activity will be treated. The frequency of this pathology is difficult to be evaluated. This affection is often founded in the family history of the patients. The incidence increases with an high tobacco consumption. Some authors have shown that 50% of women suffer from primary amenorrhea. This pathology should be considered as a public health problem. Another problem is disability, amongst 10% of those 50% are disabled. 70% are teenagers. An American study has shown that this leads to 600 million work-hours lost per year. In the case of organic etiology, endometriosis is the 1st cause, after a followed by genital infection or a uterine malformation. The different treatments will be exposed set out: Progestins, COC, SIU, AINS and the specific etiology treatments.

Attitudes and knowledge of HCPs from 4 Latin American countries regarding intrauterine contraception for parous and nulligravidas women

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Objective: To assess attitudes and knowledge about intrauterine contraceptives (IUC) for nulligravida women among 400 HCPs from 4 LA countries.
Methods: A survey was conducted online and answers from 100 Mexican, 100 Argentinian, 100 Brazilian and 70 Colombian Ob-Gyns and 30 Colombian GPs were analysed
Results: 50–64% and 16–35% had office based and hospital-based practice, attending from 20 to 200 patients on contraception/day. 24–45%, 33–38% and 17–40% had 1–10 years; 11–20 and more than 20 years of experience. 76–90% inserted IUC by themselves as well as trained and supervised insertion by other HCPs. 32–71%, 19–25%, 5–10% and 2–10% inserted 1–5; 6–10; 11–15 and 15–20 IUC/month. The main drivers and barriers for IUC in parous were very similar, with different priorities, being more relevant the concerns on PID and infertility in nulligravidas than in parous. Only 9–18% considered IUC when counselling on contraception to nulligravidas <18 years old and 28–66% 18–29 years old, versus 33–62% and 67–82% when counseling parous women of similar ages. On user request, only 15–32% of HCPs placed IUCs in nulligravidas <18 years old and 49–67% in 18–29 years old, versus 41–65% and 74–82% of parous of similar ages. About the risk of PID, 6–10% considered much higher and 58–66% a little higher in nulligravidas than in parous. Regarding difficulty and pain on insertion, 47–76% considered a little bit more difficult, 57–75% considered a little more pain and 12–16% much more pain when inserting an IUC in nulligravidas vs. parous. About perforation and expulsion: 29–48% and 17–54% consider a little higher and 3–7% and 3–8% much higher risks of perforation and expulsion in nulligravidas vs. parous
Conclusion: Misperceptions about IUC for nulligravidas and parous are widespread in LA HCPs, even between Ob-Gyns. These miscerceptions are more notorious related to nulligravidas women

Expression of matrix metalproteinase 9 and cyclin d1 in hyperplasia of endometrium of women of reproductive age

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Research Objective: assessment of expression of matrix metalproteinase 9 (MMP-9) and cyclin D1 in hyperplasia of endometrium of women of reproductive age.
Materials and methods: 107 women of reproductive age have been examined; among them 41 patients with simple hyperplasia of endometrium (HE), 30 patients with complicated hyperplasia of endometrium and 36 women without pathology. Immune histochemical research of expression of matrix metalproteinase 9 (MMP-9) and cyclin D1 was carried out.
Results: At complicated HE the tendency to increase in expression of MMP-9 in comparison with simple HE was revealed (3.8 $\pm$ 0.7 and 3.5 $\pm$ 0.9 points respectively), without reliable distinctions at recidivous HE ($p>0.05$). Increase of cyclin D1 expression in comparison with endometriun of proliferation stage is revealed (3.8 $\pm$ 0.6 and 2.2 $\pm$ 0.9 points, respectively, $p<0.05$). The expression made 3.6 $\pm$ 0.5 and 4.1 $\pm$ 0.2 points at simple and complicated HE respectively, at recidivous HE 4.1 $\pm$ 1.1 points.
Conclusions: molecular and biological processes of tissue remodeling in hyperplasia of endometrium are characterized by the increase in activity of MMP-9 and cyclin D1 that leads to violation of processes of growth, differentiation and death of cages of mucous uterus body. Expression of MMP-9 reflects severity of HE, and expression of cyclin D1- recurring of the process.

Regulation of PTEN, AMPK and PI3K pathways in Sprague-Dawley rats with insulin resistance and endometrial hyperplasia

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Context: Epidemiologic and genetic evidence links between insulin resistance and endometrial cancer. Endometrial atypical hyperplasia is a precancerous stage of endometrial cancer.

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Objective: To evaluate in rat animal model whether insulin resistance (IR) and endometrial hyperplasia (EH) affect the expression of tumor-suppressor phosphatase and tensin homologue (PTEN) and AMP-activated protein kinase (AMPK) and phosphoinositide 3-kinase (PI3K) signaling pathways.
Methods: Female Sprague-Dawley (SD) rats were fed on a high-fat diet (HFD) and administered high-dose 17β-estradiol (E2) to establish an IR and EH model. Uteri biopsies were HE stained and the expression of proteins were evaluated by immunostaining and immunoblotting.
Animals: 45 female SD rats (8 weeks old) were included.
Interventions: Rats were randomly divided into 5 groups ($n = 9$ for each group) of Control (C), standard diet (StD) and ovariectomy (OVX) (NO), StD and E2 (NE), HFD and OVX (FO), HFD and E2 (FE). Following 48 weeks of feeding, rats were subjected to OVX (except group C). NE and FE groups were administered E2 for 4 weeks.
Main Outcome Measures: The degree of insulin resistance and hyperplasia of endometrium. The protein expression of estrogen receptor (ER), progesterone receptor (PR), PTEN, AMPK, p-AMPKα, PI3K 85α, AKT, p-AKT in endometrium.
Results: Squamous intraepithelial metaplasia were appeared in endometria of NE and FE groups. The Endometria of all groups were ER and PR positive. Compared with other groups, PTEN and p-AMPK was significantly down-regulated in FE group, but PI3K 85α and p-AKT were significantly up-regulated.
Conclusions: Insulin resistance induced by feeding rats with a high-fat diet is associated with endometrial cell metabolism that including the loss of PTEN protein and the activation of AMPK and PI3K signaling networks in endometrial hyperplasia even in endometrial cancer.

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Role of Toll-like receptors 2, 4, 9 in the endometrium in chronic endometritis

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Context: The first line of defense against infection are the effectors of congenital immunity due to the formation of local inflammatory makes reactions with subsequent reparation of damaged tissues. One of the main role in this process is played by TLR. TLR2 is the highest specificity. TLR4 recognizes the patterns of the microorganisms and the host fibronectin. TLR9 recognizes demetilirovanie repeats CpG DNA of bacteria, viruses and owner's immunoglobulin G.
Objective: To study the expression of TLRs 2, 4, 9 in the endometrium in chronic endometritis (CE).
Patients and Interventions: The investigation included 60 reproductive-aged patients. All the patients underwent morphological and microbiological examinations of endometrial biopsy specimens. The expression of TLRs 2, 4, 9 was investigated by immunohistochemistry. The patients were divided into 2 groups: 45 women with morphologically verified CE and 15 apparently healthy women (proliferative-phase endometrium).
Results: Group 1 showed a significant increase in the expression of TLRs in all structure of the endometrium primary in epithelian cells as compared to Group 2 ($p < 0.05$). Comparative analysis revealed no statistical difference in TLR expression in the women with CE in the presence and absence of infective agents in their endometrial biopsy specimens.
Conclusion: Investigation of the expression of TLRs 2, 4, 9 in the endometrium has allowed to specify the fact that the following is necessary to prevent chronization of inflammation the endometrium: to rapidly eliminate the pathogen, to prevent its persistence, to restore the normal architectonics of the uterine mucosa, and to suppress TLR overexpression predisposing to the creation of the vicious pathogenetic circle.

Insulin modulates in vitro decidualization of human endometrial stromal cells via transcriptional inhibition of Forkhead box protein O1 (FOXO1)

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Context: Polycystic ovary syndrome and obesity are associated with insulin resistance, hyperinsulinemia and reduced fertility. However, the information on the possible effect of insulin on the decidualization, differentiation of endometrial stromal cells is scarce.
Objective: The aim was to investigate the effect of insulin on the regulation of FoxO1, one of the most important transcription factors during decidualization.
Patient(s): Endometrial biopsies were taken from six healthy, regularly menstruating women.
Methods: Endometrial stromal cells were isolated and decidualized *in vitro*. mRNA levels of putative FoxO1 target genes were measured with Real-Time PCR following FoxO1 inhibition or insulin treatment. PI3K inhibition was used to identify the possible mechanism behind regulation. Subcellular localization of FoxO1 was analyzed with immunofluorescence.
Main Outcome Measure(s): mRNA expressions of six putative FoxO1 target genes were measured.
Result(s): All the genes were evaluated as FoxO1 target genes in decidualizing stromal cells. Insulin modulated the decidualization process by significant alteration of gene expressions of these genes. Insulin regulated FoxO1 target genes by transcriptional inactivation and nuclear export of FoxO1 via PI3K pathway. Insulin did not inhibit the morphological transformation of endometrial stromal cells via transcriptional inactivation of FoxO1.
Conclusions: This study provides new insights on the action of insulin on endometrial function via regulation of FoxO1. In hyperinsulinemia dysregulation of a high number of FoxO1 controlled genes may contribute to menstrual disturbances, decreased fertility or pregnancy complications. Our findings may illuminate possible reasons to unexplained infertility.

(OP09) Pre-gestational, gestational and intrapartum management of risks pregnancy

Experimental study of fetal metabolic programming induced by maternal obesity

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Context: Maternal obesity during pregnancy is associated with increased metabolic risks, including proinflammatory and lipid peroxidation state and hormonal imbalance. Besides them, it has long-term consequences for the offspring, metabolic programming appearing during early life with major physiopathological impact.
Objective: To prove that maternal obesity has metabolic impact not only on the fetus, but also later in the adult life studying diet-induced obesity in female rats.

Methods: Using an animal model, we showed that maternal obesity induces fetal inflammation resulting in accelerated adipogenesis in the offspring of rats. We studied the possibility of metabolic reprogramming by submitting obese rat females to interventional therapies like changes and anti-inflammatory supplements.
Patients: Female Wistar rats with high-calorie/high-fat diet induced obesity, divided in 5 groups, depending on the supplements received and the diet modifications. Lipid peroxidation was estimated through malonyldialdehyde and total thiols value while the antioxidant status through glutathione value on fetal liver, pancreatic and placental fhomogenates. These organs have been also histopathologally analyzed. The adipokine secretion was estimated from maternal blood through leptine and adiponectin values.
Main Outcome Measures: We established associations between maternal diet and fetal-placental metabolic status.
Results: Maternal overnutrition caused fetal organ dysfunctions and altered metabolic status, predisposing the offsping to childhood and later adult obesity, through a chronic low grade inflammation status, which has been given the description of metainflammation.
Conclusions: Fetal exposure to maternal metainflammation is a mediator for programming insulin tissue resistance in the fetus with metabolic phenotype manifestations in adult life.

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Monochorionic diamniotic twin pregnancy with a discordance in Pena-Shokeir Type I phenotype.

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Context: Pena-Shokeir syndrome is a rare, early lethal disorder with an estimated incidence of 1:12.000. The fetal akinesia/hypokinesia sequence is characterized by multiple joint contractures, facial anomalies and pulmonary hypoplasia. The common feature of this sequence is decreased fetal activity.
Objective and *Methods*: We here report the first case of discordant Pena-Shokeir phenotype observed in monochorionic diamniotic twins.
Patient: A 41-year-old woman, pregnant with twins, was referrend at 12 weeks' gestation because the combined test was altered. Serial ultrasonographic examination suggested that twin A may have had arthrogryposis, micrognathia, kyphoscoliosis, fixed flexion of the limbs, polyhydramnios, myocardial ventricular hypertrophy, lack of visualization of the stomach, pulmonary hypoplasia, decreased movements, low-set ear, hypertelorism and rocker-bottom feet with a 10% restriction of growth. Twin B showed normal growth, no structural abnormalities, but a severe oligohydramnios.
Interventions: At 31 weeks of gestation a selective reduction of twin A was performed. At 32 weeks of gestation, the twins were delivered by cesarean section. Autopsy findings of twin A were consistent with the diagnosis of Pena-Shokeir phenotype.
Results: Fetus B had an Apgar index of 7–9. Fetus A presented severe thanatological alterations and all the phenotypic characteristics of the Pena-Shokeir syndrome. Assessment of organs revealed hypoplastic lungs and cryptorchidism. Microscopically iliopsoas muscle was characterized by fibrosis with fatty infiltration, lungs showed borderline hypoplasia and testis showed atrophy of testicular tubules, fibrosis and hypertrophy of Leydig-cells.
Conclusions: We suggest that cerebral injury during early gestation is a possible cause for the occurrence of the Pena–Shokeir phenotype through an anoxic-ischemic mechanism.

Medical prevention of preterm birth

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Context: Preterm birth (PTB) is associated with poor quality of life of preterm babies and economic costs. The risk of PTB is ~30% in women with the history of PTB, and ~25% in women with cervix ≤25 mm.
Objective: To determine if vaginal progesterone (Utrogestan®) reduces risk of preterm birth and associated neonatal complications in women with asymptomatic sonographic short cervix in the mid-trimester or a history of preterm birth.
Study design: International multi-center open-label study on the effectiveness of vaginal progesterone in the prevention of PTB (III phase) in "asymptomatic" singleton pregnant women with sonographic short cervix (10–25 mm) at 18–23 6/7 weeks' gestation and/or with a history PTB.
Patients: 220 patients aged 20–42 years (median 30.0) were distributed equally: 110 with a sonographic short cervix (group 1) and 110 with history of PTB (group 2). Gestational age at enrollment 21.15±1.6 weeks. The average number of pregnancies 2.64±1.74. Intervention: Utrogestan® was prescribed vaginally daily, from 18–23 weeks 6/7 to 33 6/7 weeks or amniotic fluid discharge or childbirth – which event occurs first.
Results: The PTB relative risk in group 1 compared to similar population risk was 0.22 (95% CI 0.1–0.48), RR reduction 0.8 (95% CI 0.52–0.9), OR 0.17 (95% CI 0.07–0.40, $p < 0.003$). NNT= 5 (95% CI 4–8). The relative risk of PTB in group 2 compared to similar population risk was 0.22 (95% CI 0.1–0.48, $p < 0.0028$.), RR reduction was 0.78 (95% CI 0.52–0.9), OR 0.17 (95% CI 0.08–0.40). NNT=5 (95% CI 4–8). The incidence of neonatal mortality and morbidity also decreased due to PTB rate reduction in both groups.
Conclusions: Utrogestan® in pregnant women with asymptomatic sonographic short cervix in the mid-trimester and/or history of PTB significantly reduces the incidence of preterm birth and, respectively, neonatal morbidity

Serum 25-hydroxyvitamin D levels in pregnancies complicated with preterm labour

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Objective: To measure serum 25-hydroxyvitamin D [25(OH)D] and C-reactive protein (CRP) levels and leukocytes in gestations complicated with preterm labour (PL).
Methods: Circulating serum 25(OH)D and CRP levels and leukocytes were measured in singleton pregnancies complicated with PL ($n = 59$) before tocolytic treatment and compared to controls without PL matched for gestational age ($n = 64$). Additionally, comparisons were also made in accordance to outcome of PL cases.
Results: Mean serum 25(OH)D levels were similar between cases and controls (25.8 ± 11.7 vs. 25.0 ± 10.8 ng/mL, respectively), while median white blood cell count and CRP levels were significantly higher in women with PL (11.1 [4.3] vs. 9.4 [2.8] x 10○6/mL; and 0.4 [0.7] vs. 0.3 [0.4] microg/mL, $p < 0.05$, respectively). PL cases delivering preterm

displayed shorter mean cervical lengths, higher median serum CRP levels (0.8 [1.2] vs. 0.4 [0.3], $p = 0.003$), and lower mean serum 25(OH)D levels (22.6 ± 12.4 vs. 29.1 ± 10.2, respectively, $p = 0.03$) as compared to those cases delivering at term. Two multiple linear regression models were analyzed to determine factors relating to gestational age at delivery (pooled analysis and only those with PL). In both models gestational age positively correlated to cervical length and inversely to CRP levels; whereas, in the PL model, only 25(OH)D levels correlated positively with gestational age.

Conclusion: Women complicated with PL showed similar serum 25(OH)D yet higher CRP levels. PL cases delivering preterm displayed lower 25(OH)D levels and higher CRP levels.

The current investigation was supported by the grant PI-0487/2011 from the "Fundación Pública Andaluza Progreso y Salud" for Financiation of Biomedical Research in Health Sciences in Andalusie.

An early-customized low glycaemic-index (GI) diet prevents both the gestational diabetes mellitus (GDM) and the large for gestational age (LGA) babies occurrence in overweight/obese pregnant women

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Context: The current clinical practice of providing lifestyle advices to overweight/obese pregnant women is not sufficient to reduce the GDM occurrence and other pregnancy complications.

Objective: To determine whether a detailed prescription of a behavioural program and a close follow-up prevents GDM and other adverse pregnancy outcomes through a better adherence to the healthier lifestyle.

Methods: Prospective, open-label, RCT. Follow-up was at 18, 24, 30 and 35 weeks. At enrollment and at 35 weeks, Food frequency Questionnaire (FFQ) was filled-in.

Patients: Between the 9 and 12th week, 238 women with BMI≥25 were enrolled. Forty-seven refused to participate.

Interventions: Intervention (I=96: 1800 Kcal/day + 30 minutes/day of physical activity-PA) or Controls (C=95: leaflet of lifestyle advices on diet and PA).

Main Outcome Measures: GDM and LGA occurrence.

Results: Miscarriages occurred in 6.8%, dropout in 24.6%, leaving 131 women. Both GDM (I:13, 18.8% vs. C: 23, 37.1%; $p = 0.019$) and LGA (I: 1, 1.4% vs. C: 7, 11.3%; $p = 0.019$) were lower in the I group. At logistic regression analysis, GDM was explained by both group allocation (OR = 3.9, CI 95%: 1.1–14.4) and lower BMI (OR = 2.6, CI 95%: 1.1–6.4), after correcting for the confounders. Pregnancy induced hypertension (2, 2.9% vs. 13, 21%; $p = 0.001$) and preterm birth (0 vs. 5, 8.1%; $p = 0.016$) were lower in I group. According to FFQ, I showed more adherence (40, 57.9%) respect with C group (24, 38.7%; p:0.028). Significant changes in the consumption of each investigated food were observed only in I group. Small for gestational age newborns were equally distributed. I group showed fewer interventions at parturition.

Conclusions: A customized low-GI diet started early in pregnancy in such at risk population increases the adherence to the behavioural program, thus reduces GDM, LGA babies occurrence and other adverse pregnancy outcomes.

Advantage for labor induction with oral prostaglandin-E1 treatment compared to vaginal prostaglandin-E2 gel in primiparous women and women with an unripe cervix

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Objective: To compare labor induction with oral prostaglandin-E1 treatment to vaginal prostaglandin-E2 gel in primiparous women and women with an unripe cervix.

Methods: The WHO International Classification of Diseases (ICD)-10 diagnoses and the obstetric records for all women who had labor induced with oral prostaglandin-E1 treatment ($n = 265$) or vaginal prostaglandin-E2 gel ($n = 252$) at the Department of Womeńs and Childreńs Health, Karolinska University Hospital, Solna, Sweden during 2012 and 2013 were examined.

Results: In primiparous women, oral prostaglandin-E1 resulted in vaginal birth within 24 hours in 40.2% compared to 41.4% with vaginal prostaglandin-E2 ($p < 0.001$), whereas cesarean section was necessitated in 25.0% compared to 41.4% ($p < 0.001$). In women with Bishop score 0–2, oral prostaglandin-E1 resulted in vaginal birth within 24 hours in 42.7% compared to 46.1% with vaginal prostaglandin-E2 ($p < 0.001$), and cesarean section in 27.3% compared to 38.2% ($p < 0.001$). The induction to vaginal delivery interval was 3–5 hours longer with oral prostaglandin-E1. The rates of obstetric bleeding >1000 mL, chorioamnionitis, uterine hyperstimulation and neonatal Apgar score < 7 at 5 min were comparable with the two methods ($p > 0.05$).

Conclusions: Oral prostaglandin-E1 treatment was less efficacious than vaginal prostaglandin-E2 gel in achieving vaginal birth within 24 hours in primiparous women and women with an unripe cervix, and resulted in a 3–5 hours longer induction to vaginal delivery interval. However, oral prostaglandin-E1 was advantageous in terms of safety compared to vaginal prostaglandin-E2 gel in these subgroups, since this method resulted in fewer CS.

Thyroid hormone function in pregnant women with polycystic ovary syndrome treated with metformin or placebo

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Context: Polycystic ovary syndrome (PCOS) and hypothyroidism are related conditions which both are associated with adverse pregnancy outcome. Little is known about thyroid hormone function and the possible influence of metformin on thyroid hormone levels in pregnant women with PCOS.

Objective: To investigate the prevalence of overt and subclinical hypothyroidism and the effect of metformin on serum levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT4) during pregnancy in women with PCOS.

Methods: A *Aim*: analysis of thyroid hormone status in women with PCOS, randomized to metformin or placebo during pregnancy. These women participated in two randomized controlled studies.

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Patients: Two-hundred eighty-seven women with PCOS, aged 18–42 years and singleton pregnancies.
Intervention: Metformin 850–1000 mg twice daily or placebo.
Main Outcome Measures: The prevalence of overt and subclinical hypothyroidism and serum levels of TSH and FT4 at each trimester.
Results: The overall prevalence of overt and subclinical hypothyroidism in the first trimester was 1.5% and 8.6% respectively. Among non-levothyroxine-treated patients, the mean level of TSH during pregnancy was comparable between metformin and placebo groups, whereas the mean level of FT4 in the 2nd and 3rd trimester was significantly higher (but within the normal range) in the metformin group compared to placebo ($p < 0.001$, $p < 0.05$, respectively). Among the 15 patients on levothyroxine treatment, the mean level of FT4 in the 3rd trimester was significantly higher in the metformin group compared to placebo ($p < 0.05$).
Conclusions: Subclinical hypothyroidism was highly prevalent among pregnant women with PCOS in the present study. This should be taken into consideration when managing this patient group in early pregnancy. The clinical significance of higher levels of FT4 in the metformin group needs to be further investigated.

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Estetrols' potential for neuroprotection following the injury to the developing brain: preclinical studies

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Context: Hypoxic-Ischemic encephalopathy (HIE) remains a major cause of perinatal brain injury. The brain rapidly increases in size, shape and complexity during the second and third trimesters. A sentinel event in late pregnancy or the intrapartum period may have an acute profound effect on a previously neurologically intact fetus, leading to the development of (HIE). The nature of the deficits is dependent on the gestational age and severity of the insult, though it is seldom reported in preterm infants. Studies in animal models of HIE may provide important information for the development of treatment for this pathological condition. Estetrol (E4) is a recently described estrogen with four hydroxyl-groups that is synthesized exclusively during pregnancy by the human fetal liver.
Objective: In this study, we evaluated E4's neuroprotective and therapeutic potency in neonatal (*in vivo*) HIE model of the immature 7-day-old newborn rat.
Methods: Rat pups body temperatures were examined along with their body and brain weights. Brains were studied at the level of the hippocampus and cortex. Intact cell counting and expressions of markers for neuronal early grey matter damage (microtubule-associated protein-2 (MAP-2)), neurogenesis (doublecortin (DCX)) and angiogenesis (vascular-endothelial growth factor (VEGF)) were evaluated by histo- and immunohistochemistry. The serum levels of two markers of brain damage (S100B and glial fibrillary acidic protein (GFAP)) were measured by ELISA.
Results: Our results demonstrate that E4 has a significant neuroprotective and therapeutic effects. Estetrol decreases the early gray matter loss, and promotes neuro- and angiogenesis *in vivo*. Estetrol treatment has no effects on body weight, brain weight or body temperature.
Conclusion: Taken together, E4 might become an important safe and physiological substance to treat neonatal HIE.

The mutual effect of pregestational BMI, maternal hyperglycemia and gestational weight gain on pregnancy outcomes

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Context: Obesity, gestational diabetes (GDM) and gestational weight gain (GWG) are well known risk factors for adverse pregnancy outcomes.
Objective: To investigate the mutual effect of the above mentioned on adverse pregnancy outcomes: large for gestational age, primary cesarean section and composite outcome of both.
Methods: Charts of patients who delivered in our hospital between 6/2001–6/2006 were reviewed. Maternal hyperglycemia categories were defined as: normal GCT, abnormal GCT, Impaired glucose tolerance-one abnormal OGTT value and GDM; Adequacy of GWG was calculated according to the 2009 IOM guidelines for each pregestational BMI category.
Patients: Singleton, live births above 24 weeks of gestation were included.
Interventions: None.
Main Outcome Measures: Univariate and multivariate logistic regression was used to assess pregnancy outcomes.
Results: 8595 women were included. Frequency of composite outcome increased with increasing BMI, increasing hyperglycemia and above recommended GWG. In the multivariate logistic regression analysis, there was a gradual significant increase in the odds for composite outcome with higher pregestational BMI (compared to normal BMI in overweight women OR = 1.23, (95%CI 1.06–1.44), in obese OR = 1.86 (1.51–2.31) and in severe obesity OR = 2.97 (2.15–4.11); With higher degrees of maternal hyperglycemia: compared to normoglycemia, abnormal glucose challenge test OR = 1.46 (1.20–1.79), impaired glucose tolerance OR = 1.65 (1.14–2.4) and GDM OR = 1.56 (1.16–2.10); and in women with GWG above recommended OR = 1.58, (1.37–1.81).
Conclusions: Higher pregestational BMI, maternal hyperglycemia and above recommended GWG independently contribute to adverse pregnancy outcomes. Furthermore, there is mutual effect between these factors and adverse outcomes. Appropriate pregestational weight and adequate GWG might reduce risk for adverse pregnancy outcomes.

(OP10) Premature Ovarian Failure

Insulin sensitivity in women with 46,XX spontaneous primary ovarian insufficiency (POI)

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Objective: to assess the insulin sensitivity in 46, XX karyotype women with primary ovarian insufficiency.
Methods: Anthropometric measurements, FSH, estradiol, thyroid hormones (TSH, fT4), antithyroid antibodies, fasting glucose and insulin, model for insulin resistance (HOMAIR), glucose and insulin at 60′ and 120′ of OGTT were collected. Study group consist of 98 patients aged between 18 and 39 with spontaneous POI and 75 healthy controls at the same age range. Retrospective study of patients hospitalized in Department of Gyneacological Endocrinology bewteen 2012 and 2015. The laboratory parameters were measured using Enzyme Linked Fluorescent Assay technique. Serum anti-TPO and antiTG levels were measured by electrochemiluminescent assay.

Results: For the 98 patients with 46, XX karyotype, presenting with POI, the mean age at diagnosis was 30 ± 6.3 years. The mean body mass index was not significantly compared to control group (23.5 ± 2.8 vs. 23.2 ± 2.5 kg/m^2). Thyroid autoimmune disease was associated with POI in 33 *Patients*: 1– Graves' disease and 32 (32.7%) – Hashimoto's thyroiditis.
Hyperinsulinemia was noted in 21.4% of the POI group. Only 4 patients revealed abnormal glucose tolerance and 4 – impaired fasting glucose. Not significant difference was also observed in HOMAIR between the study and control groups (1.45± 0.8 vs. 1.31± 0.6). Statistical analysis of subgroups: POI and autoimmune thyroiditis (APS-3) and POI without thyroiditis showed hyperinsulinemia after 1 hour of OGTT; 78.5 ± 76.5 vs. 52.9 ± 6.0 IU/ml, $p < 0.05$. Similarly, statistically significant differences were obtained in the subgroup POI and autoimmune thyroiditis vs. the control group (48.0 ± 26.6 IU/ml; $p < 0.05$).
Conclusions: Autoimmune thyroiditis encourages to a higher incidence of hyperinsulinemia and metabolic disorders in women with POI. HOMAIR does not correspond with hyperinsulinemia in POI patients.

Androgen levels in women with spontaneous primary ovarian insufficiency (POI)

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Objective: Aim of this retrospective study was to assess androgen levels in 46,XX karyotype women with primary ovarian insufficiency (POI) in comparison with age and body mass index (BMI) matched healthy subjects.
Methods: Patients were hospitalized in Department of Gynecological Endocrinology, Medical University of Warsaw between 2012–2015. Study group consisted of 90 patients, aged between 18–39 with spontaneous, karyotypically normal primary ovarian insufficiency (POI) FSH >40 mIU/ml. POI patients were matched with 61 healthy controls at the same age range. Antropometric measurements, blood sampling of: FSH, estradiol, testosterone, androstendione, DHEAS, SHBG were analyzed. Free androgen index (FAI) was calculated. The laboratory parameters were measured using Enzyme Linked Fluorescent Assay technique by BioMerieux.
Results: In study group the mean age at diagnosis was 31± 5.4 years, mean FSH level was 71.37 ± 25.97 mIU/ml. The mean body mass index (BMI) did not significantly differ between the groups. There were statistically relevant differences between POI and control group in androstendione (2.32 ± 1.11 vs. 2.9 ± 0.96 ng/ml; $p < 0.005$); DHEAS (5.26 ± 2.42 vs. 6.46 ± 2.18 ng/ml; $p < 0.01$); 17-OHP levels (0.73 ± 0.58 vs. 0.96 ± 0.54 ng/ml; $p < 0.05$). Statistical analysis showed that there were no significant differences between study and control group in testosterone (0.41 ± 0.25 vs. 0.37 ± 0.11 ng/ml) and SHBG levels (53.93 ± 31.96 vs. 63.86 ± 29.48 nmol/l). Nevertheless, free androgen index (FAI) was significantly higher in POI group (3.6 ± 3.44 vs. 2.34± 1.22; $p < 0.01$).
Conclusions: Androgen levels in women with premature ovarian insufficiency are lower in comparison with healthy women. However, FAI may be above the limit, probably due to low estradiol level and its indication on SHBG. This makes FAI inappropriate method of measuring androgens in POI patients.

Nanocapsulated quercetin: evaluation of preventive and therapeutic potential in the management of primary ovarian insuffiency

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Context: Sedentary lifestyle and exposure to environmental ovotoxic chemicals cause a serious threat to ovarian lifespan.Studies suggest a causative role of reactive oxygen species(ROS) and mitochondrial dysfunction in the pathogenesis of premature ovarian failure. Ovotoxicant vinylcyclohexene diepoxide(VCD), destroys specifically oocytes contained in primordial/primary follicles in rats. Quercetin is a ROS scavenger well known for down regulate lipid peroxidation,at high doses.
Objective: To investigate an envisioned protective role of nanocapsulated quercetin (NQC) in attenuating the mitochondrial apoptotic pathway and preventing the VCD-mediated follicular apoptosis.
Methods: Effect of VCD was evaluated in COV434 cell line pretreated with/without NQC(5μM) for 12h followed by culture for another 12h in the presence/absence of VCD(30μM). The *in vivo* effect was studied in 23-day-old female rats that were dosed daily with VCD (80mg/kg/day) for 15days.On completion of the treatment, the rats were injected with/without NQC(2.5 mg/kg) on every third day for 15days. Follicular growth and atresia were assessed,and ovarian microenvironment was evaluated with estradiol, lipid peroxidation(LP), antioxidant enzyme activity and western analysis of mitochondrial pro and anti apoptotic molecules.
Result: NQC prevented membrane permeability pore formation leading to cytochrome-C release from mitochondria due to VCD insult. *In vivo* results showed prevention of the rate of follicular atresia and decay by NQC. The NQC-treated rats exhibited restored the peripheral level of estradiol with increased expression of mitochondrial anti-apoptotic factors; while the apoptosis mediating molecules were downregulated. NQC treatment also attenuated the rate of LP with increased enzyme activity.
Conclusion: NQC perhaps could rescue mitochondria from VCD mediated ovotoxicity leading to restoration of follicular atresia.

Down-regulated miR-106a promotes ovarian granulosa cell apoptosis by targeting ASK1 in diminished ovarian reserve patients

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Context: Women with diminished ovarian reserve (DOR) were suffered with less fertility. Differently expressed miRNAs in the serum and ovarian granulosa cells may contribute to the DOR process.
Objective: To detect the differentially expressed miRNAs in the serum and granulosa cells between DOR patients and normal cycling women, and explore whether miR-106a is involved in the proliferation and apoptosis of the granulosa cells.
Patients: All patients who less than 40 years old underwent their first *in vitro* fertilization (IVF) or intracytoplasmic sperm injection-embryo transfer (ICSI-ET) cycle due to tubal and/or male factors from October 2011 to December 2014 were included. Granulosa cell and serum were obtained from DOR patients ($n = 30$) and normal ovarian reserve infertile patients ($n = 30$).

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Methods: MiRNAs expressions were profiled using oligonucleotide microarray chip and bioinformatic methods and conformed by qRT-PCR. Granulosa cells proliferation and apoptosis were detected after miR-106a overexpression/inhibition and ASK1 siRNA transfection. The expression of ASK1 and p38 were detected by Western Blot and qRT-PCR. Luciferase Reporter Assay was used to determine whether the miR-106a can bind to the ASK1 mRNA directly.
Results: MiR-106a was down-regulated both in serum and granulosa cells of DOR patients. Overexpression of miR-106a promoted proliferation and attenuated apoptosis, while downregulation of miR-106a inhibited proliferation and increased apoptosis in granulosa cells. ASK1 was the target of miR-106a by Luciferase Reporter Assay. Downregulation of miR-106a increased phospho-p38, while ASK1 siRNA could attenuate the upregulation.
Conclusions: MiR-106a targets ASK1 to play an important role in regulating the apoptosis of human ovarian granulosa cells through p38 signaling pathway, and this may associated with ovarian aging.

Prevalence of autoimmune polyglandular syndrome type 3 among patients with premature ovarian insufficiency

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Context: Premature ovarian insufficiency (POI) is defined as the occurence of hypergonadotropic hypoestrogenic amenorrhoea in women under the age of 40 years. Autoimmune polyglandular syndrome (APS) is defined as multiple endocrine gland insufficiency accompanied by autoimmune diseases. Type 3 of the APS consists of autoimmune thyroid diseases associated with other autoimmune diseases (excluding Addison's disease and/or hypoparathyroidism)
Objective: The aim of the study was to investigate the prevalence of autoimmune polyglandular syndrome type 3 among the patients with premature ovarian insufficiency.
Patients: Retrospective study included 41 women with a diagnosis of POI defined as: amenorrhoea, hypoestrogenism, hypergonadotropism, age under 40 years old. Exclusion criteria: following oophrorectomy, chemotherapy and pelvic radiation, karyotype disorders. Controls: 28 healthy, regularly menstruating women at hormonal balance. There were no statistically significance differences between the experimental and control groups according to age and obstetrics history.
Results: The mean age of amenorrhoea manifestation was 31.6 (range from 19 to 38 years old). The frequency of APS type 3 presented as hypothyroidism and hypogonadism among patients with POI was 28% (eleven of thirty-nine women). In comparison, the frequency of hypothyroidism among control group were 14%. One woman has coeliac disease, and another was diagnosed with vitiligo.
Conclusions: The prevalence of autoimmune thyroiditis among patients with premature ovarian insufficiency is 28%. It should be taken into consideration that patients presented APS type III have to be routinely evalueted for the other APS components including: coeliac disease, diabetes type I, adrenal insufficiency, pernicious anemia etc.

The impact of premature ovarian failure following bone marrow transplantation on young women quality of life

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Introduction: Different types of cancer appear every year and they affect people regarding age or other feature. Hematological malignancies are among them and sometimes don't respond to traditional treatment, requiring aggressive regimens as for bone marrow transplantation (BMT). The treatment is highly active on malignant remaining cells, but the damage could go beyond its purpose and could affect any organ. Ovarian toxicity is an important and common side effect following BMT curative chemo/radiotherapy.
Methods and Patients: This research is a part of an ongoing retrospective study started in 2014 and includes a number of 14 women, after signing an informed consent. They were asked to complete a questionnaire, focusing on late psychological effects following BMT, menopausal symptoms, sexual activity, health-related quality of life, fertility preservation procedures, estrogen replacement therapy (ERT).
Results: The analysis of the data revealed significantly disturbing symptoms of hypoestrogenism, including hot flashes, sweats, irritability, dry skin and eyes, vaginal dryness, discomfort during sexual intercourse, decreased libido and energy. Those symptoms associated to premature ovarian failure (POF) were partially improved by ERT. Together with depression, forms of isolation, hair loss, memory and concentration alteration, difficulties in having or keeping a relationship, incapability of having a child (basis of a family), long-term consequences of POF following BMT can impact their quality of life and self-esteem dramatically.
Conclusions: Physical and psychological effects of BMT, life that follows after overcoming a malignancy are challenging and most of the times incomplete understood by surrounding people. The young women survivors are facing not only the symptoms of premature menopause, but also the social, financial and personal aspects that follow.

Analysis of data from the Premature Ovarian Insufficiency Database

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Context: The primary ovarian insufficiency (POI) database has been used to collect international data in an effort to avoid fragmented research and improve our understanding of this rare disease.
Objective: Retrospective and prospective database analysis of women with POI.
Methods: Analysis of data collected using an online pro forma for the POI database.
Patients: Women $<$ 40 years old with POI.
Interventions: Nil
Main Outcome Measures: Data extracted on patient ages, aetiology, months to diagnosis, symptom profile and bone mineral density (BMD) based on POI aetiology.
Results: Seven-hundred eighty-four patients were identified, with an average age at diagnosis of 32.3 years and the most common age range being 36–40 years. The aetiology was idiopathic in 55.5% of patients. When assessing the average number of months to diagnosis we found the youngest age group 15–20 years took the longest to diagnose at an average of 20 months. In general, patients with different aetiologies had a similar average number of symptoms (range 3.2–3.6). The most common symptoms usually being flushing, night sweats and tiredness across all aetiologies. Patients with a genetic cause for POI had the worst BMD at diagnosis (average DEXA scan *t*-score -1.49). Overall 28% of patients had osteopenia and 4.5% of patients had osteoporosis.
Conclusions: Younger POI patients take longer to diagnose and also have the lowest BMD. The most common aetiology is an idiopathic cause and presents with an average of three symptoms. The POI database has proved successful in data collection internationally as shown by the number of patients in this study. More health care professionals should be encouraged to engage with data collection to optimize quality and quantity of data. Further data will be presented on other aspects of POI presentation and management.

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Screening for osteoporosis in women with estrogen deficit of different age: bone and fat interplay

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Context: There is controversial data on role of fat in osteoporosis.
Objective: To work out non-instrumental screening for low bone mineral density (BMD) in women with estrogen deficit based on clinical, biochemical and molecular-genetic markers.
Methods: Patients: 54 women with secondary hypothalamic amenorrhea (HA), 55 with premature ovarian insufficiency (POI) and 191 postmenopausal women (without metabolic syndrome and prior HRT) were enrolled in cross-sectional study. Interventions. We evaluated BMI, BMD (by DXA), levels of reproductive hormones, markers of bone and lipid metabolism. SNPs of genes that regulate differentiation and function of bone cells and adipocytes (COL1A1, CYP19A1, ESR1, ESR2, LEP, LEPR, LRP5, TNFRSF11B, RANKL, SOST, VDR, PPARG, FTO, INS) were assessed by PCR.
Main Outcome Measures: Correlation analysis, logistic regression analysis.
Results: 48.2% of women with HA and 23.6% with POI had low BMD. There were positive correlations between BMI and BMD in all groups. We worked out a screening for low BMD in women with amenorrhea: y=2.67 + 0.22* (duration of amenorrhea, years)-0.29*(BMI) + 0.74* (atherogenic index). AUC 0.79 (95%CI 0.68–0.89), $p < 0.001$. Probability (P)>50% (y>0) -high-risk group (Sp = 85%, PPV=70%); $p < 27\%$ (y<-1.0) -low-risk group (Se=87%, NPV=88%). The probability of postmenopausal osteoporosis: y=6.65–0.07*(body mass, kg)-0.97* (LEPR, rs8179183) + 0.56* (RANKL, rs9594759). AUC 0.75 (95% CI 0.68–0.82), p=3*10–9. y>0 -high-risk group (Sp = 73%, PPV=85%); y<-1.0 -low-risk group (Se=97%, NPV=83%). There was a significant influence of LEPR (rs8179183) on BMD in underweight women with HA and postmenopausal women with obesity ($p < 0.05$).
Conclusions: Significant associations of bone and fat were found in women with estrogen deficit with the key role of leptin receptor, connecting reproductive system, fat and bone, that led to new screening approaches.

(OP11) Breast cancer: from epidemiology to patient needs

Physicians' knowledge about hereditary familiar cancer

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Context: Mutations in BRCA1, BRCA2, MSH2, MLH1, MSH2, PMP2 genes are responsible for hereditary syndromes associated with gynecologic, breast, and other cancers.
Objective: To evaluate the knowledge and the attitude towards BRCA and Lynch syndromes among physicians.
Methods: We administered 59 questionnaires on BRCA and Lynch syndrome to Gynecologists, General Surgeons, Pathologists, Oncologists, Geneticists and Radiologists during a Congress on the topic.
Patients: Foery-five physicians completed the survey (76% response rate) (17 Gynecologists, 16 General Surgeons, 5 Oncologists, 4 Geneticists, 2 Radiologists, 1 Pathologist).
Intervention and main outcomes measures: we investigated about cancer screening in Lynch Syndrome, indications to prophylactic surgery for both syndromes and the use of hormonal contraceptives in women with BRCA mutation.
Results: About Lynch syndrome surveillance, half of the Physicians (44.4%) suggest screening with annual transvaginal ultrasonography, endometrial biopsy and colonscopy. As regards prophylactic surgery for Lynch Syndrome, 64.5% of the Physicians suggest bilateral hysteroannessiectomy while 40% do not recommend gynaecological surgery but only surveillance with colonscopy. Regarding breast cancer treatment in BRCA+ patients, most of the respondents (60%) recommends mastectomy for the affected breast and concurrent prophylactic contralateral mastectomy; conserving treatment is indicated only by 4 (8.8%) Physicians. About oral contraception in healthy BRCA+ women, only 2 Physicians completely disagree for the fear of increasing breast cancer risk while most of the respondents (84.5%) prescribe it, considering also the protective effect on ovarian cancer.
Conclusion: No agreement exists on the management of patients with hereditary syndromes and a great effort must be done to improve the knowledge among physicians.

Cytoskeleton remodeling and migration of T47D breast cancer cell enhanced by prolactin

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Objective: This study aimed at determining the effects of prolactin in the cell migration of the T47D breast cancer cells and analyse T47D Actin rearrangement and modulation of cytoskeleton by prolactin.
Methods: For this purpose, the cells, cultured In 6 well dishes with supplemented medium, were divided in 4 different assays: Assay1 (T47D-control); Assay2 (T47D+25ng/ml of prolactin); Assay3 (T47D+50ng/ml of prolactin) and Assay4 (T47D+100ng/ml of prolactin). The migration analysis, as well the immunoblotting evaluation of Focal Adhesion Kinase (FAK) and Membrane-Organizing Extension Spike Protein (Moesin), were performed 24 hours after the treatment. The actins' cytoskeleton modulation were analysed, by immunofluorescence, 30 minutes after the treatment.
Results: The results showed that prolactin, in Assay3 (50 ng/ml) and Assay4 (100 ng/ml), enhanced the migration of T47D cells. Furthermore, the expression of FAK and Moesin as well as the cell membrane thickness were increased in those Assays ($p < 0.001$).
Conclusion: In summary, prolactin enhanced T47D breast cancer cell motility. This result is probably related to an activation of Actin adjustment on the cytoskeleton and formation of focal adhesion complexes. Our findings may extend the knowledge about the physiological and pathological processes associated with prolactin and cell motility, nevertheless further studies are necessary to better understand these correlations.

Progestogens and risk of breast cancer: a link between bone and breast?

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This article reviews the data supporting the role of receptor activator of the nuclear factor kappa (RANK) and its ligand, RANKL, in progestogen-induced breast cancer. Both experimental and clinical studies have been included. The expression of both RANK and RANKL has been described in epithelial cells of both mice and humans. Experiments of gain and loss of function in mice have shown that RANK/RANKL mediate alveologenesis during pregnancy or the estrous cycle. The involvement of RANK/RANKL in the proliferation of breast epithelium and the regulation of the system by sex hormones have fed the hypothesis of the implication of RANK/RANKL in hormone-dependent breast cancer. That hypothesis has been further supported by work with animals. Transgenic mice have been shown to develop an increase in pre-neoplastic lesions. Moreover, the treatment of mice with the carcinogen DMBA and medroxyprogesterone acetate, a progestogen, has induced, i) a 2000-time increase in the production of RANKL mRNA in RP+ luminal cells, ii) proliferation of mammary epithelial cells and stem cells, and iii) a higher incidence of ductal hyperplasia, intraepithelial neoplasia and adenocarcinoma. These data suggest that the RANK/RANKL system may act as a promoter of breast tumors in mice, and that it may mediate the oncogenic role of progestogens in the breast. Interestingly, the blockade of RANK reduces the incidence of progestogen-induced tumors in 90% of the cases. This possibility might open the door to treatments based in the blockade of RANKl or RANK. The translation to clinical oncology, however, has to be made with caution yet.

Reproductive concerns and fertility preservation options in breast cancer patients

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Although the incidence of breast cancer (BC) is more common among older women, an increase in the incidence rate of BC in women in their 20s and 30s has recently been reported due to earlier diagnosis in many western countries of the world. Considering an increasing number of BC survivors with more women in the past decades delaying of childbearing until their 30s or later, there appears to be an increased BC risk with advancing maternal age at first childbirth facing with reproductive concerns prior to completing their family. Up to 76% of young childless women with BC intended to have a child in the future and 35% of the survivors who already had at least one child wanted to have another. Among the standard options random-start ovarian stimulation protocol represents a new technique, which significantly decreases the total time of the *in vitro* fertilisation cycle. Cryopreservation of embryos and oocytes are nowadays deemed the most successful techniques for fertility preservation in BC patients. GnRH agonists during chemotherapy represent an experimental method for fertility preservation due to conflicting long-term outcome results regarding its safety and efficacy. Cryopreservation of ovarian tissue, IVM of immature oocytes and other strategies are considered experimental and should only be offered within the context of a clinical trial. Although many young women (68%) with BC do discuss fertility issues with their physicians before starting therapy and more than a half (51%) are concerned about becoming infertile after treatment, only a minority of women (10%) chooses to pursue available fertility preservation strategies.

Pregnancy-associated breast cancer: a single centre experience

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Objective: This study aims to evaluate pregnancy associated breast cancer (PABC).
Methods: Retrospective study from 2001 to 2014. Three groups were considered: PABC group (diagnosis of invasive breast cancer occurred during pregnancy or within a year of childbirth); group of breast cancer in pre-menopausal patients; and group of breast cancers diagnosed in post-menopausal patients.
Results: 4670 invasive breast tumors were included, 12 were PABC proving to be the 1.23% of pre-menopausal breast cancers or 0.3% of whole invasive breast cancers. The 12 cases of PABC group were found to be significantly younger than the other two groups. The following characteristics were significantly different in PABC group than the other two groups: reduced prevalence of invasive ductal carcinoma and increased of other invasive breast cancers, reduced prevalence of luminal A and increased of luminal Her, increased prevalence of comedo-like necrosis, perivascular invasion, high Ki-67/MIB-1 and high tumor grading. There were also more frequent in PABC lymph nodes macrometastases and extracapsular lymph node invasion. In PABC group the overall survival at 5 years was found to be 83.3% (95% CI: 64.7–100.0%) but excluding the two cases with stage IV at diagnosis the overall survival at 5 years was 100% and there were no local or distant recurrences in this group with a mean follow-up of 75.77 months ($\pm$ 44.96), while in the groups of breast cancer occurred in pre- and post-menopausal periods the overall survival at 5 years was respectively 96.2% (95% CI: 94.8–97.6%) and 94.9% (95% CI: 94.1–95.7%) and disease-free survival was found to be respectively 90.2% and 92.5%.
Conclusions: Despite a local advanced disease and unfavorable biological characteristics the PABC group, excluding metastatic disease at diagnosis, has a favorable outcome with a survival rate of 100% at five years follow up.

Impact of vaginal estriol on breast cancer cells in postmenopausal patients treated with aromatase inhibitors

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Introduction: Recently, we have shown that vaginal estriol to overcome side effects of aromatase inhibitor treatment does not influence serum hormone levels in postmenopausal patients with breast cancer. However, concern still exists regarding vaginal estriol use during endocrine treatment of breast cancer. To further elucidate this issue we investigated the impact of vaginal estriol on breast cancer cells *in vitro* using sera of postmenopausal patients with breast cancer treated with aromatase inhibitors.
Methods: To investigate the sensitivity of breast cancer cell growth and apoptosis in human serum, we cultivated MCF-7 cells as well as MDA-MB-231 cells in sera of 6 pre- and 6 postmenopausal women. To investigate the impact of vaginal estriol on breast cancer cells, we cultivated MCF-7 cells as well as MDA-MB-231 in sera of 10

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postmenopausal breast cancer patients treated with aromatase inhibitor before and after 2 weeks of daily vaginal estriol application. In both experiments, proliferation was measured by Cell Titer Blue cell viability assay, apoptosis was measured by Caspase Glo 3/7 assay and mobility of cancer cells was measured by a scratch assay. All experiments were done in triplets.
Results: The pre test showed significant higher proliferation of MCF-7 as well as MDA-MB-231 cells when cultivated in sera of premenopausal women compared to sera of postmenopausal women. No difference in apoptosis or mobility could be observed. Two weeks of vaginal estriol lead to a non-significant increase of proliferation of MCF-7 cells and a significant increase of proliferation of MDA-MB-231 cells. No impact of vaginal estriol on apoptosis or mobility of breast cancer cells could be observed.
Conclusion: Even though 2 weeks of vaginal estriol did not change measured hormone serum levels, it did impact on breast cancer cell proliferation.

Safety of fertility preservation indicated by a diagnosis of breast cancer – a Swedish registry-matched cohort study

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Context: The number of women that perform fertility preservation (FP) before initiating chemotherapy for treatment of breast cancer is increasing. Efficacy of FP has been documented but reports of safety aspects are scarce.
Objective: To investigate the safety of fertility preservation with and without hormonal stimulation in the incidence rate of breast cancer relapse.
Methods: Matched cohort study.
Patients: Women who performed FP treatments at the Reproductive Medicine clinic of Karolinska University Hospital ($N = 187$) and age-matched controls ($N = 319$) who did not perform FP. Controls were identified at the Swedish National Quality Registry for Breast Cancer.
Intervention: Women underwent fertility preservation by using hormonal stimulation for freezing embryos or oocytes or without hormone stimulation (89% and 19% of FP cases, respectively).
Main Outcome Measure(s): Risk of breast cancer relapse in the cases cohort vs. controls' cohort.
Results: There was no evidence of non-proportional hazards with respect to the effects of fertility preservation on the risk of relapse in the whole FP cohort, irrespective if the women underwent hormonal stimulation or not for FP, or of receptor status or tumour size at diagnosis. A stratified Cox regression model that allowed separate baseline hazard functions for each level for the investigation of the effect of number of involved lymph nodes was performed. In this model, the effect of fertility preservation on the risk of relapse was virtually unchanged (IRR: 1.02, 95% CI:0.56–1.84).
Conclusion: Our preliminary results indicate that fertility preservation either using hormone stimulation or not is unlikely to cause substantially increase recurrence risk of breast cancer, irrespective of the receptor status, tumor size of lymph node compromise.

Oocyte cryopreservation in breast cancer Patients: a retrospective analysis of single university centre

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Background: Cancer can be a devastating diagnosis. Oncological patients survive at increasing rates, but successful treatment in younger patients often lead to risk of developing a number of late sequelae, including impaired fertility. Among fertility preservation options oocyte cryopreservation is considered no more an experimental technique. One of the most important challenges in ovarian stimulation for oocyte banking is time required to complete the therapy and hyperestrogenism especially in those estrogen-dependent cancer such as breast cancer. Different stimulation protocols are now disposable in order to achieve this purpose.
Objective: The study is retrospective analyses of fertility preservation program in 15 breast cancer patients occur to our centre, Department of Reproductive Medicine of The University of Pisa, in order to do oocyte cryopreservation protocol after breast surgery and before anticancer treatment. Study design: Cancer patients start fertility preservation program anytime during menstrual cycle after Gnrh antagonist induced luteolysis in order to not postpone the beginning of anticancer treatment. Ovarian stimulation consistents in administration of a combined letrozole-gonadotropins protocol. The outcomes are: duration of stimulation, cumulative dosage of gonadotropins number of oocyte retrieved, percentage of mature oocytes and expecially estrgen blood levels. We compared the effects of this ovarian stimulation protocol to those used in 15 cancer patients without an estrogen dependet cancer.
Results: The results show any differences between two groups if we consider days of stimulation, total amount of gonadotropins administered, the number of oocyte retrieved and the number of mature oocyte obtained. The estradiol blood levels on hCG administration are statically significant lower than in other group despite a similar good oocyte retrival.

Estradiol therapy and breast cancer risk: a systematic review and meta-analysis

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Objective: The aim of our study is to review the evidence on breast cancer risk associated with estradiol-only therapy and estradiol therapy combined with different types of progestin, to provide some suggestions for confused patients and physicians.
Methods: A comprehensive computerized literature search of Embase, Pubmed and Cochrane Library for articles published up to February 2015 with English abstracts was performed, studies meet our inclusion criteria were included, the reference lists of retrieved literatures were viewed and a meta-analysis was conducted. Odds ratio (OR) values and 95% confidence intervals (CI) were calculated by Stata 12.0 software.
Results: Thirteen studies (5 RCTs, 8 observational studies) were included in our study. In estradiol-only therapy analysis, meta-analysis resulted a pooled OR =0.89, 95% CI (0.41, 1.97) from the RCTs and pooled OR =1.01, 95% CI (0.94, 1.09) from observational studies. However, in the analysis of estradiol-progestin therapy, the risk of breast cancer increased significantly (OR =1.57, 95% CI (1.34, 1.83)), no matter the sequential estradiol-progestin therapy (OR = 1.86, 95% CI (1.24, 2.80)) or continuous estradiol-progestin therapy (OR = 3.04, 95% CI (1.62, 5.69)), and the duration with more than five years (OR = 2.43, 95% CI (1.79, 3.29)) presented a higher risk than using less than five years (OR = 1.49, 95% CI (1.03, 2.15)).

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Conclusions: Estradiol-only therapy carries no risk for breast cancer, while estradiol-progestin therapy is associated with an increased risk of breast cancer, the risk rise progressively by prolonged use, furthermore, comparing to sequential therapy, continuous therapy carries a higher risk. Although the overall effect of estradiol therapy on breast cancer risk is approximately determined, more individual features must be fully considered before clinical application.

(OP12) Polycystic ovary *Patients*: life and risks

The facial expression of emotions recognition in patients with polycystic ovary syndrome.

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Context: A facial expression of emotions (FEE) recognition is one of the basic psychological abilities. Sex steroids are able to strongly modulate the process of interpretation of facial expressions.
Objective: The aim of this study was the assessment of ability to interpret the FEE in women with hyperandrogenemia associated with polycystic ovary syndrome (PCOS).
Methods: Participants completed a visual emotional task in which they were asked to recognize the FEE of 80 randomly chosen facial expressions from NimStim set (Tottenham et al., 2009). With dedicated software we were able to assess the accuracy of patients FEE recognition (in comparison to NimStim validation set) and time required to provide the answer. Patients with psychotic personality have been excluded using Eysenck Personality Questionnaire (EPQ). All the patients underwent also hormonal tests including gonadotropins, estradiol and androgen concentrations.
Patients: Sixty women diagnosed with PCOS and hyperandrogenemia were included to the study. The control group consisted of 60 healthy women matched by age.
Intervention: Each patient underwent visual FEE and EPQ tasks using specifically designed software.
Main Outcome Measures: The accuracy rate (AR) and time required to recognize emotion (TE) of following emotions: anger, disgust, fear, happiness, sadness, surprise, calm and neutral has been measured.
Results: Patients with PCOS showed significantly reduced AR for calm (0.76¬+/-0.09) and surprise (0.67+/-0.18) in comparison to controls (0.81+/-0.09, 0.79+/-0.08 respectively). The TE for the anger was higher in PCOS group. Estradiol concentrations showed a statistic tendency ($p = 0.07$) for correlation with TE for the happiness in controls.
Conclusions: In this study we showed for the first time that patients affected by hyperandrogenism shows signs of disturbed recognition of FEE.

Insights into the influence of subclinical hypothyroidism on polycystic ovary syndrome patients' characteristics. A meta-analysis of observational studies

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Objective: To examine whether patients with SCH should be initially excluded from patients with PCOS diagnosis or not.
Design: Meta-analysis of published observational studies.
Methods: A Medline, Scopus, Embase, Webmed Central search was performed to identify the studies comparing PCOS and PCOS patients with SCH (PCOS-like-SCH) patients. In the end, 9 papers were selected; 7 with cross-sectional design and 2 case-control studies.
Results: A total of 1842 patients were included, 1508 with PCOS and 334 with PCOS-like-SCH. The results were expressed as raw mean differences (RMD) and standard error (SE), using the random effects model. The Cochrane's heterogeneity (Q) and I^2 statistics are presented. Anthropometrical parameters waist circumference ($p = 0.671$), waist–hip ratio ($p = 0.597$), and body mass index ($p = 0.409$) were equal in both groups. Total cholesterol levels were higher in PCOS-like-SCH than PCOS patients ($p = 0.036$) (Tau^2=0.148; Q=33.24; I^2=78.94; $p = 0.000$), and high-density lipoprotein cholesterol level was lower in the PCOS-like-SCH group ($p = 0.018$), (Tau^2=0.003; Q=10.10; $I^2 = 40.6\%$, $p = 0.120$). Triglyceride levels were also higher in PCOS-like-SCH patients ($p = 0.012$), also including eight heterogeneous studies ($Tau^2 = 0.086$; Q =28.54; $I^2 = 75.48$; p =0.000). Fasting glucose was lower in PCOS patients ($p = 0.022$), pooled from eight homogeneous studies ($Tau^2 = 0.000$; Q=7.55; $I^2 = 7.37$; $p = 0.022$). All androgen levels were similar between PCOS and PCOS-like-SCH patients; most studies were heterogeneous.
Conclusions: Because heterogeneity among studies the results of some parameters should be interpreted with caution. Standardization of the TSH cut-off level for the exclusion of women with thyroid dysfunction from PCOS patients is required. This meta-analysis provided enough data to be considered in future studies addressing PCOS diagnosis and exclusion/inclusion criteria.

Variations on lipid profile among different phenotypes of adolescent girls with polycystic ovary sydrome

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Context: The diagnosis of PCOS (Polycystic Ovary Syndrome) to an adolescent girl is a lifelong health burden. According to literature, disturbances to the metabolic profile of patients start at an early age and are associated with increased long-term risk of cardiovascular disease.
Objective: We evaluated the lipid parameters of adolescent PCOS patients and examined differences among various PCOS phenotypes.
Methods & Patients: One hundred eighy-six adolescent girls, between 13 and 21 years old, fulfilling the Rotterdam criteria were included. Patients were assorted to phenotypes created by the combination of Rotterdam criteria (anovulation, hyperadrogenism (HA), polycystic morphology) they presented at first visit. Anthropometric, biochemical and imaging data were measured and analyzed.
Main outcome & Results: Patients with hyperandrogenic phenotypes presented with less favorable metabolic profile than patients with non-hyperandrogenic phenotypes. Lean girls with HA had higher total cholesterol serum levels ($p = 0.036$) than lean PCOS girls without HA. Overweight adolescent patients with HA present with increased LDL ($p = 0.03$) and total cholesterol levels ($p = 0.03$), whereas obese patients with HA demonstrate high triglycerides ($p = 0.075$) and lower HDL ($p = 0.03$).
Conclusions: Lipoproteins are well-established markers of atherosclerosis and CVD risk. In literature, regarding adult women with PCOS, hyperandrogenism is indicated as a key element in developing metabolic disorders. However, data regarding adolescent PCOS patients are scarce and contradicting. In the present study, we demonstrated an unfavorable lipid profile in adolescents with hyperandrogenic PCOS phenotypes. It is of great importance to identify most severely affected PCOS subgroups, in order to provide a

more thorough follow up and encourage these patients to a adopt a healthy lifestyle even from the first reproductive years.

Hepatic steatosis in polycystic ovary syndrome

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Context: Polycystic ovary syndrome (PCOS) is often accompanied with obesity and recent reports have found an increased prevalence of hepatic steatosis.
Objective: To study the effect of a randomized life-style intervention on hepatic steatosis in PCOS.
Patients: Women fulfilling all 3 Rotterdam criteria of PCOS, aged 18–40 years and BMI $\geq$ 27.
Intervention: Randomization to a 4-month active life-style intervention supported by a personal training coach and a dietician, or passive treatment with standard life-style recommendations.
Methods: Twenty-one women underwent magnetic resonance (MR) imaging-estimated proton density fat fraction/percent (PDFF) of the liver at baseline and at the end of the intervention. Hepatic steatosis was defined as a MR Imaging-PDFF threshold of $\geq$ 6.4%.
Main outcome measure: MR Imaging-PDFF threshold of $\geq$ 6.4% before and after the intervention.
Results: Mean BMI at baseline was 36.7 $\pm$ 6.1 and mean MR-PDFF was 8.8 $\pm$ 5.7%. Ten of the 21 women (46%) had hepatic steatosis and this finding was more common in those with amenorrhea (6/7), than those with oligomenorrhea, 4/14 ($p < 0.001$). After intervention, there was no difference in MR-PDFF or prevalence of hepatic steatosis between the groups. BMI was lower after intervention, 35.6 $\pm$ 6.3 ($p < 0.01$), but no change in MR-PDFF or the proportion of women having steatosis (43%) was found. Hepatic fat percent correlated positively with BMI ($r = 0.68$, $p < 0.01$) and mean BMI was higher among women with hepatic steatosis than those without, 39.3 versus 32.7 ($p < 0.01$). Hepatic steatosis was only found in women with BMI 32.5 or higher.
Conclusions: Hepatic steatosis is common in obese women with PCOS, but it was not affected by our short-term life-style intervention. The prevalence of hepatic steatosis correlated positively with BMI and was higher in women with amenorrhea than in those with oligomenorrhea.

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Investigating the linkage between vitamin D and PCOS: development of new rat model

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Context: Not only hiperandrogenic status, but vitamin D deficiency can lead to the elevation of cardiovascular risk. These two symptoms are both frequent in polycystic ovarian syndrome.
Objective: In our present examination we investigated the joint action of hyperandrogenic status and vitamin D decficiency. Instead of dihydro-testosterone treatment, now we reached the hyperandrogenic status with direct testosteron treatment, which is more similar to the human PCOS.
Methods: To explain the early pathophysiological changes of PCOS, we created a chronic (8-week) transdermal testosterone treatement protocol. 46 adolescent female Wistar rats were grouped into 4 groups. For testosterone and vitamin D treateted groups, transdermal tesostosterone gel (5 times a week) and oral cholecalciferol (weekly) was given.
Main Outcome Measures: Bloodsamples were taken (4–6-8th week) to measure sexual steroid, vitamin D, cholesterol and triglicerid plasma levels with high performace liqiud chromatography method. Oral glucose test. insulin ELISA test (6th week), pulse wave variance test and forced swim test (7th week), were performed. Heart ultrasound, invasive bloodpressure, heart- and adrenal gland ovariumweight were measured (8th week). Histology samples from the ovarii and the heart were also taken.
Results: Significantly higer testosterone and vitamin D plasma levels were observed after the 8-week treatment. Hiperandrogenic rats had reduced oral glucose tolerance and showed signficant depressive behavioral changes with forced swim test. Higher body- and heart-weight, and smaller adrenal gland and ovarium weight were observed.
Conclusions: With direct trandermal testosterone protocol a hyperandrogenic PCOS rat model was produced. Oral vitamin D substitution was efficient.

Oxidative stress markers in patients with polycystic ovary syndrome during adolescence

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Context: PCOS is not the most common cause of oligomenorrhea in girls, but also a metabolic disorder related to oxidative stress.
Objective: To investigate the relationship between oxidative stress markers and hormonal profile in adolescent girls with PCOS and controls.
Patients: The study included 65 girls with PCOS according to the Rotterdam criteria and 15 healthy girls with regular menstrual cycle in control group from 15 to 17 years old.
Methods: Complete examination; hormonal profile (LH, FSH, E2, T, PRL, DGA-S, 17-OHP, androstenedione (A), AMG); levels of CRP, Mg2+, Fe2+, malondialdehyde (MDA); glucose tolerance test. The level of glutathione (GSH), the oxidized glutathione ratio (GSSG)/GSH was studied by spectrophotometry; determination of catalase, glutathione peroxidase activity in plasma (GPx) was performed using specific reactions.
Results: The difference was observed between the PCOS and Control groups for levels of LH, IU/L (7.4 $\pm$ 3.8 vs. 4.1 $\pm$ 1.8, $p \leq 0.05$, Kolmogorov-Smirnov test), T, nmol/L(1.7 $\pm$ 0.7 vs. 0.9 $\pm$ 0.2, $p \leq 0.01$), A, ng/ml (19.4 $\pm$ 10.6 vs. 8.3 $\pm$ 2.0, $p \leq 0.001$), AMG, ng/ml (12.7 $\pm$ 13.9 vs. 5.4 $\pm$ 2.4, $p \leq 0.001$).
In PCOS compared with Control group significant indicators of oxidative stress were revealed: level of MDA, μM (8.2$\pm$1.4 vs. 9.5 $\pm$ 0.9, $p \leq 0.001$, Mann–Whitney *U*-test), level of total GSH, μM (1449.6$\pm$677.4 vs. 1267.0$\pm$677.4, $p \leq 0.05$), the level of reduced GSH, μM (1441.6 $\pm$ 677.0 vs. 1020.5 $\pm$ 198.5, $p \leq 0.05$) GPx, μmole/min (22.1 $\pm$ 1.1 vs. 25.9 $\pm$ 2.2, $p \leq 0.05$). Significant positive correlations were observed between tGSH μM, GSSG μM levels and AMG (0.31; 0.42; $p \leq 0.05$, Spearman Rank Order), CRP levels with the parameters of MDA, GSSG μmole/g Hb, and negative with Mg2+ (0.57; 0.32; −0.34, $p \leq 0.05$).
Conclusions: This study supports the hypothesis of association of PCOS with impaired homeostasis of glutathione-dependent antioxidant protection in the background of oxidative stress.

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Endometrial expression of progesterone receptor membrane component 1 and 2 in obese women with polycystic ovary syndrome

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Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. It is associated with an increased risk of endometrial hyperplasia and cancer. Progesterone protects the endometrium from estrogen stimulation via genomic and non-genomic signaling pathways. However, endometrial expression of non-genomic progesterone receptors in obese women with PCOS is not known.
Aim: To study receptors of non-genomic progesterone signaling in the endometrium of women with PCOS as compared to BMI-matched controls.
Material and Methods: Endometrial levels of mRNA and immunostaining of progesterone receptor membrane component 1(PGRMC1) and 2 (PGRMC2) were evaluated in obese women with PCOS according to all three Rotterdam criteria ($n = 18$) and BMI-matched controls ($n = 10$) on cycle day 21–23. Luteal phase was confirmed on the basis of an elevated level of progesterone (<17 nmol/l).
Results: All women with PCOS, both those with confirmed luteal phase ($n = 6$) and those who were anovulatory ($n = 12$), displayed a higher PGRMC1 mRNA level, as well as stromal PGRMC1 immunostaining, on cycle day 21–23 than the BMI matched controls ($p < 0.001$ and $p < 0.05$, respectively). Moreover, stromal immunostaining of PGRMC2 was higher in anovulatory women with PCOS as compared to controls ($p < 0.05$).
Conclusions: Endometrial expression of PGRMC1 and PGRMC2 is altered in obese women with PCOS compared to BMI-matched controls. We propose that higher expression of PGRMC1 in the luteal phase, might indicate impaired progesterone action and thereby endometrial dysfunction in obese PCOS women.

Induction of ovulation with clomiphene vs. clomiphene with bromocriptine in PCOS patients: a prospective, randomized, controlled clinical trial

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Objective:The purpose of this study was to compare the effects on the outcome of ovulation-induction of bromocriptine(Brc) combined with clomiphene citrate(CC) vs. CC alone in patients with polycystic ovary syndrome.
Methods: Prospective, randomized, controlled clinical trial.
Patients: One hundred polycystic ovary patients with infertility who needed ovulation-induction to assistant to get pregnancy.
Interventions:Patients were randomly divided into two groups, one group received 50 mg CC from day 3 to day 7, the other group was given 50 mg of CC from day3 to day7 along with 2.5mg of Brc daily for full cycle. Both the groups were treated for one cycle.
Main Outcome Measure(s): The outcomes were measured by the hormonal status, follicular size, endometrial thickness, ovulation rate, and pregnancy outcomes.
Results: The baseline level of hormones between two groups was no different before treatment. After intervention, the rate of ovulation in CC group was 72.0% and in CC+Brc group was 75.4% ($p > 0.05$), the rate of ongoing pregnancy in CC+Brc group was higher than that in CC group (18.4% vs. 8.0%). At HCG day, there were no statistical differences between two groups regarding to level of FSH, E2 and P ($p > 0.05$), but PRL and T was significantly decreased (respectively $p < 0.001$, $p < 0.01$), and LH was also decreased but with no statistical significance($p > 0.05$). At HCG day 7, level of P and E2 was no difference in the two groups, but PRL was decreased ($p < 0.001$) and the endometrial thickness was increased significantly ($p < 0.01$).
Conclusions: Use of bromocriptine with CC could improve the outcome of ovulation-induction more than use of CC alone for infertile PCOS patients, which may be brought about through dopamine agonists efficacy in reducing LH, PRL, vascular resistance and increased uterine blood supply to the uterus.

(OP13) Menopause: women, biology and treatments

Subclinical atherosclerosis and GFR variations in postmenopausal women

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Context: Cardiovascular damage has long been related to the development of renal morbid- and fatal events and vice versa.
Objective: To evaluate the effect of renal function variations within normal limits, estimated using levels of glomerular filtration rate (GFR), on vascular structure, before the development of hypertension.
Methods: Hemodynamic parameters and markers of vascular structure were associated with markers of renal function and levels of GFR.
Patients: One-hundred forty-one postmenopausal women without evidence of renal dysfunction or hypertension.
Interventions: Ultrasound evaluations included the intima-media thickness (IMT) and atheromatous plaque presence of carotid and femoral arteries. Blood drawing was performed to evaluate markers of renal function and for GFR estimations (using standard [GFR_epi] and newer creatinine and/or cystatin calculations [GFR_cr_cystatin, GFR_cystatin]).
Main Outcome Measures: Mean IMT values, presence of atheromatous plaques, levels of GFR and biochemical markers of renal function.
Results: Multivariate analysis indicated that carotid bulb (CB)-IMT was predicted by GFR_epi levels (b-coefficient $= -0.212$, p-value $= 0.020$) and age, while femoral-IMT was predicted by GFR_epi levels (b-coefficient $= -0.293$, p-value $= 0.001$). Logistic analysis indicated that GFR_epi levels <25th percentile associated with lower odds of atherosclerotic plaques presence (CB: OR = 0.146, p-value=0.006; carotid arteries combined: OR = 0.249, p-value=0.043), both in association with levels of body mass index.
Conclusions: The extent of structural vascular disease was independently associated with renal function within normal limits of GFR, in this sample of postmenopausal women. Levels of creatinine presented a more sensitive marker compared to Cystatin C, with respect to the assessment of GFR concerning the association with IMT and atherosclerotic plaques in this population.

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Thyroid hormones are associated with indices of adiposity in euthyroid postmenopausal women

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Context: Affected by aging and menopause, thyroid function is related with many adverse health outcomes and changes in body weight.
Objective: To evaluate the impact of thyroid hormones on the distribution of fat accumulation, in euthyroid, postmenopausal women.
Methods: We examined potential associations between levels of thyroid hormones and measures of anthropometric parameters or abdominal fat layers.
Patients: One-hundred ninety-four healthy, euthyroid, postmenopausal women
Interventions: Blood drawing for hormonal evaluation; determination of anthropometric parameters; sonographic assessment of abdominal fat layers.
Main Outcome Measures: Abdominal fat layers included the subcutaneous (SF) and preperitoneal fat (PF) mass (defined as high vs. low, according to the median value of every assessed parameter); thyroid hormones included thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4); anthropometric parameters included waist-to-hip ratio (WHR) and body mass index (BMI).
Results: Higher SF associated with lower FT4 levels and higher FT3/FT4 ratio, adjusting for traditional risk factors (FT4: Exp(B)=0.035, *p*-value= 0.020; FT3/FT4: Exp(B)=2.374, *p*-value =0.018). Higher PF associated with higher FT3 levels (Exp(B)=2.815, *p*-value =0.032). BMI associated positively with TSH (Exp(B)=1.829, *p*-value =0.018). Finally, SF associated with FT3, only among women with higher BMI (FT3, b-coefficient=0.259, *p*-value =0.040), or higher WHR (b-coefficient=0.309, *p*-value =0.020), but not among women with lower values of BMI or WHR.
Conclusions: SF and PF associated with levels of thyroid hormones, and in particular FT3, in euthyroid postmenopausal women. This effect was mainly evident in women with higher BMIs. Among traditional indices of adiposity, only BMI correlated positively with TSH. Larger prospective studies are necessary to evaluate the significance of our findings.

The effect of a monthly parenteral formulation of 17β-estradiol/progesterone using novel non-polymeric microsphere technology over menopausal symptoms and quality of life in climacteric women

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Context: HT is still the most effective option for the relief of vasomotor and other symptoms related to the menopause. Current consensus highly recommends the use of lower dosages and the non-oral route. Monthly IM administration would be an advantage.
Objective: To evaluate the short term effect of a monthly parenteral formulation of 17β-estradiol (E)/progesterone (P) using novel non-plymeric microsphere technology over menopausal symptoms and quality of life in climacteric women.
Methods: Secondary analysis of a multicenter randomized, single-blind, parallel, clinical trial.
Patients: Peri- and postmenopausal women with moderate to severe vasomotor symptoms (at least 3 hot flashes per day or 21 episodes per week).
Interventions: Monthly intramuscular injection of 0.5 mg E + 15 mg P (Group A), 1 mg E + 20 mg P (Group B), or 1 mg E + 30 mg P (Group C), for 6 months.
Main Outcome Measures: Menopausal symptoms were assessed with the Greene Climacteric Scale (GCS) and Quality of life (QoL) with the Utian Quality of Life Scale (UQoLS).
Results: One hundred three women were randomized (Groups A, B & C: 38, 29, 36). A 56% of women were peri- and 44% postmenopausal, median age was 49 years (range 38–62), a 59% were overweight and 22% obese. After six months, all treated groups displayed a significant improvement in QoL expressed by an increase in total scores of the four domains of the UQoLS ($p < 0.05$), particulary in emotional and sexual domains ($p < 0.05$). Regarding menopausal symptoms, as compared to baseline, mean scores for all the clusters of the GCS significantly decreased in all treated groups at the end of the study.
Conclusion: The three low-dose continuous sequential intramuscular monthly formulations of E/P microspheres exerted a positive effect short term over menopausal symptoms and QoL. Efficacy and safety must be confirmed in phase III randomized, placebo-controlled trials.

Estrogen enhances glucose transporter 4 and insulin substrate 1 expressions in SGBS-adipocyte submitted to low and high glucose concentration

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Context: New findings show that the estrogen therapy, via Estrogen Receptor Alpha (ERα) activation, may influence the metabolic homeostasis of insulin-dependent tissues and modulate the expression of proteins involved in the insulin signaling. However, it is not clear which proteins partake in this activity and how they are expressed. A possible crosstalk between Erα and Insulin Receptor could help increase glucose uptake and promote energy advantage for the cell.
Objective: This study aimed at determining the effects of estrogen on activation of insulin signaling pathway.
Methods and Results: We here show that SGBS-adipocyte cells treated with estrogen and exposed to low (1000 mg/L) and high (1800 mg/L) concentrations of glucose, with or without insulin, display an elevated Glucose Transporter 4 (GLUT4) expression. Furthermore, the concomitant administration of estrogen and insulin enhanced the expression of ERα and Insulin Substrate 1 (IRS1) both at low and high glucose concentrations.
Conclusions: In conclusion, estrogen therapy may regulate the expression of GLUT4 and IRS1, which are involved to insulin signaling pathway. Although these findings broadens the understanding of estrogen actions in SGBS-adipocyte, further studies addressing glucose uptake are needed to better comprehend its actions on insulin-dependent cells

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Treatment of steroidopenia is a key of the new method of hypercholesterolemia management

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In 2002 we suggested a new hypothesis of hypercholesterolemia. There are very few publications regarding the association of steroidopenia and hypercholesterolemia. The goal of our presentation is to determine if the correction of steroidopenia with hormonorestorative therapy (HT) to youthful levels will normalize total cholesterol (TC) levels. We analyzed our two retrospective studies in women with high cholesterol (78 and 31 patients), where we used hormonorestorative therapy as a basic element of treatment. Laboratory workup included lipid profile, serum pregnenolone, dehydroepiandrosterone sulfate, total estrogen, progesterone, cortisol, total testosterone, and vitamin D-3 levels at presentation with follow up ranging from 3 to 9 months. HT therapy included a combination of several agents such as pregnenolone, dehydroepiandrosterone (DHEA), triestrogen, progesterone, testosterone, hydrocortisone, and vitamin D-3. Cholesterol levels decreased in all 109 patients treated with HT. Mean serum TC dropped by 23.6% (from 246.1 mg/dL before to 191.6 mg/dL after treatment) in the first study group (78 patients). Mean age 54.2. Serum TC completely normalized in 63.4%. 36.6% of patients still have a minimal elevation of serum TC due to an incomplete optimization of steroid hormone levels. In the second study, in women, mean age 57.0, HT statistically significantly lowered mean TC from 229 mg/dL to 186 mg/dL (19%) ($p < 0.05$). These results were associated with statistically significant elevations in pregnenolone, DHEA Sulfate, testosterone, progesterone but not total estrogen, cortisol, or vitamin D-3 changes in both men and women. During the follow up no patients exhibited adverse complications related to HT and most described marked global quality of life improvement. The acute morbidity of HT was zero. Our studies showed that the correction of steroidopenia with the use of hormonorestorative therapy is an effective strategy for normalizing and maintaining cholesterol homeostasis. HT can significantly decrease the level of TC without any side effects and can be recommended for clinical use.

The salivary cortisol level as the marker of psychological disorder assessed in accordance with menopause rating scale on the perimenopausal women in medan – Indonesia

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Background: The perimenopausal period is marked with the decrease of estrogen hormone level that often causes a very disturbing symptom. Based on the Menopause Rating Scale, one of the factors affecting the perimenopausal symptoms is psychological factor. The factor is closely related to cortisol level in which the stressful circumstance relates to neuroendocrine system. As the product of this mechanism, the cortisol hormone is often used as biomarker to learn stress. The diagnosis from menopausal symptoms to date is still limited on the complaint that tends to be subjective. Therefore, it requires a biomarker in diagnosing the psychological disorder.
Method: It is the analytic research with cross-sectional design and diagnostic test. In order to avoid bias, the research was conducted in Haji Adam Malik General Hospital in Medan with outpatient paramedics as its samples, starting from July 2015 to September 2015. It was conducted by assessing the psychological disorder on the scoring of Menopause Rating Scale (MRS) and it was associated with the salivary cortisol level.
Result: This research shows the result that there is existence or absence of meaningful difference between salivary cortisol level and psychological disorder with the p value < 0.01. There is also meaningful difference between salivary cortisol level with its respective levels of psychological score group on MRS with p value = 0.008. The cut-off point value of salivary cortisol level as the marker of psychological disorder is on 9.02 ng/ml with the sensitivity value of 80% and the specificity of 90%.
Conclusion: The examination on salivary cortisol level as the marker of psychological disorder is on 9.02 ng/ml with the sensitivity value of 80% and the specificity of 90%.

Keywords

Salivary cortisol, psychological disorder, Menopause Rating Scale.

Serum follicle-stimulating hormone level is a predictor of changes in lipid profiles in postmenopausal women with hormone replacement therapy

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Context: Menopause-associated dyslipidemia is a potential coronary risk factor for post-menopausal women. The exact mechanism still remains unclear whether menopausal lipid changes in relation to menopausal changes in endogenous hormones.
Objective: The aim of this study is to investigate the relationship of serum hormone levels and the lipids profiles in Chinese postmenopausal women before and after HRT.
Methods: A cross-sectional study was conducted on 200 healthy Chinese postmenopausal women, aged 42–60 years, who were without contraindication of hormone replacement therapy. The serum levels of FSH, estradiol, TG, TC, LDL-C, and HDL-C were detected before and after 12 month HRT. Written informed consent was obtained from each subject prior to data collection.
Result(s): 1. The average age at menopause was 49.1 years, and the mean elapsed time since menopause was 3.0 years. 2. These postmenopausal women were divided into two groups according to the median value of basal FSH: the low FSH group, the high FSH group. The serum levels of TG, TC and LDL-C were significant higher, and HDL-C were lower in high FSH group, however, there were no significant differences in estradiol between two groups. 3. The HRT treatment of these postmenopausal women for 12 months decreased the serum FSH levels and increased the serum estradiol significantly in both groups, but decreased the serum levels of TC and LDL-C significantly only in high FSH group.
Conclusions: After treatment with HRT, postmenopausal women with high baseline serum FSH levels had a greater decrease in FSH levels than those with lower baseline FSH levels. These finding suggest that HRT in postmenopausal women with higher basal FSH levels may have better preventive effects, and those women might be encouraged to take HRT in the postmenopausal years.

Effect of HRT on inter-vertebral disc height: data from a prospective randomised trial

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Context: Inter-vertebral discs have an important function in acting as shock absorbers in the spine, thereby helping to reduce the risk of vertebral body compression fractures. Previous cross-sectional studies

have shown that loss of estrogen following the menopause is associated with a reduction in disc height whereas treatment with hormone replacement therapy (HRT) helps to maintain disc height.
Objective: We now report findings from a prospective randomised clinical trial of HRT.
Patients and *Interventions*: 75 healthy postmenopausal women aged (mean±SD) 56.5±4.6 years were randomised to HRT with estradiol 1 or 2 mg plus dydrogesterone or to placebo.
Methods: DXA measurements (Lunar DPX) were obtained at baseline and following 2 years of treatment.
Main outcome measure: Inter-vertebral disc height was measured in discs between D12 to L3 using the bone densitometer ruler.
Results: Treatment with HRT resulted in a significant increase in total disc height 13.6±7.7 – 19.0±3.1 cm, $p < 0.001$) whereas there was no significant change with placebo.
Conclusions: These results confirm the previous cross-sectional findings of a beneficial effect of estrogen on inter-vertebral discs. This may be in part responsible for the anti-fracture efficacy of HRT on vertebral fractures.

An innovative LC-MS/MS-based method for determining CYP 17 and CYP 19 activity in the adipose tissue of pre- and postmenopausal and ovariectomized women using 13C-labeled steroid substrates

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Aim: To clarify whether adipose tissue produces sex steroid hormone like an endocrine organ, we estimated several key steroid hormone levels, as well as CYP17 and CYP19 activity, in ovariectomized, pre- and postmenopausal women by liquid chromatography-tandem mass spectrometry (LC-MS/MS).
Subjects and methods: The subjects were 19 premenopausal ($n = 12$), postmenopausal ($n = 4$), and ovariectomized women ($n = 3$) aged 27–68 years. Serum, visceral adipose and sc adipose samples were taken from these subjects and stored at -70°C. The levels of cortisol, cortisone, progesterone (Prog), androstenedione, dehydroepiandrosterone, estrone, estradiol (E2), and T in serum and adipose tissue were estimated simultaneously by LC-MS/MS. CYP17 and CYP19 activity in tissues were assayed with the use of (13)C-labeled steroid precursors and LC-MS/MS-based estimation of the metabolites.
Results: E2 and Prog levels in the sera of postmenopausal or ovariectomized women were less than 10% of those in premenopausal women. No marked variations were seen in other hormones. Estrone, androstenedione, dehydroepiandrosterone, and Prog levels in the visceral and sc tissues of postmenopausal and ovariectomized women were 9–60 times higher than those in serum, whereas E2 and T levels were 3- to 7-fold higher than those in serum, and cortisol and cortisone levels were 20% of those found for serum. CYP17 in adipose tissue was found to have 17-hydroxylase and 20.17-lyase activity, with each catalytic activity being essentially equal.
Conclusion: Our findings suggest that adipose tissue acts as an endocrine organ, with CYP17 and CYP19 activity playing an essential role in sex steroid hormone biosynthesis.

(OP14) Polycystic ovary: glucose metabolism and insulin

Biomechanical properties and structural changies of coronary arterioles in chronic rat PCOS model

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Contex: Polycystic ovarian syndrome (PCOS) one of the most frequent gynecological illnesses influencing about 8% of fertile women worldwide. Vitamin D hypovitaminosis occurs in 70–80% of women suffering from PCOS.
Objective: Our goal is to describe the biomechanical changes of small coronary arterioles and to show the possible linkage between PCOS, hyperandrogenism and vitamin D status with a new rodent model.
Methods: Forty-six adolescent (21–28 day-old), 90–110 gram-weighed female Wistar rats were grouped randomly in 4 groups: 24 animals recieved vitamin D supplemented diet, from which 12 animals went under transdermal testosterone treatment. 22 animals recieved vitamin D deficient diet, from which 11 were treated with testosterone. After 8 weeks of treatment, arterioles (*in vivo* diameter of 100–200 micrometer) from left anterior coronary artery were obtained.
Main Outcome Measures: Isolated coronary arterioles were examined, *in vitro*, with pressure miography method. With videomicroscopic angiometry, the inner and outer radii of the arteriole was evaluated. Such biomechanical properties as tangential stress, normal myogenic, maximal passive vasorelaxative and vasoconstrictive tone of the arterioles were obtained and statistically analysed.
Results: Actual vitamin D status caused significant differences in the vessel's maximal smooth muscle relaxant potential, tromboxane induced contraction capacity and normal myogenic tone. Mean wallthickness was greater in vitamin D deficient animals.
Conclusions: In D hypovitaminosis lower relaxation capacites and higher wallthickness could cause the rigidity of the coronary arterioles and lead to the elevation of cardiovascular risk. Supplementation of vitamin D could improve myogenic tone and relaxation, which holds cardiovascular benefits.

Insulin resistance of coronary arteries in a rat PCOS model

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Context: The connection between androgen hormones and insulin resistance (with 70% occurence) were investigated by several researches in the past decade. In policystic ovarian syndrome (PCOS) insulin resistance could be the underlying cause of early onset hypertension and diabetes mellitus.
Objective: We investigated the effects of vitamin D status on vascular insulin resistance in PCOS in a rat model.
Methods: Forty-six adolescent female Wistar rats were divided into 4 groups and treated for 8 weeks according to the following protocol:
• vitamin D supplemented groups with and without transdermal testosterone treatment

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• vitamin D deficient groups with and without transdermal testosterone treatment

On the 6th week of the treatment oral glucose test (OGTT) was performed according to the standard method of De Vigneaud and Karr. On the 8th week coronary arterioles (diameter of 100–200 micrometer) from left anterior coronary branch were measured with pressure miography method.

Main Outcome Measures: During OGTT blood sugar levels and (0–60–120 min) and plasma insulin levels were measured (0 and 120 min) with ELISA. With videomicroscope assisted microangiometry diameter and insulin induced relaxation of the coronary arterioles were registered and analyzed with statistical tests.

Results: In both vitamin D-deficient groups, fasting plasma glucose levels were elevated compared to vitamin D treated ones. Decreased insulin induced arteriolar relaxation was detected in both testosterone treated and vitamin D-deficient groups.

Conclusions: Higher fasting plasma glucose and insulin levels, which occur in hyperandrogenisms and vitamin D deficiency, can be combined with damaged insulin induced arteriolar relaxation in coronary arteries.

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NUCB2 gene polymorphism and its relationship with nesfatin-1 levels in polycystic ovary syndrome

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Context: Nesfatin-1, encoded by the nucleobindin-2 (NUCB2) gene, is an anorexigenic protein related to energy metabolism, obesity, and insulin resistance.

Objective: The aim of this study was to evaluate NUCB2 gene polymorphism (rs757081) and its association with serum levels of nesfatin-1 in obese and nonobese women with PCOS.

Methods: The patients were recruited from the outpatient clinics of the Department of Obstetrics and Gynecology, Balikesir University School of Medicine over a 10-month period. The diagnosis of PCOS was made based on the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) criteria.

Patient(s): In the study population, we analyzed 60 patients with PCOS and 26 age-matched healthy women as controls. The patients with PCOS were divided into two groups based on body mass index (BMI): obese group ($n = 28$) or nonobese group ($n = 32$).

Intervention(s): NUCB2 was genotyped using the polymerase chain reaction-restriction (PCR) technique. Serum nesfatin-1 level was measured by enzyme-linked immunosorbent assay (ELISA).

Main outcome(s): Nesfatin-1 levels, NUCB2 genotypes, cardiometabolic risk factors.

Results: Nesfatin-1 levels in the obese PCOS group were significantly lower than those in the nonobese PCOS and control groups. There was no statistically significant difference in the distribution of NUCB2 genotypes among the groups, whereas nesfatin-1 levels in the CC and CG genotypes were lower than those in the GG genotype.

Conclusion: Nesfatin-1 decreases in PCOS, especially in obese women, and is negatively correlated with cardiometabolic risk factors. Although genotype disturbances of NUCB2 were similar among the groups, CC and CG genotypes accompanied lower nesfatin-1 levels. C allele of NUCB2 gene polymorphism and nesfatin-1 may play a role in the pathophysiology of PCOS.

MTNR1B melatonin receptor gene polymorphisms and carbohydrate metabolism in young women with polycystic ovary syndrome

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Context: The polycystic ovary syndrome (PCOS) has a pathophysiological mechanism seemingly related to decreased insulin sensitivity. Melatonin, through its receptor type 2 (MT2), interferes in insulin secretion by pancreatic beta cells, has an antioxidant action on the ovaries and, in PCOS, its levels increase. Therefore, it may be involved in the pathogenesis of the syndrome. Polymorphisms of the MTNR1B gene, which codifies MT2, have been connected with fasting glucose as well as with risk for gestational and type 2 diabetes mellitus. PCOS increases the risk for type 2 diabetes, so the study of biomarkers which can aid in the early identification of disorders of carbohydrate metabolism is of great importance. OBJECTIVE. The aim was to identify four polymorphisms of the MTNR1B gene – rs10830963C/G; rs12804291C/T; rs3781638A/C; rs1387153C/T – in young women with PCOS, correlating them with carbohydrate metabolism.

Methods: Cross-sectional study.

Patients: One hundred sixteen ambulatory patients under 24 years of age who had PCOS by the Rotterdam criteria.

Main Outcome Measures: Assessments were made of body mass index (BMI), fasting and after 2 hours of oral overcharge of 75g of glucose glycemia and insulinemia. Genetic sequencing was performed.

Results: The presence of rs10830963C/G was associated with higher levels of fasting glucose and 2 hours after overcharge insulin and that of rs3781638A/C, with higher levels of insulin 2 hours after overcharge. No differences were found in the other parameters (including BMI) or for rs12804291C/T and rs1387153C/T polymorphisms.

Conclusions: Young women with PCOS and the rs10830963C/G or rs3781638A/C polymorphism may have greater disturbances of carbohydrate metabolism, thus putting them at a higher risk of developing insulin resistance and even type 2 diabetes.

Investigation of the effects of JNK inhibitor (SP600125) on serum oxidative stress and inflammatory parameters in a rat model of polycystic ovary syndrome

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Context: c-Jun N-terminal kinase (JNK) pathway which was shown to modulate the actions of insulin in type 2 diabetic patients may have a role in the pathogenesis of PCOS which is a dilemma.

Objective: To investigate whether there is a change in serum insulin and androgen levels as well as oxidative stress and inflammatory markers as a result of inhibition of JNK pathway with SP600125.

Method: The study included 5 experimental groups as Group 1, control; Group 2, sham; Group 3, PCOS; Group 4, PCOS + SP600125 and Group 5, SP600125.
Patient(s): Fifty female, Wistar albino rats.
Intervention(s): Group 2 was consisted of the rats injected with only 0.2 ml sesame oil. In Group 3, polycystic ovary was formed with a single dose of im 4 mg estradiol valerate (EV) injection and the rats were sacrificed 60 days later. In Group 4, 60 days later following the single dose of EV injection,15 mg/kg intraperitoneal SP600125 was given for a period of 4 days and the rats were sacrificed at the 65th day. In group 5, following 15 mg/kg intraperitoneal SP600125 administration for 4 days, the rats were sacrificed at the fifth day.
Main Outcome Measure(s): Serum gonadotropin, total testosteron, insulin, adenosine deaminase (ADA) and oxidative stress.
Result(s): The number of follicular cysts and levels of total testosteron, insulin and ADA decreased significantly in PCOS group with the administration of SP600125. Serum aril esterase, xanthine oxidase, paraoxonase, total antioxidant capacity, total oxidant status measurements and oxidative stress index values did not differ between the groups ($p > 0.05$).
Conclusion: The inhibition of JNK pathway via SP600125 may improve the findings of PCOS by decreasing the levels of androgen and insulin which play critical roles in the pathogenesis. Future studies are needed to elucidate the potential roles of JNK inhibitors in the treatment of PCOS.

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Hormonal response to different intensive schedule of insulin therapy in premenopausal women with type 1 diabetes mellitus

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Introduction: It is known that type 1 Diabetes Mellitus (T1DM) is associated with polycystic ovary syndrome and other ovarian dysfunctions.Continuous subcutaneous insulin infusion (CSII) therapy improves metabolic control and reduces risk of hypoglycemia in comparison with multiple daily injection (MDI).Glycated Hb (HbA1c),body mass index and inflammatory parameters are usually considered as metabolic outcomes. However, few data are available on pituitary and gonadal hormone responses,which are involved in metabolic processes. To gain insight these relationships during CSII or MDI treatments, we evaluated dehydroepiandrosterone sulphate (DHEAS), luteinizing hormone (LH), sex hormone binding globulin (SHBG), testosterone (T) levels in a cohort of T1DM patients, comparing these two different kinds of intensive insulin administration.
Methods:We enrolled 24 women,in premenopausal period,aged 20–60 ys; 12 were treated by MDI (group1) and 12 by CSII (group2). The groups were similar for age, BMI, duration of DM.LH, SHBG, T and DHEAS were assayed by Chemiluminescent Microparticle ImmunoAssay.
Results: Despite similar glycemic control (mean$\pm$SD % HbA1c:7.8$\pm$1.2 in group 1; 7.3$\pm$0.7 in group 2), we found in group1 a trend toward higher DHEAS levels (2320.09$\pm$1638.52 vs. 1949.67$\pm$786.84 ng/ml, $p < 0.05$), T levels (0.8$\pm$1.6 vs. 0.4$\pm$0.2 ng/ml) and LH levels (16.9$\pm$18.3 vs. 6.3$\pm$5.2 mUI/ml); SHBG values were significantly lower in group 1 than group 2 (100.4$\pm$93.7 vs. 131.2$\pm$38.4 nmol/l).
Conclusion: These preliminary data seem to indicate a differential hormone response in women treated by CSII or MDI, despite similar glycemic control, with lower androgen levels and increased SHBG levels during treatment with insulin pump. Further studies are needed to clarify these complex hormonal–metabolic relationships, the prevalence of different kinds of hyperandrogenism and their prognostic/therapeutic implications.

Testosterone may influence GIP plasma level among lean women with polycystic ovary syndrome

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Context: Glucose-dependent insulinotropic peptide (GIP) belongs to the incretins which are responsible for 70% of the insulin release after oral glucose intake. Its impaired secretion was noted in several conditions involving insulin resistance, including polycystic ovary syndrome (PCOS) known as the state with increased testosterone level.
Objective: To investigate whether free androgen index (FAI) may influence basal and meal stimulated level of GIP in lean women affected by polycystic ovary syndrome.
Methods: Basal fasting blood samples were tested for lipid profile and hormonal parameters. Serum GIP, glucose and insulin concentrations were determined both at fasting and at 60 minute of the test. Statistical analyses were carried out using STATISTICA 10.
Patients: Fifty age and BMI-matched lean women were divided into two groups. Patients with phenotype with FAI<5 were classified as group 1, PCOS patients with FAI>5 formed group 2.
Interventions: All participants of the study underwent standard meal test that contained 300 kcal, 54% carbohydrates, 30% lipids and 16% protein.
Main Outcome Measures: Comparison of GIP 0′ and GIP 60′ blood concentration in two groups, relationship between FAI and GIP 0′ as well as GIP 60′ levels.
Results: Mann–Whitney test indicated a statistically significant difference in medians values between groups on fasting (36.4 pg/ml vs. 59.6 pg/ml; $p = 0.0007$) and at 60 minutes after meal test (50.1 pg/ml vs. 72.5 pg/ml; $p = 0.006$). Spearman test indicated significant correlation between FAI and GIP levels at 0′ and 60′ in total study population (0′:$R = 0.37$;$p = 0.008$; 60′:$R = 0.28$; $p = 0.049$).
Conclusions: Excess androgen activity might be a factor contributing to alter secretion of incretins in lean PCOS women. An increased GIP levels may induce hyperinsulinemia and play an additive to insulin resistance role in progression to diabetes mellitus type 2 (DMT2).

Molecular cues to cardio-metabolic risks in polycystic ovarian syndrome.

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Context:Polycystic ovary syndrome(PCOS), a leading cause of infertility,encompasses broad spectra of metabolic syndrome. Reports suggest that PCOS women are at increased risk of cardiovascular diseases(CVD), furthermore hyperhomocysteinemia (HHcy), a potential cause of CVD, is frequently associated with PCOS.
Objective: The present investigation mapped the molecular cues of HHcy to untangle the complex relationship between PCOS,CVD and HHcy.
Methods: The study protocol used experimental rat model of HHcy induced by gavaging homocysteine at a dose of 50mg/kg/day for 12weeks, and human hepatocytes, HepG2, in the presence/absence of Hcy(5mM). The state of homocysteinemia was assessed with respect to levels of homocysteine and its thiolactone,with expression of MTHFR. Evaluation of insulin and lipid profile with expression of plasminogen activator inhibitor-1(PAI-1), hepatic lipase(HL), sterol regulatory element-binding protein 2 (SREBP2), HMG-CoA reductase, LDL

receptor(LDLR) and proprotein convertase subtilisin/kexin9(PCSK9) addressed the issue of metabolic disturbance. The expression of insulin signalling molecules including PI3K, AKT, GSK3-β characterised the state of hyperinsulinemia.
Results: Elevated Hcy and Hcy-thiolactone levels marked the state of HHcy in rats. The HHcy rats developed hyperandrogenemia, glucose intolerance, hyperinsulinemia, and dyslipidemia which replicated the morphologic and metabolic features of PCOS.RT-PCR/western analyses showed alteration of the PI3K-Akt signalling cascade that marked attenuation of the insulin signalling pathway. HHcy inhibited expression of LDLR with a concomitant increase in SREBP2 and its target genes, HMG-CoA reductase and PCSK9. Western analysis showed increased expression of PAI-1 and HL that evidenced increased cardiovascular risk.
Conclusion: The study suggests an etiologic role of HHcy in the pathogenesis of PCOS with a possible risk of CVD.

The combined therapy with Myo-Inositol and D-chiro-inositol (40:1) is able to restore ovarian and metabolic profile in PCOS patients

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Polycystic Ovary Syndrome (PCOS), a relevant cause of infertility, is a heterogeneous, endocrine disorder affecting up to 10% of women in reproductive age. Currently, the diagnosis is based on the outcome of a consensus meeting held in Rotterdam in 2003. Although the consensus decided to exclude insulin resistance (IR) from the diagnostic criteria, this metabolic condition is found in 16% to 80% of PCOS patients and insulin-sensitizing agents are among the treatments routinely used in clinical practice. Two inositol isoforms, Myo-inositol (MI) and D-chiro-inositol (DCI), counteracting downstream consequences of IR, are used in the treatment of PCOS. In particular, they play different roles on glucose metabolism: MI promotes glucose uptake whereas DCI mediates glycogen synthesis. Furthermore, at ovary level, MI regulates glucose uptake and follicle stimulating hormone (FSH) signaling, whereas DCI is devoted to the insulin-mediated androgen production. The synergetic activity of the two stereoisomers results in an enhancement of insulin sensitivity and consequently in a decrease in circulating insulin, and, in the ovary, in a restored FSH sensitivity and an improved oocyte quality. In order to define the optimal clinical dosage of the two isoforms, the physiological concentrations of MI and DCI in plasma in normal women was identified and resulted in a 40:1 (MI/DCI) ratio. Some clinical trials, by adopting the formulation based on this MI:DCI ratio, evidenced the suitability of this combined approach, and provided promising. *Results*: Moreover, it was recently published a review about the results from International Consensus Conference on the use of MI and DCI which supported the efficacy of combined therapy to treat the multiple aspects of PCOS.

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(OP15) Endometriosis: from basic science to clinical management

Interconnection between eutopic and ectopic endometrium on gene expression and signalling pathways levels

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Context: Development and progression of the endometriosis can be explained only in highly individual way. The lack of a unified theory of the etiology and pathogenesis, which describes all known cases of the disease, is making the relevance to study the disease on a molecular level.
Objective: To identify all specific changes at the gene expression level and changes of intracellular signaling pathways activity in eutopic and ectopic endometrium.
Methods: Transcriptome has been investigated by microchip hybridization (CustomArray B3 Synthesizer). The profiles of activation/repression of intracellular signaling pathways (ISP) were calculated using bioinformatics method OncoFinder. We compared the profiles of activation/repression of the ISP in eutopic and ectopic endometrium.
Patients: Fifty women (average age 32 years) with different forms of endometriosis, which were not treated with hormonal medicines before surgery. To date, we have fully analyzed data of 6 patients (6 eutopic, 6 ectopic and 2 normal endometrial samples).
Intervention: laparoscopic removal of eutopic and ectopic foci, hysteroscopy with endometrial scraping.
Main Outcome Measures: We have identified the most differentially up- and down-activated signaling pathways in endometriosis foci compared to the normal endometrium (list of top-30 pathways).
Results: The primary analysis of 6 samples of eutopic and ectopic endometrium suggests qualitative changes in the regulation of gene expression and intracellular signaling pathways level.
Conclusions: Evaluation of changes in the eutopic endometrium may serve as a marker of tissue condition in ectopic foci (hysteroscopy versus relaparoscopy). The analysis of changes in the ISP activity in eutopic endometrium can be used as a reliable monitoring method of the effectiveness of the therapy and can be further used for the selection of optimal therapeutic methods.

Investigation of endometriotic lesions of different localization by direct mass spectrometry methods

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Context: Pathogenesis of endometriosis is still unknown, there is a lack of early diagnostic markers and current therapies are only symptomatic. One of the most promising methods of screening and differentiation of tissues is direct high-resolution mass spectrometry.
Objective: The aim of this work was applying the methods of direct mass spectrometry for the analysis of endometriotic tissues of different localization.
Methods: Tissue samples (endometriotic lesions and endometrium) were collected during surgical procedures. The first part of each tissue sample was analyzed by histology and the second part by mass-spectrometry. In the developed direct-spray-from-tissue ion source,

molecular species are extracted from the tissue surface by a solvent and simultaneously ionised in the electrospray. The solvent was constantly delivered to the sample to provide stable ion current. MS and MS2 spectra were registered by Thermo Finnigan LTQ FT Ultra – a combined linear trap and ICR cell mass spectrometer. Both high- and low-resolution spectra were obtained.
Patient(s): Our study included 25 patients with ovarian cysts, 22 patients with peritoneal endometriosis and 7 patients with deep infiltrative endometriosis. We have also analyzed the endometrium of women with endometriosis using mass spectrometry.
Result(s): It is shown that the mass spectrometric profiles of tissues from different endometriotic foci localization significantly different from each other.
Conclusions: We have found interesting peaks of lipids and fatty acids in women with endometriosis. In the future, the results of these studies can be used to determine the optimal treatment of patients with endometriosis and early diagnosis.

Endometriosis in a caesarean section scar – a case study literature review

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Endometriosis is defined as the presence of endometrial glands and stroma outside the uterus. It is associated with a large array of symptoms and complications and is estimated to effect from between 2 and 10% of premenopausal women, to 50% of infertile women. The most commonly affected sites are the pelvic organs and peritoneum, although other parts of the body are rarely affected. In this case study, a 35-year-old, paragravida two woman, presented with a 6-month history of sharp cramping pelvic and lower back pack pain as well as a 6 cm mass on her anterior lower abdominal wall. Her previous two deliveries were by caesarean section and she had no other past medical history. The mass was confirmed on clinical examination and ultrasound guided biopsy confirmed endometriosis. MRI scanning detected two areas of speculated soft tissue lesions encroaching the underlying rectus muscle in the anterior abdominal wall, just inferior to the umbilicus (4.4 $\times$ 2cm) and 1.2 $\times$ 2.2cm). Laparoscopy demonstrated that these were isolated lesions in the previous caesarean section scar and there was no evidence of endometriosis within the pelvis or peritoneum. A mini laparotomy was performed to excise the lesions which were then sent for histopathology examination. It was confirmed as being an endometrioma. With the ever increasing number of caesarean sections, we need to consider the maternal complication that may follow. The pathophysiology of endometriosis is uncertain. One theory is that degenerating endometrial components undergo metaplastic transformation when introduced into the abdominal cavity whilst the implantation theory, assumes the relocation of endometrial tissue with the consequential implantation and growth of live cell of the endometrial mucosa. Both these theories may theoretically happen when the uterine cavity is opened during caesarean section.

Is there a role for endocrine disruptors in endometriosis? Analysis of 9 urinary phtalate and bisphenol a metabolites

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Context: Endocrine disrupting chemicals (EDC) are substances that may interfere with the actions of endogenous hormones and may be associated with estrogen-related diseases such as endometriosis.
Objective: Test the association between phthalate and bisphenol A exposure and endometriosis by evaluating the urinary metabolites concentrations(mono-methyl phthalate, mono-isobutyl phthalate, mono-butyl phthalate, mono-cyclohexyl phthalate, mono-(ethylhexyl) phthalate, mono-isononyl phthalate, mono-octyl phthalate, mono-benzyl phthalate and bisphenol A) as biomarkers of exposure in women with endometriosis in comparison to a control group.
Patients and Methods: prospective cohort study of consecutive women with histologically proven endometriosis ($n = 30$) and a control group ($n = 22$) operated on for benign gynecological conditions without endometriosis. All particpants signed an informed consent.
Interventions: Participants answered a structured questionnaire to collect clinical and surgical data as well as food and alcohol consumption, and smoking history. Urine sample analysis was performed using liquid phase microextraction (LPME) and gas chromatography coupled with mass spectometry. Statiscal analysis included ROC curve, chi-square test and odds ratio (OR) . The study protocol was approved by the local IRB.
Results: Women age ranged from 20 to 45. Body mass index, eating and smoking habits did no differ between groups. All nine metabolites were found in different concentrarions in the urine samples in both groups. The sample contained at least one of the compounds. The values of metabolite concentrations did not differ betwen groups.
Conclusion: We could not find an association between endometriosis and biomarkers of exposure of bisphenol A and phthalates.

Innovative PCR real time-based method for endometrial hyperplasia neoplastic transformation prognosis

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Context: Currently endometrial carcinoma (EC) and endometrial hyperplasia (EH) prognostic criteria development is one of the most significant goals to work out approaches for individual treatment. Meanwhile, types of EH can cause EC in different ways even when histologically similarly verified. Thus, more accurate diagnostic and prognostic tool should be created.
Objective: We identified the malignant potential of EH variants using significant for endometrial neoplastic transformation genes mRNA expression.
Methods: Clinical laboratory evaluation, histology, real time-PCR (quantification of PTEN, MKI67 (KI67), CCNB1, BIRC5, AURKA, MYBL2, CDKN2A (p16), NDRG1, BCL2, BAX, BAG1, CTSL2, MMP11, ESR1, PGR, CD68, PTGS2 (COX2), CYP19A1, SCUBE2 mRNA).
Patients: One-hundred eleven patients were recruited into experimental group (58 patients with endometrial hyperplasia ((simple EH ($n = 31$), complex EH ($n = 15$), atypical EH ($n = 12$)), comparison group (16 patients with EC grade 1) and control group (47 patients with normal endometrium (proliferative ($n = 26$)/secretory ($n = 21$)). Intervention:endometrial biopsy/curretage.
Results:Statistic model involved PTEN, PGR, NDRG1, CTSL2, SCUBE2 expression level was created with binary logistic regression to predict EC occurence. The area under ROC curve was 0.984 ± 0.16, $p < 0.0001$. Using this model made possible to clearly classify morphologically verified EC in 93.8%; 19% of simple EH, 20% of complex EH and 42% of atypical EH were classified as having a high neoplastic potential.
Conclusion: PTEN, PGR, NDRG1, CTSL2, SCUBE2 were defined as the most significant among 19 studied genes. They were included into statistic model (linear equation) for high oncologic risk patients identification. Thus,more attention should be paid to such patients who need follow-up diagnostic monitoring, risk factors modification, long and adequate hormonal therapy or surgical treatment.

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Identification of kisspeptins in endometrial cell culture from patients with endometriosis and ex vivo

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Ott Research Institute of Obstetrics, Gynecology and Reproductology

Objective: External Genital Endometriosis (EGE) has a high prevalence in women of reproductive age. Kisspeptin (KISS) and kisspeptin receptor (KISS1R) regulate the function of metalloproteinases (MMP), which play an important role in the invasion processes. Despite this, KISS/KISS1R activity in EGE has not investigated yet.
Methods: Immunohistochemistry. Paraffin sections were incubated for 1 h with primary antibody to kisspeptin (Abcam, UK, 1:100), KISS1R (Abcam, UK, 1:300). The cells culture (CC) was isolated by enzymatic digestion (collagenase II, Gibco, USA) from human endometrial samples. Incubated at 37oC in DMEM/F-12 supplemented with 10% FBS.
Patients: In CC were studied 10 patients with EGE (mean age 32.3) classified as having stage II EGE, according to the AFA. The 19 biopsies with II-III EGE were studied immunohistochemically. As a control group 8 endometrial samples of healthy women (mean age 31.5) were investigated.
EGE: underwent laparoscopic excision for endometriosis. *Control*: endometrial pipelle biopsy. For statistical analysis, Mann–Whitney *U* test was performed using Statistica 7.0 software.
Results: CC: KISS expression was detected in half of the culture studied, and the KISS1R was detected in 6 of 10 samples. IHC: Significant KISS1/KISS1R expression was detected in 14 out of the 19 samples of women suffering from EGE. In the group of early secretary phase ($n = 3$) reaction was higher than in the middle ($n = 11$). In late phase ($n = 5$) the response was weak or absent. In control, KISS1/KISS1R expression was detected in 5 of the 8 samples.
Conclusions: The obtained CC can be used as a model for studying of EGE. Expressions of KISS/KISS1R were found. So, synthetic KISS could be used to suppress MMP activity in endometrial cells.The expression of KISS/KISS1R in 14/19 samples of EGE suggests that this system may play a role in the pathophysiology of EGE.

Differences in peripheral blood cytotoxic T-cell levels during the menstrual cycle in women with peritoneal and ovarian endometriosis relative to healthy women

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Context: Our study aimed to evaluate peripheral blood lymphocyte subpopulations during the menstrual cycle in women with peritoneal and ovarian endometriosis relative to healthy women.
Objective: The etiology of endometriosis remains unknown, but increasing evidence suggests that immune regulation may be important.
Methods: The study was prospective, case controled.
Patiens: In this study, 65 women with peritoneal and ovarian endometriosis (37 in the follicular phase and 28 in the luteal phase of the menstrual cycle) and 61 healthy women (33 in the follicular phase and 28 in the luteal phase) were enrolled. The inclusion criterion for study group was peritoneal and ovarian endometriosis. In the control group included healthy women at reproductive age.
Interventions: Flow cytometric analysis measured peripheral blood lymphocyte subpopulations. The serum levels of and cortisol were also determined.
Main outcome measure: Women with endometriosis do not exhibit fluctuations in the concentration of cytotoxic and activated peripheral blood lymphocytes during the menstrual cycle. However, a marked increase in regulatory T cell concentration in the luteal phase was detected only in endometriosis patients.
Results: In healthy controls, we detected an increased concentration of cytotoxic (CD8+) T cells and activated (HLA-DR) T cells in the luteal phase compared with the follicular phase of the menstrual cycle, whereas no such fluctuation was detected in endometriosis. Women with endometriosis had higher levels of serum cortisol, which correlated with the concentration of regulatory T cells.
Conclusions: The marked fluctuation of regulatory T cells detected in endometriosis could be attributed to altered immune response. Our data support the hypothesis that women with endometriosis lack effective cytotoxic destruction of the endometrial cells present in the peritoneal cavity.

Impact on ovarian reserve of hemostasis using a new dual wavelengths laser system (DWLS) versus bipolar coagulation after surgical stripping of monolateral endometrioma: preliminary results

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Context: Laparoscopic excision of ovarian endometrioma may reduce ovarian reserve.
Objective: The aim of our study was to assess the loss of ovarian parenchyma by dosing the Anti-Mullerian Hormone (AMH) after monolateral ovarian endometrioma ablation using a new approach on haemostasis control: a dual wavelengths laser system (DWLS), which was compared to classical bipolar coagulation (BC).
Materials and methods: Women presenting to our Unit were recruited between January and July 2015. The most part of endometrioma was excised following the conventional stripping technique. The haemostasis of residual ovarian tissue was performed using the DWLS, with a conic fiber of 1000 micron or classical bipolar forceps.
Patient(s): Thirty women with monolateral endometrioma of $\geq$ 35mm in diameter before intervention were randomized in two groups: Group 1 (DWLS haemostasis, $n = 15$) and Group 2 (bipolar coagulation, $n = 15$).
Main outcome measure: The primary aim was to estimate whether the DWLS haemostasis of the ovary is superior to bipolar coagulation in preserving ovarian reserve as assessed by use of AMH levels. The hormone assay was performed before surgery (T0), 4–6 weeks (T1) and 6–9 months after surgery (T2).
Results: Ovarian reserve showed a reduction in serum AMH levels after surgery. At both T1 and T2, BC and DWLS groups were associated to lower AMH levels ($p < 0.0001$) than baseline, with mean AMH levels at T1 of 1.23 and 1.98 ng/ml, respectively. However, while AMH levels at T2 remained decreased from baseline in the BC group (mean 1.45 ng/ml, $p < 0.0001$), in the DWLS group the AMH levels seemed to increase towards baseline levels (mean 2.36 ng/ml, $p < 0.0001$), and this difference was statistically significant between T1 and T2 ($p < 0.0001$).
Conclusions: Laser haemostasis could prevent follicular reserve loss after surgery for ovarian endometrioma.

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Increased miR-196a expression in eutopic endometrium of infertile women with minimal or mild endometriosis represses progesterone receptor by increased activation of MEK/ERK signal pathway

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Context: Progesterone resistance, mainly caused by aberrantly expressed progesterone receptor (PGR), is considered as a key factor of decreased endometrial receptivity in endometriosis.
Objective: To explore miRNA-mediated mechanism underlying aberrant PGR expression in eutopic endometrium of endometriosis.
Methods: Gene expression profiling of eutopic endometrium of minimal or mild endometriosis were examined by microarrays. qRT-PCR was used to validate the highest different expressed miR-196a. Bioinformatics analysis predicted miR-196a target PGR 3′UTR. The relationship between miR-196a level and PGR expression was studied; the role of MEK/ERK signal pathway was investigated meantime.
Patients: The study was conducted at West China Second University Hospital of Sichuan University. 22 infertile women with r-AFS I-II endometriosis and 20 disease-free subjects were enrolled.
Interventions: Microarrays, qRT-PCR, cell transfections, luciferase reporter assays, and western bolt were used.
Main Outcome Measures: The relationships between miR-196a level and PGR mRNAs in ESCs; The direct effect of miR-196a on PGR in 293T cell; Regulation of miR-196a and P-MEK/P-ERK inhibitor on P-MEK/P-ERK and PGR protein.
Results: miR-196a and P-MEK/P-ERK were significantly upregulated in eutopic endometrium of endometriosis. PGR and PGR-B mRNA were inhibited by miR-196a overexpression and upregulated by miR-196a inhibition. Luciferase reporter failed to confirm the target regulation of miR-196a on PGR.P-MEK/P-ERK protein up-regulated, PGR protein down-regulated, and PGR-A/B protein ratio up-regulated after miR-196a overexpressed. Inhibiting P-MEK/P-ERK increased PGR protein, and decreased PGR-A/B protein ratio.
Conclusions: Aberrantly expressed miR-196a dysregulates PGR expression byMEK/ERK in eutopic endometrium of minimal or mild endometriosis.

Posters

Brain/Neuroendocrinology/Gonadal Dysfunction/Adolescence/Menstrual Cycle/Thyroid

P1 Prognostic criteria menstrual cycle recovery in patients with anorexia nervosa after weight restoration

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Background: Amenorrhea is a persistent feature of Anorexia Nervosa (AN). So far not identified prognostic criteria recovery menstrual cycle after weight gain. The lack of consensus on the appointment of HRT to patients with amenorrhea despite weight restoration, creates the need to find an objective prognostic criteria for progress of the disease.
Objectives: To develop a method of forecasting of menstrual cycle restoration at AN patients after weight gain.
Patients and methods: Serum levels of leptin (L), BMI and L/BMI ratio were investigated in 20 healthy adolescents girls (control) and in 89 AN diagnosed patients (I group) at the first visit, through 3 and 6 months. On the basis of the retrospective analysis of medical cards, I group has been divided on 2 subgroups depending on a disease outcome: A – 42 patients with persistent amenorrhea; B – 47 patients with restored menstrual cycle.
Results: Through 3 months from the beginning of treatment L levels in B group exceeded the similar indicator A group in 3.5 times and exceeded the basic levels in 6.3 times. No one of the research periods L values and L/BMI ratio of A group did not come nearer to indicators of control and were below values B group. Absence of the dynamics of leptin/BMI ratio within 3 months from a starting of treatment, despite BMI increase, can be used as a criterion of the adverse forecast of restoration of menstrual cycle. On the basis of a comparative analysis of the L levels in two subgroups through 3 months from the treatment beginning, using ROC analysis we estimate diagnostic Cut-off of L and L/BMI ratio for predicting the future course of the disease.
Conclusion: At proceeding amenorrhea and presence of the criteria defining the adverse forecast of menstrual function restoration, in 3 months from a starting of treatment at achievement by the patient of the set weight, necessity of HRT is proved.

P2 Peculiarities of sheehan syndrome in the Moroccan Women

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Context: Sheehan syndrome (SS) or post-partum pituitary necrosis is a very significant cause of maternal morbidity and mortality in developing countries although.
Objective: The aim of the present study was to determine the clinical characteristics of Sheehan's syndrome in our population
Patients and Methods: In this study, we reviewed 15 cases retrospectively who were diagnosed and followed as SS in our clinic from 2010 to 2015. All patients had a history of massive hemorrhage at delivery and physical signs of Sheehan's syndrome.
Results: The patients aged 38–42 years with a mean age of 36 ± 2.3 years (mean $\pm$ SD). Time to make a definitive diagnosis of the disease ranged between 2 and 15 years with a mean of 4.8 years. There were 7 subjects with disturbances in consciousness associated with hyponatremia or hypoglycemia on admittance. Endocrine testing of the pituitary revealed secondary hypothyroidism in 13 patients, adrenal cortex failure in all patients, hypogonadotrophic hypogonadism in 14 patients . Prolactin levels were low in 6 patients. Diabetes insipidus has not been found in any patient. None of our patients had a dynamic testing. All of the patients were imaged with pituitary MRI. Twelve patients had empty sella. The obstetrical factors related to the occurrence of Sheehan syndrome were not precise in our patient.
Conclusion: SS is still a common problem in our country, especially in rural areas. Considering the duration of disease, important delays occur in diagnosis and treatment of the disease. Almost half of our cases were diagnosed at the emergency department where the identification of patients is critical. The most important clues for diagnosis of Sheehan's syndrome are lack of lactation and failure of menstrual resumption after a delivery complicated with severe hemorrhage.

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P3 Difficulties of sheehan syndrome diagnosis at the emergency department

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Introduction: Sheehan Syndrome (SS) is a rare but potentially serious complication of post-partum hemorrhage. While most cases are diagnosed based on subtle symptoms, a minority has a more acute and potentially lethal form.
Objective: We present the cases of 3 women with rare clinical presentations in order to keep in mind the SS diagnosis in women with a history of post-partum hemorrhage and to discuss the physiopathology behind this unusual presentations.
Patients: Patient 1: 29 y.o women who were admitted to the emergency department for management of a myxoedema coma associated with acute adrenal insufficiency. After initial management, the neurologic examination found a cerebellar syndrome. She had suffered a post-partum hemorrhage 5 years ago. On laboratory assessment, low hormones levels suggested panhypopituitarism. The diagnosis was confirmed by MRI of the sella. Patient 2: 36 y.o women who presented with generalized tonic-clonic seizures secondary to vomiting, dehydration and hypoglycemia. She had suffered a post-partum hemorrhage 8 months ago. The laboratory work-up confirmed hyponatremia with hypopituitarism. The CT scan showed a sellar arachoid cyst. Patient 3: A 46 y.o woman who presented with cardiac arrest secondary to a ventricular tachycardia. After recovery, Initial evaluation found a severe hypoglycemia, hyponatremia and hypokalemia. Electrocardiogram revealed prolonged QT interval. Due to the past history of post-partum hemorrhage, the patient was suspected of having pituitary insufficiency. On further hormonal assessment, this was confirmed. The patient was started on hormonal replacement therapy. She responded well and was discharged home.
Conclusion: I dentification of patients affected with Sheehan syndrome is critical to avoid delays management. Appropriate replacement therapy is able of yielding complete remission of symptoms.

P4 Bone health in young women with central hypogonadism is similar or worse than in healthy postmenopausal women

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Decreased estrogen level in perimenopausal age is associated with the increased bone mineral density (BMD) loss and is a pathogenic base of osteoporosis in the aged group of women. However BMD loss can occur not only in postmenopausal period but also in different hypoestrogenic conditions in younger women. Study aim was to estimate markers of mineral turnover and BMD in young women with the central hypogonadism and to compare them with healthy young women of similar age, and also with healthy postmenopausal women of middle/advanced age. One hundred seventy women were examined: 73 patients with the central hypogonadism (CH), isolated hypogonadism $n = 35$, hypopituitarism $n = 38$, age 25 [21.2; 30.5] y.o., amenorrhea duration 5.2 [2.3; 10.1] years; 47 healthy women (HW) with regular menstrual cycles, age 24 [23.1; 28] y.o. ($p = 0.93$ in comparison with CH) and 50 healthy postmenopausal women (HPm), age 56 [53; 58] y.o., postmenopause duration 6 [2.1; 10] years ($p = 0.9$ in comparison with CH). In CH concentrations of Ca++ and alkaline phosphatase as well as serum collagen type 1 cross-linked C-telopeptide were significantly higher than in HW of similar age however did not differ from those in HPm. BMD was significantly lower in both skeleton sites in CH in comparison with HPm (T-criteria ≤ -2.5SD in lumbar vertebras 55% and 28% respectively $p<0.001$, in a hip 27% and 7% respectively $p = 0.002$). The factors promoting lower BMD in CH were the amenorrhea duration, low levels of the total testosterone, and primary amenorrhea. Distinctions of mineral turnover markers and BMD in isolated hypogonadism and a hypopituitarism was not revealed. Thus, metabolic parameters of bone health in young women with central hypogonadism is similar to those in postmenopause and BMD is even lower than in postmenopause at the corresponding middle age.

P5 Central hypogonadism in young women is associated with premature aging

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Natural menopause is a trigger of a physiological aging due to loss of protective effects of estrogens. Premature menopause is associated with the earlier start of maturing progression. Central (hypogonadotropic) hypogonadism in women could also be a cause of persistent amenorrhea and hypoestrogenemia. Aim of study was to evaluate clinical, hormonal and biochemical parameters in women with central hypogonadism and to reveal signs of premature aging. One hundred sixty young women (25 [21; 30] y.o.) with central hypogonadism (CH), 53 healthy young women (24 [23; 28] y.o.) and 50 healthy postmenopausal women (56 [53; 58] y.o.) were examined. Frequency of psychoemotional, neurovegetative and urogenital complains was significantly higher in patients with CH compared with the healthy young women and was similar to those in postmenopausal women. Hormonal concentrations were (respectively CH, healthy young and postmenopausal women): E2 38 [33; 58] pmol/l, 167 [114; 248] pmol/l and 57 [50; 73]; total T 0.45 [0.1; 1.01] nmol/l, 1.1 [0.8; 1.4] nmol/l and 0.54 [0.49; 0.6] nmol/l, free T 8.63 [2.7; 10.8] pmol/l, 12.4 [9.15; 16.5] pmol/l and 8.6 [8.0; 9.7] pmol/l; DHEAS 2300 [230; 5690] nmol/l, 5430 [4490; 6750] nmol/l and 2311 [2160; 2900] nmol/l. So sex steroid levels were considerably lower in patients with CH than in healthy young women however were comparable with those in postmenopausal women. Prevalence of hypercholesterinemia and hypertriglyceridemia was very low in healthy young women but was high in women with CH as well as in postmenopausal women. Thus, clinical and hormonal features in young women with central hypogonadism were comparable in many aspects with those in healthy postmenopausal women of middle/older age. We can conclude that untreated central hypogonadism in young women should be considered as a model of premature ageing.

P6 Clinical features of macroprolactinemia phenomena in hyperprolactinemic women from moscow region

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According to guidelines on diagnosis and treatment of hyperprolactinemia (2011) asymptomatic patients with hyperprolactinemia should be assessed for macroprolactin. Prevalence of macroprolactin in serum (>40%) is a cause of low biological serum activity in

patients with elevated total prolactin levels. Such disassociation could be a reason of misinterpretation of clinical and hormonal data in patients with hyperprolactinemia. We analyzed clinical data and macroprolactin levels in 85 women with hyperprolactinemia: NonTumor hyperprolactinemia (NT, $n = 31$), age 33 [27; 40] y.o., MIcroadenomas (MI, $n = 32$), 32 [28; 40] y.o., MAcroadenomas (MA, $n = 22$), 36.5 [25; 46] y.o. Prolactin levels 1716 [1150; 2700] mIU/l; 2974 [1190; 3665] mIU/l and 3546 [1312; 48209] mIU/l, accordingly. Monomeric prolactin in serum was tested after polyethylene glycol precipitation. Prevalence of macroprolactin in serum was found in 16/31 (51.6%) NT, 9/32 (28.1%) MI, and 2/22 (9%) MA. A relative amount of monomeric prolactin in patients without or with macroprolactinemia was 20.5 [10; 24] % and 86 [78; 90] % accordingly. Normal levels of monomeric prolactin were found in 10/16 NT, 4/9 MI and 1/2 MA; though only 6 NT and 4 MI were asymptomatic, other patients had menstrual irregularities and/or infertility. On the other hand, there were asymptomatic cases among patients with elevated monomeric prolactin levels. In symptomatic compared with asymptomatic patients total prolactin levels did not differ in NT subgroups and were higher in MI ($p = 0.012$).
There was no clear correlation found between clinical symptoms and monomeric prolactin levels in patiens with macroprolactinemia. To avoid misunderstanding we support assessing for macroprolactin in all patients hyperprolactinemia regardless of symptoms – at least in women without pituitary lesions and microadenomas.

P7 New insights in clinical importance of macroprolactinemia

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Context: Macroprolactin is an antigen-antibody complex of a higher prolactin (PRL) molecular mass, consisting of monomeric PRL and immunoglobulin G isotype. The term macroprolactinemia is suspected for cases when the concentration of macroprolactin exceeds 60% of the total serum PRL concentration. The prevalence in hyperprolactinemic populations varies between 15 and 35%.
Objective: In majority of cases macroprolactin is of extrapituitary origin. It is possible that some changes in the pituitary PRL molecule represent an increased antigenicity to the immune system leading to the production of anti-PRL antibodies. A mild hyperprolactinemia usually occurs because macroprolactin is not readily cleared from circulation due to its higher molecular weight. Hypothalamic negative feedback mechanism by autoantibody-bound PRL is inactive because macroprolactin cannot access to the hypothalamus and therefore results in hyperprolactinemia. Reduced *in vivo* bioactivity of macroprolactin may be the reason for the lack of hyperprolactinemic symptoms. It also seems that anti-PRL autoantibodies may compete with the PRL molecule for receptor-binding thus resulting in low bioactivity. Additionally, the large molecular size of macroprolactin confined in the intravascular compartment prevents its passage through the capillary endothelium to the target cell, which may be the reason for the absence of the symptoms. In these cases when excess of macroprolactin occurs with clinical manifestations of hyperprolactinemia, macroprolactinemia should be regarded a pathological biochemical variant of hyperprolactinemia. An individualized approach and pituitary imaging, dopamine treatment, and prolonged follow-up should be applied. In cases of exclusion of all the causes and negative pituitary imaging idiopathic hyperprolactinemia should be established.

P8 Pituitary adenoma in Turner's syndrome patient under neuroleptic treatment – case report

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Context: Turner syndrome (TS) is a genetic trait related to total or partial lack of the one of X chromosomes. Interestingly, TS is more frequent in schizophrenic women compared to the general female population. Schizophrenia treatment consists of antipsychotic drug (APD) administration that can lead to drug-induced hyperprolactinemia (HPRL) and possibly to pituitary tumors.
Objective: The aim of this case report is presentation of the patient with TS, schizophrenia, hypothyroidism and pituitary adenoma and discussion of the importance of the differential diagnosis of HPRL in patients undergoing APD treatment.
Methods: Medical history, hormonal tests, neuroimaging and G-banding karyotype was collected.
Patient: Thirty-six years old woman diagnosed with TS because of short stature. In the past, she has been treated with recombinant growth hormone and after 2 years started hormonal replacement therapy. The patient had hypothyroidism and at age 30 she was diagnosed with schizophrenia. At admission she was under risperidone treatment and presented HPRL.
Intervention: Hormonal evaluation before and after APD withdrawal.
Main Outcome Measures: Serum fasting PRL concentrations, magnetic resonance imaging (MRI).
Result: In the basic state the serum PRL concentrations were 105 ng/ml. After 3 days of APD withdrawal they remained elevated (90 ng/ml). In MRI we found anterior pituitary adenoma of 2.5 mm diameter. After the psychiatric consultation the patient was prescribed aripiprazole and cabergoline treatment.
Conclusions: The TS patient may develop PRL secreting pituitary adenoma. It is important to perform differential diagnosis in patient with HPRL under APD treatment to exclude the possible organic changes. In case of concomitant pituitary adenoma interdisciplinary approach is needed and we suggest the use of long-lasting dopamine agonist and possible switch to prolactin-sparing APD.

P9 Delayed puberty revealing an uncommon genetic disease: about one case

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Context: Kallmann syndrome is a rare genetic disease which can affect both men and women. It combines hypogonadotropic hypogonadism which characterised by a failure to start or to fully complete puberty naturally; olfactory disorders such hyposmia or anosmia, impaired color vision, deafness, unilateral or bilateral renal aplasia and midline anomalies.
Objective: We report a case of this rare syndrome, responsible of delayed puberty view of infertility.
Patient – Intervention: A patient of 23 years, from a non-consanguineous marriage, consultant for delayed puberty with a Tanner stage to P2G2, without cryptorchidism or hyposmia.
Intervention: We realized a hormonal exploration, with a morphological exploration of hypothalamic–pituitary region.
Main outcome measure: We have suspected this diagnosis through the absence of development of secondary sex characteristics. The definitive diagnosis relies on the detection of the genetic anomaly, not available to our level, hormonal explorations,olfactometry, abnormalities on MRI Kallmann syndrome.

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Result: Hormonal exploration showed hypogonadotropic hypogonadism. MRI is in favor of a predominant Hypoplastic right olfactory tract and the olfactory grooves, with a normal rod.
Conclusion: With the correct diagnosis and treatment, fertility can be achieved in many cases and the risk of osteoporosis reduced.

P10 Uterine and ovarian morphology, Tanner scale and hormones in pre-menarchal girls

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The aim of our study is to investigate the uterine and ovarian ultrasonography morphology in pre-menarchal patients refered at the Paediatric Endocrinology Outpatient Clinic who needed a gynaecological evaluation between January 2014 and July 2015. This is a retrospective study performed on 50 girls with the mean age of 11.3 years. Total uterine length (TUL), maximum ovarian diameter (OD), Tanner scale (B and P), hormonal measurements were stratified according to various pubertal stages. The pelvic ultrasound evaluation was present in 49 of 50 patients, the average uterine longitudinal diameter was 44.8mm, the average maximum ovarian diameter was 25.6 mm. The presence or absence of follicles was reported in 33/50 patients. The mean measures with Tanner scale B1P1 were: TUL 34.3 mm, OD 21.6 mm; FSH 2.3 U/L, LH 0.99 U/L. In B2P2 TUL was 48.5 mm, OD 25.5 mm, FSH 6.5 U/L, LH 3.4 U/L. The data may be useful in screening cases around puberty when continuos changes take place.

P11 Routine pelvic exams: women's attitudes and beliefs in light of new guidelines

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Context: Routine pelvic exams have been a fundamental part of the annual female exam. Recent guidelines from the American College of Physicians (ACP) recommend against routine pelvic exams in asymptomatic, non-pregnant, average risk women.
Objective: To evaluate women's attitudes and beliefs about pelvic exams and how knowledge of new guidelines affects attitudes and beliefs.
Methods: A descriptive cross-sectional study was performed using a self-administered written survey. The survey was developed through a literature review, pre-tested and revised based on staff suggestions.
Patients: All non-pregnant women aged 21 years or more presenting to outpatient clinics at Mayo Clinic Arizona and Rochester were given the survey.
Interventions: After inquiring about pelvic exam practices and beliefs, participants were informed of the ACP guidelines to determine the effect on attitude and beliefs regarding pelvic exam frequency.
Main outcome measure: Self-reported responses on frequency of pelvic exam screening.
Results: Six-hundred seventy-one mostly Caucasian, married, educated female participants completed surveys. Pelvic exams were described as reassuring and respectful, and a majority believed they were useful in detecting ovarian cancer (74.6%), were necessary to screen for sexually transmitted infections (STIs)(71%) or prior to initiating contraception (67%). 54% believed they should have yearly pelvic exams, and 49% reported having yearly pelvic exams. Once presented with the ACP guideline, a significantly lower percentage planned to continue yearly pelvic exams (34.9%, $p < 0.0001$).
Conclusions: Women report pelvic exams are reassuring, important and despite evidence to the contrary, believe them necessary for STI screening or contraception initiation and useful for ovarian cancer detection. After education on screening guidelines, fewer women planned to continue yearly pelvic exams.

P12 No intra-cycle variations in markers of systemic inflammation in healthy regularly menstruating reproductive age women

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Context: Some studies demonstrated that ovulation is similar to inflammation and that cyclic variations in sex hormones modulate secretion of inflammatory biomarkers. Data available reveal conflicting results with relatively small groups studied.
Objective: To investigate the menstrual cycle-associated changes in selected markers of systemic inflammation: interleukin-6 (Il-6), endothelial leukocyte adhesion molecule (E-selectin) and high sensitivity C-reactive protein (hs-CRP).
Patients: This was a prospective study of 46 healthy and regularly menstruating women (29 ± 5 yrs of age; BMI 22.7 ± 3.9 kg/ m^2) evaluated throughout the single, natural menstrual cycle at the early follicular (EFP – 3rd-5th day), late follicular (LFP – 11th-14th day), and midluteal phase (LP – 19th–22nd day).
Methods and *Interventions*: We performed blood sampling at each visit (8–9 am) for hormonal evaluations (FSH, LH, estradiol and progesterone) and transvaginal ultrasound scans to confirm biphasic cycle. Serum concentrations of Il-6, E-selectin and hs-CRP were measured with specific ELISAs. Data analysis included repeated measures ANOVA and Pearson correlation test.
Main Outcome: Evaluation of menstrual cycle related changes in inflammatory biomarkers and their possible associations with endogenous sex steroids.
Results: There were no significant intra-cycle (EFP:LPF:LP) differences between Il-6, E-selectin and hs-CRP serum concentrations. No significant correlations were observed between these biomarkers and sex steroids.
Conclusions: Physiological cycle-related sex hormone changes had no significant influence on the variations in the systemic inflammatory markers. Inflammatory biomarkers are detected at measureable levels, but their menstrual cycle-related variations are minimal and probably not clinically relevant.

The study was supported by Polish National Science Center (N407 297640).

P13 Physiological changes of adipokines during the menstrual cycle

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Context: The cyclical effects of hormones during the menstrual cycle (MC) are responsible for driving ovulation. The information about roles

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of adipokines within the scope of MC are not definite. Leptin plays a role in sexual function and regulating the onset of puberty. Thin girls often fail to ovulate or release an egg from an ovary during menstruation cycles.
Objective: The aim of our study was to describe physiological changes of selected steroids and adipokines at women during the MC.
Methods: Their hormonal spectrum and adipokines were measured by RIA, IRMA and BioPlex.
Patient(s): Twenty-seven women with regular menstrual cycles (cycle length 28±2 days) were included in the study. The women used no hormonal contraceptives or other medicines influencing the production of steroid hormones, and were non-smokers.
Intervention(s): Fasting blood samples were taken in the morning between 7 and 8 am. The first sampling was done at the start of the menstrual cycle (1st or 2nd day). Subsequent samples were taken at regular intervals every three days.
Main Outcome Measures: During the MC we found increased levels of testosterone, estradiol, progesterone, and 17-hydroxyprogesterone during ovulation. There was a significant decrease in resistin levels during ovulation.
Results: Classical changes in gonadotropins, estrogens and progesterone during the menstrual cycle are accompanied by less striking but significant changes in 17-hydroxyprogesterone and testosterone. Adipokines show a tendency to increase during ovulation.
Conclusions: Our results demonstrate that changes to adipokines during the menstrual cycle are not substantial. Precise descriptions of physiological changes in healthy women are important in helping us understand the significance of the changes accompanying various pathological states.

P14 Menstrual disturbances in patients with disorders of lipid metabolism

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Objective: To evaluate the menstrual and hormonal abnormalities in association with hepatobiliary disorders (HBD) in women with disturbance of lipid metabolism.
Materials and methods: Of the total of women who addressed to the medical center for various reasons, 94 patients aged 18–38 years with obesity and/or dyslipidemia were included in a study. All patients underwent clinical, laboratory examination, abdominal and pelvic ultrasound.
Results: Patients were divided into 3 groups: group 1 – 45 obese patients with dyslipidemia; group 2 – 30 obese patients with normal lipid levels; group 3 – 19 patients with normal weight and dyslipidemia. In group 1 menstrual irregularities were detected in 68.8%, group 2 – 30%; group 3 – 78.9%. Obese patients had a variety of menstrual disorders: abnormal uterine bleeding, oligomenorrhea and amenorrhea. In women with dyslipidemia and normal weight the oligomenorrhea/amenorrhea predominated. Menstrual disorders in groups 1 and 2 were associated with hyperandrogenemia; in patients with normal menstrual cycle the hyperestrogenemia prevailed. In group 3 the amenorrhea with hypoestrogenic status was found in 1/3 of patients. Leptin levels were directly associated with BMI. The signs of HBD were identified in 19 cases (non-alcoholic fatty liver disease, gallbladder cholesterolosis or cholelithiasis). The HBD in group 1 among patients with menstrual irregularities were determined in 47.3%, in patients with normal menstrual cycles – in 33.3%; in group 2 – in 37.5% and in 22.2%; in group 3 – in 38% and not detected in any case, respectively.
Conclusion: Violations of lipid metabolism are highly associated with the ovarian dysfunction and should be taken into account in the management of menstrual disorders. Patients with ovarian dysfunction combined with lipid metabolism disturbances are at the risk group of early development of HBD.

P15 Serum leptin concentration in women of reproductive age with euthyroid autoimmune thyroiditis

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Context: Autoimmune thyroid disease (AITD) with elevated antithytoid peroxidase antibody (aTPO) levels appears in 12–25% of all women, apart from thyroid dysfunction. High titers of aTPO are more common in women with polycystic ovary syndrome and endometriosis. Elevated aTPO has been associated with infertility and poorer quality of life among euthyroid women, and may be related to other factors.
Objectives: The aim of the study was to measure differences in serum leptin concentration between AITD+ and AITD- patients.
Methods: All testing was completed during the follicular phase of the menstrual cycle (3–7 days after last menses) to avoid hormonal fluctuation and were measured by Chemiluminescent Microparticle Immunoassay (CMIA) and ELISA kits from Biovendor (depended on measured parameter).
Patients: The sample was comprised of 74 women who were hospitalized in the Department of Gynecological Endocrinology, Medical University of Warsaw.
Intervention: We included into the study only women who had pituitary-ovarian imbalance (World Health Organisation – WHO – group II). We excluded women with polycystic ovarian syndrome (PCOS), premature ovarian insufficiency (POI) and hyperprolactinemia.
Main outcome measure: Data collected included age, BMI, and serum antithyroid peroxidase antibodies (aTPO), serum TSH, serum fT4, serum FSH, serum estradiol and serum leptin. AITD positive status was defined as serum aTPO greater than 5.6 mIU/ml.
Results: Serum leptin concentrations were significantly higher in AITD+ patients compared to AITD− patients (17.13 ng/ml [SD 7.66] vs. 12.78 ng/ml [SD 7.28]; $p < 0.05$). No differences by AITD status were found in age, BMI, TSH, FSH, estradiol and fT4.
Conclusions: Serum leptin concentrations were higher in patients with AITD than in patients without AITD.

P16 Novel composite heterozygous mutation of the receptor for hCG and LH leading to 46XY disorder of sexual development

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Context: Intrauterine differentiation of the male genital organs depends on testosterone secretion, which is closely regulated by the LHCGR, the target receptor for both hCG and LH. Dysfunction of the LHCGR leads to Leydig cell hypoplasia, which, in its most severe form, corresponds to a phenotype of 46,XY disorder of sexual development (DSD).
Objective: We report a case of DSD due to a novel composite heterozygous mutation of the LHCGR.
Patient and method: The 16-year-old patient was referred for a pediatric consultation for the exploration of pubertal delay and primary amenorrhea. Clinically, the patient was tall for her age and parental heights(178.8cm, >P97) with normal weight (79 kg). There were no signs of pubertal development (B1P1–2 Tanner stage). Hormonal assessment found very low estradiol, low progesterone and testosterone, high LH (32.6UI/l) and normal FSH. Pelvic imaging revealed the absence of mullerian derivatives and localized inguinal testicles bilaterally. Patient's karyotype was found to be 46,XY. To avoid malignant transformation, gonadectomy was performed.

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Intervention: Genetic analysis of the LHCGR gene was performed.
Results: A composite heterozygote mutation of the LHCGR gene was found: deletion of 4 aminoacids and substitution of leucine 16 of the signal peptide on one allele and duplication of 9 aminoacids from the signal peptide on the other allele. The first two genetic anomalies were inherited from the father, while the last from the mother.
Conclusions: We report a case of DSD in a 46,XY patient with an inactive LHCGR. As hCG intrauterine action is necessary for testosterone secretion, differentiation of male genital organs and testicular descent, the patient's phenotype was female. Mutations in the signal peptide of the LHCGR are rare and the genetic anomaly found in our patient has never been previously reported.

P17 Severe bone alteration in young anorexic women: impact of weight recovery on bone density

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Introduction: Anorexia nervosa (AN) is characterized by an extreme fear of gaining weight, a body weight under 85% of expected, a distorted self-image, and the absence of three consecutive menstrual periods1. AN causes various endocrine changes leading to a low bone mineral density2 (BMD). Osteoporosis (OP) in premenopausal patients is defined as a low BMD, combined with chronic malnutrition, eating disorders, hypogonadism, glucocorticoid exposure, and previous fractures3. Consequently, early diagnosis and intervention are important to minimize bone loss. M&M A prospective clinical study that analyses bone alteration in AN patients compared to lean controls that evaluates the influence of weight recovery on bone status. Forty-five anorexic women aging between 14 and 44 years were enrolled. All patients underwent a bone evaluation by dual-energy X-ray absorptiometry (DXA) as well as BMI, BMD, body fat distribution and hormonal level assessment. A cohort of 15 patients had DXA examinations at 6 and 12 months during a dietary protocol to restore body weight. Results Patients with AN had amenorrhea for a year and showed a significantly lower BMI and body fat compared with lean controls ($p < 0.01$ and 0.001 respectively). T and Z-scores of vertebral and femur neck were significantly lower in the AN group ($p < 0.05$ and $p < 0.01$). Moreover, 50.1% of AN patients had osteopenia and 34.6% had OP. At 6 months, AN patients who followed a weight gain dietary regime showed a partial menstrual cycle recovery (46.1%), 5% increase in BMI and 34% increase in body fat. The menstrual cycle was restored in 45% of the patients.
Conclusions: AN patients have high prevalence of osteopenia- OP with a severe compromise of bone metabolism even when compared to peers with lean body mass. Weight and menstrual cycle recovery, brings an end to the pathology related gradual bone compromise

P18 Character of menstrual function disorders of adolscent girls

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Context: Primary amenorrhea can be related to the insufficient secretion of gonadotropins or with primary ovarian insufficiency and also with the physical health of adolscent.

Objective: The aim of this study was determination of types of menstrual disorders for teenagers and to identify possible reasons of their development. Studies were undertaken among 543 student girls of colleges. Examination, anthropometric measuring, count of index of body weight, degree of development of secondary sexual characters was conducted.
Methods: Age was ranged from 15 to 17. In all from a number inspected different menstrual disorders are educed at 8.5%. Among them 1.1% in age 16 had primary and 0.9% had secondary amenorrhea by duration from 8 months to two years. Hypomenstrual syndrome was observed at 2.2%, algomenorrhea at 4.2%.
Results: Research of BMI of these girls showed that at 25% of them there were deficit of weight and 34.8% conversely had surplus mass and obesity. Normal cycle also educed with deficit of body weight (8.2%) and increase of BMI at 6.8%. At majority of them (54.3%) identified the hepatitis carried in childhood. More than 40% of adolescent in childhood were often ill by catarrhal diseases and their inspection identified the hypoplasia of thyroid gland. The ultrasound of small pelvis educed the hypoplasia of uterus of I–II degree at 80 girls with violations of cycle and among healthy educed – hypoplasia of I – degree at 12.9. Only at 1 girl (0.2%) an ultrasonic and MRI of uterus showed the small lesion up to 3 cm and small ovaries.
Conclusion: Menstrual disorders of adolescent girls often is complication of the inflammatory diseases and endocrine violations carried in childhood. Improvement of physical health of children of prepubertat age will allows to decrease the frequency of menstrual disorders for adolescent.

P19 Ectopic adrenal gland in ovarian tissue: an unusual case report

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Introduction: Developmental anomalies of the adrenal gland are classified into heteropias, renal-adrenal adherence and ectopic or accessory tissue. The adrenal cells have a double embryological origin. The cortex arises from the coelomic mesothelium and the medulla from neural crest ectoderm. Ectopic adrenocortical gland can be found in tissues such as the celiac axis, the broad ligament, the adnexa of the testes and the spermatic cord.
Case Report: We report a case of a 63-year-old obese female with hirsutism, acne and acantosi nigricans. Laboratory data highlights increased levels of androgens. Diagnostic features reveals normal morphology and function of adrenocortical gland. In view of clinical picture, menopausal status of patient and suspected diagnosis of hyperplasia of Leydig-Sertoli cells, she was subjected to bilateral oophorectomy.
Results: Histological examination shows small groups cells expressing MART-1 and some cells appear weakly positive for CKAE1AE3, with the characters of ectopic adrenal cells.
Discussion: This case reports an unusual localization of ectopic adrenal gland secreting androgens in ovarian tissue.

P20 Studio epidemiologico delle patologie mammarie negli ex-voto in ceramica di Castelli

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Introduzione: Gli ex-voto sono una particolare categoria di oggetti devozionali, ampiamente utilizzata in Italia come una forma di preghiera, o come simbolo di ringraziamento per una grazia ricevuta.

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Storicamente, le offerte votive venivano appese nelle chiese per mostrare gratitudine per un miracolo, una guarigione di una malattia o come una supplica. Gli ex-voto qui presentati sono unici al mondo: sono maioliche provenienti dalla chiesa di San Rocco nel comune di Castelli (Abruzzo). Raffigurano lesioni tridimensionali benigne e maligne della mammella, realizzando un accurato e personalizzato ritratto delle patologie mammarie; mostrano fini dettagli di ogni malattia, dimostrando una conoscenza accurata dell'anatomia femminile e delle patologie in questione.
Materiali e Metodi: Studio degli ex-voto in ceramica del XIX secolo conservati presso il Museo delle Ceramiche di Castelli (Teramo). Classificazione accurata degli ex-voto raffiguranti mammelle ed ipotesi diagnostiche ed epidemiologiche delle patologie in esse rappresentate.
Risultati: Dei 18 ex-voto mammari donati a San Rocco, in 17 casi è possibile sospettare un cancro mammario con presenza di morbo di Paget; in 7 casi si pone sospetto di mastite batterica; in 3 casi si può sospettare una ferita da taglio o una procedura chirurgica; 3 casi indicherebbero un'ulcera da allattamento; 3 casi indicherebbero dei lipomi; 2 casi mostrerebbero un eczema; 2 casi indicherebbero una lesione sifilitica o ulcera venerea; 2 casi mostrerebbero un ematoma o steatonecrosi; in 1 caso si pone diagnosi di papilloma intraduttale ed in 1 caso di ascesso mammario.
Conclusioni: La presenza di così tante mammelle in ceramica nella chiesa di San Rocco a Castelli, conferma l'importanza dell'allattamento al seno come principale fonte di vita per i figli e la sua nobile importanza tra la popolazione femminile locale. Gli ex-voto mammari indicherebbero un'alta incidenza di malattie del seno tra la popolazione locale, forse una mutazione genetica in una matriarca, degna di ulteriori approfondimenti. Ciò conferma l'utilità dell'arte nello studio epidemiologico delle malattie.

P21 About a Kallmann syndrome in women

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Introduction: Kallmann syndrome is a genetic disorder characterized by the association of hypogonadotropic hypogonadism and hyposmia or anosmia. Kallmann syndrome in women is associated in the literature to discontent of self-esteem due to altered body image in adolescent girls. We report a case of Kallmann syndrome in a young patient of 26 years.
Case report: A 26-year-old woman is seen for primary amenorrhea. She has a delayed puberty without mental retardation. She relates accompanying signs such as asthenia since the age of adolescence especially early morning and late afternoon that worsened since 2 years. Occasionally, it presents with dizziness hot flashes at a rate of once a week, especially in the evening. The patient relates also an impaired libido. On the other hand, she had no weight loss, no hair removal, no polyuria-polydipsia, no galactorrhoea and no eating disorders. Physical examination notes: BP: 110/80mmHg, fasting capillary glycemia: 0.89 g/l, BMI 21.6kg/ m^2. Tanner stage: B4P3. Axillary and pubic hair sparse with small external genitals. The balance sheet showed: FSH: 0.3mUI/ml LH: 0.50mUI/ml. Estradiol: 22.27 pg/ml PRL: 3.75ng/ml, Cortisolemia at 8am: 28microg/dl. Hypothalamo-hypophysal MRI talked about an endosellar arachnoidocèle with normal olfactory bulbs. Pelvic ultrasonography showed impaired size of the external genitalia without visualization of the ovaries. Osteodensitometry assessed an osteoporosis (Femoral T-score of: −3.5DS). The patient is currently under treatment with hormone replacement recovery cycle.
Discussion: Kallmann syndrome is rare in women. The diagnosis is based on clinical findings because the sensitivity of the genetic study is only 30%. The objective of the management is to maintain secondary sex characteristics and secondly to induce fertility.

P22 Cyproterone acetate versus leuprolide acetate in combination with transdermal estradiol in transwomen: a comparison of safety and effectiveness.

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Introduction: To retrospectively compare the effectiveness and safety of one-year administration of transdermal estradiol (E) with cyproterone acetate (CPA) or Leuprolide acetate (Leu) in transwomen. Materials and methods. Forty transwomen received 50 mg of CPA daily orally ($n = 20$; CPA+E group) or Leu at a dose of 3.75 mg i.m. monthly ($n = 20$; Leu+E group) in combination with transdermal estradiol (TE) at a dose of 1 or 2 mg daily for one year. Reproductive hormones, biochemical parameters, body composition and bone mineral density were assessed.
Results: Luteinizing hormone (LH), follicle-stimulating hormone (FSH) and total testosterone (T) levels were significantly decreased by month three of hormone administration in both groups and continued to decrease until month 12; the decrease of LH levels in the first three months was significantly faster in the Leu+E group. Prolactin was significantly increased at month 12 in the CPA+E group only. Bone metabolism parameters and bone mineral density as detected at Dual Energy X-ray Absorptiometry did not significantly change in either group, apart from a statistically significant increase of parathormone after 52 weeks of Leu administration. Total cholesterol and high-density lipoproteins (HDL) cholesterol were significantly increased in the Leu+E group and reduced in the CPA+E group. No major adverse effects were registered in either group. Psychological well-being parameters did not differ between the two groups.
Conclusions: Preliminary results suggest that CPA and Leu in combination with TE are equally effective in the suppression of gonadotropins and testosterone levels over one year. Whether the different effects on HDL-cholesterol may lead to long-term different cardiovascular safety profiles remains to be defined.

P23 3D Ultrasound and Power Doppler vascular indices in diagnosing polycystic ovarian syndrome in adolescents

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Context: Polycystic ovarian syndrome (PCOS) is the most common reproductive endocrinopathy in adolescents.
Objective: To determine the role of 3D Power Doppler vascular indices in diagnosing PCOS in adolescents.
Patients: This prospective observational study included 50 sexually active adolescents. They were divided into 2 groups: Group I: 24 adolescents with PCOS; Group II (control): 26 adolescents with regular menstrual cycles and normal ovaries on ultrasound scan.
Interventions and Methods: Pulsatility index (PI) and resistance index (RI) of the uterine artery and ovary were measured by 2D Doppler imaging. 3D Ultrasound (VOCAL™) program was used to calculate the volume of both ovaries. Power Doppler ovarian stromal histogram facility of VOCAL™ was used to measure vascularization index (VI), flow index (FI) and vascularization flow index (VFI). Serum LH and FSH were determined on cycle day 2–4. An independent-sample *t*-test was used to compare the variables. p Values <0.05 were considered to be statistically significant.
Results: Adolescents with PCOS had higher ovarian volume (13.48 cm^3 vs. 6.12 cm^3, $p < 0.001$). Uterine and ovarian arteries blood flow parameters revealed significantly increased RI and PI values and

maximal peak velocity. These parameters correlated with serum hormone levels. Stromal volume (11.52 vs. 4.88 cm^3, $p<0.001$) and stromal vascularization (FI: 36.98 vs. 31.26, $p<0.05$; VI: 4.86 vs. 3.82%, $p<0.001$; VFI: 1.62 vs. 0.96, $p<0.001$) were also increased in adolescents with PCOS. There was a positive correlation between VI, FI, VFI and LH in the PCOS group.
Conclusions: PCOS adolescents had significantly increased ovarian stromal VI, FI, VFI, and ovarian volume compared to adolescents with a regular menstrual cycles. The positive correlation between vascular indices and LH suggests that these indices may be useful in diagnosing PCOS in adolescents.

P24 Impaired endothelial function in young women with functional hypothalamic amenorrhea

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Aim of the study: Cardiovascular disease is the leading cause of death among women. Vascular endothelial dysfunction is an early marker of arteriosclerosis. Women with functional hypothalamic amenorrhea present an increased risk for cardiovascular disease, which may be attributed to the early onset of vascular endothelial dysfunction associated with sex steroid deficiency.
Materials and methods: This was a prospective study of the evaluation of flow-mediated dilation of branchial artery (vascular endothelial function) in women with functional hypothalamic amenorrhea and controls. Endothelial function was assessed in 12 women with functional hypothalamic amenorrhea and was compared with the endothelial function of 12 age-matched control women. Brachial artery diameter was measured both during hyperemia (an index of endothelium-dependent vasodilation) and in response to glyceryl trinitrate (an index of endothelium-independent vasodilation).
Results: The mean age of women with functional hypothalamic amenorrhea was 22.6 years and of controls 23.7 years (p = NS). The body mass index of women with functional hypothalamic amenorrhea was 18.97 kg/ m^2 and of controls 25.99 kg/ m^2 ($p<0.001$). Flow-mediated dilation was significantly lower in women with functional hypothalamic amenorrhea (increase by 2.96%, range 0.20–6.66%) than in control women (increase by 9.15%, range 5.71–14.29%; $p<0.001$). Glyceryl trinitrate-induced vasodilation did not differ between the groups.
Conclusions: Young women with functional hypothalamic amenorrhea have significant vascular endothelial dysfunction. Early onset of endothelial dysfunction associated with sex steroid deficiency may contribute to the increased risk of cardiovascular disease in young women with functional hypothalamic amenorrhea.

P25 Gynecological morbidity among students in dynamics of training

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Five hundred female students surveyed in the first year of the Baikal State University of Economics and Law, Irkutsk (17.2±0.03 years). Four hundred girls out of a total number of inspections in the dynamics of two years in the third year (19.3±0.04 years). Two hundred students received a therapeutic and prophylactic measures. Parts of students was assigned dydrogesterone 10 mg to 14 to 25 day cycle for 4–6 months. The proportion of female students with gynecological diseases increased from 78% in the first year of study to 85.8% in the third year, (P ($\chi 2$) <0.01). Disorders of menstruation and menstrual irregularities took first place ranking, inflammatory diseases of the of the genitals – the second, neuroendocrine syndromes – the third, the disease of the cervix and mastopathy – fourth grade. 5.8% of female students are fertile, 9.8% – is supposed fertile, 2.9% – primarily sterile, 81.5% – with unknown fertility. Most sexually active students used contraceptive methods (76.5% are sexually active). Ovarian dysfunction was 10.8% for the first time examined the students of the first course. Dysfunction of the ovaries in women in the treatment group in the 3 course was at 1.6% versus the group without treatment, 15.6% (p <0.05). The frequency of premenstrual syndrome was at 19.2% for the first time examined girls in the first year of study. The girls who received treatment, the frequency of the syndrome premenstrual tension decreased to 12.8% in the third year against 26.7% of girls who had no treatment (p <0.05). Dysmenorrhea was at 30.2% of the girls first year and 38.4% of girls of the third course, did not receive treatment. The share of dysmenorrhea in a group girls who received treatment (third year) decreased to 18.7% (p <0.05). The complex of therapeutic measures, including the appointment of progesterone helped significantly reduce the incidence of gynecological students.

P26 Anti-Müllerian hormone (AMH) correlates with luteinizing hormone (LH).

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Context: It has been demonstrated that as AMH decreases to undetectable values, the menopause appears in 5 years, being the ideal marker for ovarian reserve, even better than age because of its stability in spite of hormonal contraception, menstrual cycle or pregnancy, so it can be determined at any time. Other studies have demonstrated more specificity in LH for the diagnosis of POI while AMH has no superiority differentiating groups with elevation of FSH and women with POI.
Objectives: Demonstrate the correlation of AMH and LH to justificate the use of recombinant LH (LHr).
Methods: We studied 453 patients with infertility and determine LH and AMH serum concentrations; sample was obtained at day 3 of menstrual cycle. Statistics pack were used for analysis (SPSS 22).
Patient(s): We study 453 serum samples of women with infertility.
Intervention(s): Observational; prospective study
Main Outcome Measure(s): Sample was determined by Beckman-Coulter.
Result(s): The AMH and LH were present in 100% patients. They were associated by Pearson correlation (0.117).
Conclusions: We correlate AMH and LH; this explained by two-cells/two-gonadotropins model, which evaluates the stimulation by LH converting cholesterol to androgens in theca cells with paralleled aromatization of androgens in granulose cells. This model specifies the requirement of collaboration between theca and granulose cells. While there is elevation of FSH in some patients, others tend to increase their LH determinations, diminishing estradiol and causing initial phase of ovarian insufficiency, with deficient granulose cells and progressive increase in the production of LH. This demonstrated the need of LH replacement at low AMH levels.

P27 some demographic factors attendant to Mastalgia in patients

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Introduction: Mastalgia is a painful complaint that its physiological or pathological reason is unknown yet. Approximately, 66% of healthy women have become Mastalgia. common breast disease that causes pain include: Function and physiological disorders, inflammatory diseases, benign tumors are rarely malignant tumors. This study

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aimed to investigate some demographic and individual factors attendant to Mastalgia in patients in Rasht.
Material and Methods: This study study is a descriptive – cross sectional on 347 patients with breast pain, who referred to breast cancer specialist center in the city of Rasht in 2014. Participants were clinical examined by a gynecologist and were asked them ultrasound and mammography by a trained. Demographics and individual information that includes: age, body mass index, marital status, family history of breast cancer, history of breast problems were collected and analyzed by statistical software spss and descriptive and analytical statistical tests.
Results: The mean age and mean Age at menopause were 38/48 ± 10/72 years and 47/24±5/9 years, respectively. The majority of patients (88/2%) were married. Methods of contraception, most of patients (54%) were used withdrawal, 28 of patients(9/1%) were used hormonal methods of contraception. The most of them(82/6%) did not report a history of breast disease. Also 12/2% of them were healthy and did not have any in their breast disease and 293 of them did not have any in their relatives and family history of breast disease.
Conclusion: It is proved right now that many diseases and pains caused by the lack of balance in lifestyle, nutrition and weight. So in the mild pain, with clinical examinations to reassure that there is no serious problem and in cases of moderate to severe pain, following treatment is recommended, including psychological counseling.

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P28 Association of FSH receptor gene polymorphism with menarche age

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Context: The effect of genetic factors on menarche age is strong. There is a contribution between estrogen and estrogen receptor genes and menarche age. FSH is an important hormone that plays a major role in the regulation of folliculogenesis and estrogen synthesis.
Objective: The aim of this study was to investigate the influence of FSH receptor polymorphisms Asn680Ser and Thr307Ala on menarche age.
Methods: FSH receptor gene polymorphisms were investigated in Turkish women who were admitted to Selcuk University between May 2013 and November 2014. Information about menarche age was obtained through interviews. The study was approved by the Selcuk University Ethics Committee and supported by Selcuk University Scientific Projects fund.
Patients: Polymorphic analysis of the FSH receptor gene was performed in 209 health women who had undergone an annual health examination.
Intervention: Genomic DNA was obtained from peripheral blood leukocytes and polymorphisms were investigated using restriction fragment length polymorphism analysis.
Main Outcome Measures: Menarche age and FSH receptor genotype results were investigated.
Results: The mean age at menarche was 12.95±1.62 years. The overall frequencies for Asn680Ser variants NN, NS and SS were 40.2%, 36.4% and 23.4%, respectively whereas Thr307Ala variants TT, TA and AA were 34.4%, 41.1% and 24.4%, respectively. Menarche occurred 3.6 months earlier in TN homozygote genotype than AS homozygotes and the mean age of menarche was 2.5 months earlier in TN homozygotes when compared with all other study subjects but the differences were not statistically significant ($p = 0.966$ and $p = 0.986$, respectively).
Conclusions: The Ala307Thr and Ser680Asn polymorphisms of FSH receptor gene are not associated with menarche age in Turkish population.

P29 Swyer syndrome: how long can the surgery be postponed

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Swyer syndrome or XY gonadal dysgenesis is a condition of defective gonadal differentiation in phenotypic females with a normal set of male (XY) karyotype. The syndrome is usually indentified in puberty as phenotypic girls seek medical attention for primary amenorrhea and sexual infantilism. Affected individuals are at about 30% risk of developing a germ cell neoplasm, therefore streak gonads require surgical removal. However, it is not yet exactly clear when the surgery should be performed. We report case series of 3 patients diagnosed with Swyer syndrome and recently treated at Vilnius University Hospital Santariskiu Klinikos, tertiary care medical center, Department of Gynecology. The first patient underwent prophylactic laparoscopic gonadectomy at age of 26 years, pathologic examination revealed malignant transformation in both gonads; the second one experienced unilateral adnexectomy by laparotomy at age of 16 years due to large ovarian mass, it was confirmed benign; the third one is 6 years old at the moment, there are no changes on her pelvic ultrasound. The question is how long can the surgery be postponed? We are going to try answering this question in our poster.

P30 Hormonal gynaecological disorders associated with viral hepatitis

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In Moldova 9% of population suffer from chronic viral hepatitis (VH). The problem of correlation between VH and menstrual dysfunctions is still actual, being determined by high incidence and severity of specific to this association abnormalities. The aim of the study – to evaluate the correlation between hormonal and biochemical parameters at women of reproductive age with different types of VH. In the study were included 80 women with menstrual dysfunctions and HV, with neither pelvic nor other endocrine diseases. The severity of HV was set on the basis of clinical and biochemical blood parameters. Hormonal profile was fixed up by appreciation of level of progesterone, estradiol, prolactin, FSH, LH. The mean age of examined patient – 26.0±5 years. The biochemical parameters (level of bilirubin, transaminases, alkaline phosphatase were increased considerably (4–20 times in comparison with control group), especially in mixed VH. Changes have been observed in cholesterol level and β-lipoprotein, which are evidently decreased in all patients with all types of VH. Normal menstrual cycle was present only at 7.5±2.48% women. Hypermenstrual syndrome and uterine bleeding were found at 2.4% patients, at 22.6±1.48% patients – hypomenstrual syndrome and 67.5% – amenorrhea. The disorder was more obvious in HVC (35.3±2.3%) and mix-hepatitis (28.58±1.08%). Analysis of hormonés level denots a wide range of fluctuation of estradiol and progesterone. Hyperestrogenemia was higher in severe HVB and mixed forms (in 63.75±3.1% cases). Progesterone was dropped at 67.5±2.9% patients. Level of FSH and LH slightly exceeded. In the most of cases high prolactin level was registered. The results reveal serious disturbances in all hepatic functions at patients with viral hepatitis with direct repercussions over the ovaries, which lead to disturbance of ovarian hormone biosynthesis.

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P31 Surgical management of ovarian lesions in children and adolescents: conservative vs. non-conservative approach

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Introduction: We discuss about clinical aspects, diagnosis, and current surgical indications of ovarian masses in children, starting from a critical analysis of our own treated cases.
Materials and methods: We analyze the management of ovarian masses in a total of 159 children surgically treated for 166 ovarian lesions (7 bilateral) from January 2001 to January 2015. Operative treatments were classified as emergency versus non-emergency surgery in conformity with the clinical presentation. Surgical procedures were led to laparoscopic or open surgery and were performed using either the conservative or non-conservative approach. The conservative surgery consists in detorsion alone in case of twisted normal ovary, simple surveillance or cystectomy for functional lesions, tumorectomy in presence of benign neoplasms. The non-conservative approach consists in the removal of the ovary and, if involved, of the fallopian tube.
Results: Histological examination revealed 82 (49.4%) functional lesions, 67 (40.4%) benign neoplasms, 5 (3%) malignant ones, and 12 (7.2%) torsed normal ovaries. Ovarian torsion occurred in 42 cases (25.3%). A conservative treatment was performed in 98 (59%) girls: 75 (76.5%) treated in non-emergency and 23 (23.5%) in emergency surgery; laparoscopic approach in 49 cases (50%) and open surgery in 49 (50%). The remaining 68 (40.9%) ovarian masses underwent nonconservative surgery: 49 cases (72.1%) non-emergency and 19 (27.9%) emergency; laparoscopy in 27 patients (39.7%) and open surgery in 41(60.3%).
Conclusions: Fertility preservation should be a goal in the treatment. The management of ovarian torsion should include adnexal detorsion and recovery of the ovarian tissue. In case of benign neoplasms, laparoscopic tumorectomy should be the gold standard; in early stage malignant tumors, fertility-sparing surgery with accurate staging is preferred.

P32 Tratti di personalità e attitudini verso la ritmicità mestruale: un'indagine condotta in due Cliniche Universitarie del Nord Italia

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Introduzione: La nostra indagine ha esplorato i desideri delle donne in età fertile in tema di ciclicità mestruale, stabilendo una relazione fra tratti di personalità e preferenze per un ritmo mestruale differente da quello fisiologico o derivante dall'uso di contraccezione ormonale combinata (CHC) convenzionale.
Materiali e metodi: Studio trasversale condotto in due cliniche dell'Italia Settentrionale mediante un questionario autosomministrato in un campione di donne in età fertile ($n = 545$; età 18–44 anni) che stavano utilizzando, avevano utilizzato o non-avevano mai utilizzato una CHC.
Risultati: Il 45% del campione vorrebbe modificare la frequenza del proprio sanguinamento utilizzando una CHC. Sono soprattutto donne di età >39 anni (57%) e <30 anni (46%), mentre donne fra 30 e 39 anni sono meno favorevoli (31%) ($\chi 2$: 9.1; $p = 0.01$). Sono principalmente le pregresse utilizzatrici di CHC (51%) e le attuali (49%) a voler cambiare ritmo di sanguinamento, mentre le mai utilizzatrici hanno un'attitudine negativa (71%) ($\chi 2$:18.7; $p = 0.001$). La prima scelta ricade sul regime flessibile (33%), seguito da regimi estesi con sanguinamento ogni tre mesi (22%) e senza previsione di sanguinamento (18%). L'attitudine positiva alla modificazione della ritmicità mestruale ha come ragioni principali evitare la dismenorrea (43%) e avere maggiore libertà sessuale (36%), sportiva e lavorativa (35%), mentre l'attitudine negativa ha come ragione principale la naturalità della mestruazione (59%). Le donne con maggiore apertura mentale ($p = 0.005$) ed estroversione ($p = 0.001$) sono le più favorevoli alla modifica del pattern di sanguinamento.
Conclusioni: L'età, il pregresso utilizzo di CHC, le problematiche mestruali e una personalità estroversa e aperta al nuovo correlano con un'attitudine positiva alla modifica del pattern di sanguinamento, principalmente secondo un regime flessibile e trimestrale.

P33 Interval changes in bone mineral density over 24 months in young women with hypothalamic amenorrhoea and apparent athlete triad syndrome

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Objectives: To evaluate the bone mineral density (BMD) changes in collegiate dance students undergoing intensive training between a 24-months interval and to correlate these changes to the presence of apparent athlete triad syndrome (ATS)
Methods: Forty full time collegiate dance students were recruited from a tertiary Performing Arts Institute. All subjects had basic anthropometric measurements, hormonal profile, pelvic ultrasound, and dual energy X-ray absorptiometry (DXA) and quantitative peripheral CT scans (pQCT). The measurements were then repeated after 22–24 months. Those who had persistent oligo/amenorrhoea and were underweight with a BMI $<18.5\,kg/cm^2$ were categorized as having apparent ATS. The measurements were compared to non-exercising eumenorrheic adolescents in the same age group recruited from a general gynaecology clinic.
Results: Of a total of 40 dance students and 21 control subjects, the exercising group showed a larger interval increment in lumbar spine BMD at the 24 month interval ($0.068\,g/cm^2$ vs. $0.016\,g/\,cm^2$, $p = 0.001$) as well hip BMD values (neck of femur 0.0439 vs. $0.008\,g/\,cm^2$; trochanter 0.023 vs. $0.016\,g/\,cm^2$; Ward's triangle 0.035 vs. $0.010\,g/\,cm^2$; $p \leq 0.001$). Volumetric BMD also showed similar trends (distal radius core BMD 21.2 vs. 13.1 g/ cm^3, distal tibia core 20.5 vs. 14 g/ cm^3, $p = 0.001$). When dance students with ($n = 13$) or without apparent ATS ($n = 27$) were compared, no significant differences were seen in axial BMD values, while marginally lower radial core BMD (16.3 vs. 23.5 g/ cm^3, $p = 0.029$) and tibial core BMD (16.8 vs. 22.2 g/ cm^3, $p = 0.048$) increments were seen in the ATS group.
Conclusion: Young women undergoing regular intensive weight-bearing exercises have higher BMD increments as compared to non-exercising women, even in the presence of apparent athlete triad syndrome.

P34 Prevention of abnormal uterine bleeding relapses in female adolescents

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Objective: Abnormal pubertal uterine bleeding (APUB) is a most serious menstrual disorder of female adolescents which can often lead to

anaemic condition causing serious health hazards. The aim of this study is to examine the effectiveness of treatment and rehabilitation of patients with APUB.
Design and Methods: Cases of 79 pediatric and adolescent female patients with APUB aged 11–19 were surveyed on the clinical base of the Department of Obstetrics, Gynaecology and Pediatric Gynecology of Kharkiv National Medical University. The complex investigation comprised: general clinical and gynaecological examination, ultrasonic scanning (with Dopplerography), vaginascopy, colpositology, endocrinological (serum hormone levels) and bacteriological examination.
Results: It has been found that in 22.8% of patients APUB arose with menarche, in 36.7% – 1–3 years after it; 40.5% of female adolescents have been diagnosed with relapses of APUB. Differential schemes of treatment have been worked out; they used combined oral contraceptives with synthetic estrogen and progestogen components (3–6 months). After that APUB patients were given Dydrogesteronum (DUPHASTON) to prevent relapses.
Conclusion: Conservative hormonal therapy has demonstrated a positive clinical effect in 97.5% of all cases, APUB relapses being 3 times lower. Surgical treatment has been given to 2 patients according to vital indications.

P35 Circulating serotonin and a potential dual function: menopausal bone turnover and neuroendocrine marker

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Context: Circulating serotonin (Ser) is a euroendocrine marker of NETs (neuroendocrine tumors as stomacf, adrenals, etc). Peripheral serotonin directly inhibits bone formation, potentially serving as surrogate bone turnover marker (BTM).
Objective: Ser assay on a osteoporotic patient with adrenal masses.
Methods: evaluation of bone parameters, Ser (fasting blood withdrawn), and adrenal phenotype.
Patient: A 78-year Caucasian female with intermittent hot flushes, diffuse bone pain including lumbar associated with persistent anemia and inflammatory syndrome for the last 6 months. She affirms prior diagnosis of untreated osteoporosis.
Intervention: She was suspected for NETs but computed tomography showed bilateral AT of 5.5 cm, respective 3.5 cm and vertebral fractures. Mild persistent cortisolemia is confirmed with serum chromogranin A twice as normal. A benign gastric ulcer is detected and correlated with anemia and chronic inflammation.
Main Outcome Measure: 25-Hydroxy vitamin D is 4 ng/mL (N>30); BTM are high: osteocalcin (57ng/mL, N:15–46), CrossLaps (1.5ng/mL, N:<1.008), P1NP (105.6ng/mL, N:<74) but not Ser (119ng/mL, N:80–450).
Result: Osteoporosis is confirmed: lumbar DXA bone mineral density of 0.838g/sqcm, T-score of −3SD, Z-score of −1.4SD. The patient refused andrenalectomy and zolendronic acid plus vitamin D is given.
Conclusions: Whether serotonin will serve as an additional BTM in selected cases (especially if endocrine tumors are confirmed) it is still unclear. Similarly, classical BTM have a high individual variation so statements regarding their general use are not possible. 5-hydroxytriptamine action on bone includes a paracrine mechanism and a distant indirect central action via leptin so the monoamine blood assay might not be strictly correlated with skeleton anomalies.

Partially support of this work is from project 33878/11.11.2014.

P36 The main risk factors of menstrual disorders among adolescent girls with hypothalamic dysfunction

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Context: Amenorrhea is detected in 32.9%, abnormal uterine bleeding in 24% among adolescent girls with hypothalamic dysfunction. Objective The purpose of the study is to analyze the socio-economic and medico-biological factors of menstrual violations among adolescent girls with the hypothalamic dysfunction.
Methods: 2 × 2 crosstabs were used for risk assessment. The impact of a specific factor was evaluated by a relative risk (RR) of comparing these two groups of the exposed and unexposed. Patients The study involved 170 girls with hypothalamic dysfunction, who were admitted to the gynecological department with menstrual disorders from 2000 to 2014, the average age of girls was 14.41 ± 0.26 years.
Results: The most significant risk factors for menstrual disorders in adolescent girls with hypothalamic dysfunction were identified. The RR of the primary and secondary amenorrhea and abnormal uterine bleeding were determined. The ranking of amenorrhea risk factors was conducted. The first rank place – cardiomyopathy ($R^2 = 2.9$), retinal angiopathy ($R^2 = 2.8$), the second – duration of hypothalamic dysfunction more than 5 years ($R^2 = 2$), the third – obesity (body mass index >30 kg/m^2) ($R^2 = 1.9$), the fourth – antenatal factors: asphyxia ($R^2 = 1.7$), preeclampsia ($R^2 = 1.6$). Also significant risk factors were – extra classes with a tutor ($R^2 = 2.3$), "tense relationship" in the family ($R^2 = 1.8$), low-income in the family ($R^2 = 1.7$). Significant risk factors for abnormal uterine bleeding in girls with hypothalamic dysfunction were identified: the first rank place takes retinal angiopathy ($R^2 = 1.9$), the second – herpetic infection ($R^2 = 1.7$) and the threat of miscarriage of a mother ($R^2 = 1.7$).
Conclusions: This study showed the basic medico-biological and socio-economic risk factors in the development of menstrual disorders in adolescent girls with hypothalamic dysfunction.

P37 Structure of menstrual disorders in adolescent girls with hypothalamic dysfunction, depending on the body mass index

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Context: Menstrual disorders have a different structure in overweight and obese girls with hypothalamic dysfunction.
Objective: The purpose of the study is to determine the structure of menstrual disorders in adolescent girls with hypothalamic dysfunction, depending on the body mass index (BMI).
Methods: Characteristics of the menstrual cycle included an age of menarche, regularity and duration of menstruation, menstruation achiness. An analysis of differences in the frequencies of two independent groups was performed using $\chi 2$.

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Patients: The study involved 170 girls with hypothalamic dysfunction, admitted to gynecological department with menstrual disorders from 2000 to 2014.
Results: Sixty-six girls with hypothalamic dysfunction were found overweight, 104 – were found to be obese, BMI was 26.1±1.42 and 33.36±3.03 kg/m^2 ($p = 0.000$), average age–14.18±1.9 and 14.56±1.6 years ($p = 0.17$), respectively. The age of menarche in overweight girls was 11.42±0.89 years, in girls with obesity – 11.65±0.8 years($p = 0.17$). The regular menstrual cycle was noted in 59.1% of overweight girls and 25.0% in girls with obesity. An oligomenorrhea was diagnosed more often in overweight girls at 78.8%, against 59.6% in girls with obesity ($p = 0.09$). A secondary amenorrhea is significantly more frequent in girls with obesity in 40.4%, against 21.2% of overweight girls ($p = 0.009$). A primary amenorrhea was diagnosed in 30.8% of girls with obesity and in 16.7% of overweight girls ($p = 0.039$). Dysmenorrhea was diagnosed in 7.6% and 8.7% of girls from the respective groups ($p = 0.80$). Abnormal uterine bleeding observed in 26.0% of overweight girls and in 22.7% girls with obesity.
Conclusions: Thus, primary and secondary amenorrhea were diagnosed significantly more often in girls with hypothalamic dysfunction with obesity, than in overweight girls. Oligomenorrhea and abnormal uterine bleeding was of great impact in both groups.

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Endometrium/DUB/ Fibroids/POF/ Endometriosis

P38 Endometrial polyps in women affected by levothyroxine-treated hypothyroidism: histological features, immunohistochemical findings, and possible explanation of etiopathogenic mechanism: a pilot study.

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Context: Tertiary-care academic center
Objective: Aim of the study was to investigate the possible different expression of estrogen(ERs) and progesterone(PRs) receptors in glandular and stromal cells of endometrial polyps(EPs) in a cohort of postmenopausal women with hypothyroidism receiving levothyroxine administration compared to a cohort of euthyroid women.
Methods: A pilot case-control study on asymptomatic women referred to hysteroscopy for suspicious of large endometrial polyps (>2 cm).
Patient(s): 22 Patients: 12 women with hypothyroidism levothyroxine-treated for at least 1 year (GroupA), and 10 women with normal thyroid function (GroupB).
Intervention(s):All patients received an hysteroscopic polipectomy and all EPs were histologically analyzed. The immunohistochemical staining for PR and ER nuclear and cytoplasmic expression was performed and scored by 2 pathologists.
Main Outcome Measure(s): Stromal and glandular intensity (categorized in "low positive" and "high positive") of ERs and PRs and their percentage.
Result(s):The 2 groups were similar for ERs and PRs intensity rates in EPs glandular cells, but ERs percentage expression was 60% in 2/3 of GroupA in respect to only 1/3 of GroupB EPs. Considering stromal EPs intensity: it was "low positive" in 2 and 9 cases, "high positive" in 10 and 1 cases in GroupA and B respectively. ERs stromal expression had a different trend in our Groups, but a borderline statistical significance.
Conclusions:Our data suggest a hyper-expression of ERs pathway in hypothyroid women in replacement therapy, which may be related to a non-physiological TSH circadian oscillation. The stimulation of TSH receptors may promote the activity of iodothyronine deiodinase type2 (2DIO) and consequently the circulating exogenous thyroxine can be locally metabolized in active form by 2DIO, stimulating local ERs.

P39 Special genetic polymorphism among patients with endometrial hyperplasia

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Objective: Endometrial hyperplasia is the result of hormonal changes but hormone therapy increase the risk of thrombosis.
Methods: We analyzed the results of examination of 250 patients. Fisheŕs exact test was used to estimate the association between the presence of hypercoagulation status and genetic determinants of the thrombophilia. Genotyping was performed in 10 genes.
Results: Among the patients of the main group 18% had hypercoagulability and intravascular coagulation activation before treatment, the causes of which had to be clarified in the course of our study. The results of the investigation of polymorphism G1639A gene VKORC1 are extremely interesting. The risk of venous thrombosis among women with allele A is 2.22 times as high as in the presence of an alternative allele G (OR = 2.22, df = 1.25–3.96) on bilateral Fisher's exact test. The presence of homozygous genotype A/A increases the risk of venous thrombosis several times. There was only one case of deep vein thrombosis in this group of patients with genotype A/A of gene VKORC1 after hormonal treatment. Therefore, homozygous genotype A/A of gene VKORC1 as an additional risk factor for thrombosis is highly prevalent among patients with endometrial hyperplasia. We should try to avoid hormone therapy for carriers of homozygous genotype A/A of gene VKORC1 with endometrial hyperplasia, regardless of the presence of metabolic syndrome, as alternative – an endometrial ablation.
Conclusion: Genetic defects of coagulation and fibrinolytic systems increases the risk of venous thrombosis.

Keywords

Endometrial hyperplasia, thrombophilia, polymorphism

P40 To the problem of pathogenesis of abnormal uterine bleedings and the possibility of their correction

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In Ukraine 21–38% of women of late reproductive age suffers from Endometrial Hyperplasia (EH). Abnormal uterine bleedings (AUB) watched in this category of patients in 94% of cases are the most frequent manifestation of hyperplastic endometrial processes.

Research objective is to find out the possible molecular and cellular determinants of originating AUB in late reproductive age and the ways of their correction. One hundred twenty-two women of late reproductive age with AUB were surveyed. An estimate of nuclei ploidy of endometrial cells, immunohistochemical examination (proliferation and apoptosis markers, receptive endometrial status) in hyperplasia identification were done. The pathogenetic well-grounded choice of AUB treatment based on EH was offered. The obtained microspectrophotometric data testified to forming of various clones of endometrial cells. Thus nuclei of epitheliocytes under a genetic material content were mainly within paratriploid value that, most likely, could be due to the effect of the long-term estrogenic action. On immunohistochemical examinations it was revealed that glandular and glandular-cystic endometrial hyperplasia were characterized by a moderate expression of receptors as to estrogens and progesterone, a trend to decrease of protein p27 and p53 and the main mediator of apoptosis caspase-3. Estradiol valerate/dienogest was offered to patients with glandular and glandular-cystic endometrial hyperplasia as hormonal therapy that promoted restoring the balance of molecular-biological processes by blocking of proliferation, induction of processes of apoptosis and AUB absence both in time of taking combined oral contraceptive (COC) and after drug withdrawal.

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P41 Successful pregnancy following the complex treatment of gigantic uterine fibroids using ulipristal acetate Prof. A.L. Tikhomirov (Obstetrics and Gynecology Chair of the Medical Department of A.I. Evdokimov Moscow State Medical & Dental University, Moscow, Russia)

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Context: The pregnancy after giant fibroid treatment is presented. The effective combination of pharmacotherapy and surgery are described.
Material and Methods: On 6\04\2013 rapidly growing uterine fibroids corresponding to 30 weeks of gestation, with intramural fibroid lesion of 22 cm in diameter, menometrorrhagias and iron-deficiency anemia (2nd stage) were diagnosed in a 27-year-old young and nulliparous woman having reproductive during her examination for menometrorrhagia. Intervtntion: On 20\04\2013 the patient underwent the procedure of uterine fibroid embolization (UFE). Following the UFE (05–06\2013), the reduction of duration and volume of menstrual blood loss and belly shrinkage were observed. However, her menometrorrhagia manifestations relapsed after UFE in 06\2013. On 15\07\2013 the diagnostic curettage and hysteroscopy, which confirmed severe deformation of the uterus (histological examination: endometrium in proliferation stage), were performed. On 16\08\2013, menometrorrhagia relapse occurred. In 09\2013 the reduction of the fibroid lesion up to $15 \times 11 \times 13$ cm was observed but the uterus cavity was still severely deformed. Profusive menstruations persisted and 2nd stage anemia (Hb 77 g/L) was diagnosed. UA (5 mg per day for 3 months) was prescribed. UA caused amenorrhea and in 3 months allowed to restore hemoglobin level (up to 110 g/L). UA also allowed to decrease additionally the fibroid lesion size by 27%. On 09\01\2014, the laparotomic myommyometroectomia was performed, blood loss up to 150 ml.
Results: 15.10.1.5 Successful delivery through C-section with live female fetus (3330 g).
Conclusion: To create conditions for organ-preserving treatment and reduction of surgical intervention risks, a differential approach combining medical and surgical treatment for large uterine fibroids is required.

P42 Prospective study on the use of low doses of GnRH agonist in patients with uterine leyomiomas

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Context: Leiomyomas are the most common solid tumors in women. Although over 50% of women with uterine fibroids are asymptomatic, many of them suffer bleeding and pelvic symptoms.
Objective: To assess the improvement in symptoms of patients and the reduction in uterine and fibroids volume after using GnRH agonist injection under expanded regimen.
Methods: This prospective study followed patients with leiomyomas and pelvic pain from Gynecology clinic of the University Hospital Gaffree e Guinle in the city of Rio de janeiro–Brazil. The patients received two doses of goserelin acetate 3.6mg, by subcutaneous depot injection under expanded regimen with interval of 45 days.
Patients: 11 women with fibroids in radiologic diagnosis and uterine volume over than 200 cm^3. Intervention: The patients had their pain complaints quantified by the visual analog scale of pain, did an ultrasound to identify uterine volume and fibroid volume and did laboratory exams (haemoglobin, haematocrit, serum iron) before and after treatment. The Research Ethics Committee approved this project by the CAAE:38378814.0.0000.5258.
Main Outcome Measure(s): the uterine volume and fibroids had a significancy reduction. Dysmenorrhea, dyspareunia, pelvic pain and compressive symptoms improved comparing the results of visual analog scale of pain before and after treatment.
Results: The size reduction of uterine volume was 33% in average ($p = 0.0009766$) and decreased 38% of uterine fibroid ($p = 0.001953$), haematocrit level increased 5% ($p = 0.123$), haemoglobin increased 6% ($p = 0.1925$) and iron levels 14% ($p = 0.018$).
Conclusion: This expanded regimen is effective in reducing pelvic symptoms, increasing blood levels to turn the surgery after with less complications. The decrease of uterine volume and leiomyomas also may turn the presurgical treatment as an option to make smaller incision and to turn myomectomy possible.

P43 The evaluation of proliferation in peritoneal adhesions in patients with uterine fibroid in consideration of progenitor cells expression

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Context: Uterine fibroids (UF) are most often gynecological pathology among women of reproductive age. Prevention of adhesion formation is important part of reconstructive surgery in these group of patients.
Objective: evaluation of proliferation in peritoneal adhesions in consideration of progenitor cells expression in tissue samples in patients with UF.
Methods: Biopsies of UF, adhesions, and normal peritoneum were investigated using by immunohystochemical studies (IHC) of C-KIT.
Patients: 110 patients with UF were enrolled in the study.
Interventions: Laparoscopic myomectomy and intraoperative evaluation of pelvic adhesions was performed in all patients.
Main outcome: Strong correlation between the severity of pelvic adhesions in patients with UF and the number of progenitor cells in tissue samples were observed.
Measures: Positive IHC stain on C-KIT characterized by brown color of the nuclei and cytoplasm in cells of patients with UF. Positive C-KIT cells were revealed between adipose cells and fibrotic fibers in pelvic adhesion samples.

Results: Positive C-KIT cells were determined in a small amount in UF samples. Statistically significant differences in the expression of C-KIT between the samples of UF and peritoneum, peritoneum and adhesions ($p < 0.05$) were detected. It should be noted that women, depending on the severity of adhesions in the abdominal cavity a number of positive cells was different. In the tissue of adhesions of 1st degree positive IHC stain on C-KIT cells were in 1% in the field of view, in adhesions of 2 – 3rd degree to 7% in the field of view
Conclusion: We found strong direct correlation between the severity of pelvic adhesions in patients with UF and the number of progenitor cells in tissue samples. Thereby the progenitor cells should be an important factor for pelvic adhesion formation in patients with UF.

P44 Effect of transforming growth factor tgf-β2 cell proliferation fibroids

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One of the main growth factors involved in the pathogenesis of uterine fibroids, a transforming growth factor, which plays a key role in the implementation and regulation of proliferation, differentiation of tissues and others. Transforming growth factor beta (TGF-β) – a family of polypeptides which both stimulate and inhibit cell proliferation. Depending on the concentration can have the opposite effect. To study the role of the transforming growth factor in the pathogenesis of fibroids and its various morphological types. Studies were conducted to determine the cytotoxic activity of the transforming factor regarding temporary cell culture. To do this, we took operational materials from women of childbearing age with uterine myoma (multiple symptomatic uterine myoma, proliferative type) who underwent amputation surgery of the uterus. The average age of patients was 44.0±1.15. The indications for surgery were symptomatic uterine fibroids (a symptom of bleeding, pain and growth, the effects on adjacent organs). The resulting cell culture time were divided into five groups depending on the dose actuating. After incubation under magnification of 280 times produce a sub-account of the living, the dead and apoptotic cells. The cytotoxic activity was expressed in % of the living, the dead and apoptotic cells. The greatest efficiency of the suppression of life transformed cells found under the influence of transforming factor in a dose of 1000 mg/10•106 cells. Our studies have shown that transforming growth factor beta 2 in the growth of fibroids is able, under certain conditions, dosage, to suppress tumor growth. With pronounced dose-dependent cytotoxic effect on proliferating cells of uterine fibroids, transforming growth factor beta 2 able to induce the appearance of apoptotic cells.

P45 Features conservative treatment of uterine fibroids women of reproductive age

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Uterine myoma is a benign form of the reproductive system, it is often the cause of infertility. A new and very effective drug in the treatment of fibroids found is a se-lective progesterone receptor modulator (SPRM-ulipristal acetate-UPA). UPA is reduces the size of fibroids, inhibits proliferation and promotes apoptosis. Objec-tive: to study the effectiveness of conservative treatment of uterine fibroids in women of reproductive age with infertility. We examined 37 women aged 23 to 38 years old. Patients were divided into 2 groups: group 1 – 20 patients with large and medium nodes ranging in size from 3 to 7 cm, of whom 12 had infertility due to deformation of the uterine cavity, 2-group – 17 patients with small myoma nodes up to 3 cm in diameter, of which 8 was observed infertility. All patients performed a pelvic examination, physical ex-amination, ultrasound Doppler blood flow in and around the myoma node. The study included women with subserous and/or intramural myoma nodes distorting the uterus. Monitoring the effectiveness of conservative treatment was determined by the deterioration in the quality of blood flow in and around the nodes with the Doppler. Thus, the small nodes up to 15 mm in diameter in patients of both groups is almost disappeared, and larger than 15 mm is reduced by half or one third of its original size. Conservative myomectomy performed 12 patients of 1-group after 3 month course UPA since there was a distortion of the uterine cavity, and 8 patients of 2-group patients. Indications for reappointment UPA were clinical signs of re-lapse – an increase of nodes on ultrasound, appearance of hemorrhage, the appear-ance of pain. Modern approaches to conservative treatment of uterine fibroids is the appointment SPRM. UPA to reduce the percentage of radical operations, and increase the frequency of organ-preserving operations.

P46 The characteristic of women with primary premature ovarian insufficiency (PPOI) and sohlh2 mutation

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Introduction: PPOI is a syndrome characterized with hypergonadotropic amenhorrea and hypoestrogenism. SOHLH2 gene is situated on chromosome 13 and is testis-specific factor important for spermatogenesis, oogenesis and folliculogenesis. The aim of the study was to investigate women,s characteristic with PPOI and those with PPOI where SOHLH2 mutation was found.
Methods: The study covered ethically homogenous population of the Serbian women with equally socio-economic and alimentary status. 168 women with PPOI younger than 40 years of age, with normal cariotype was included in the study from 2007 to 2010 and was divided in two groups. First group was formed by 159 women with PPOI and the second group formed by 9 women with SOHLH2 mutation. Hormonal analysis, body height and weight was measured for all women. The difference in FSH, LH, E2, PRL, P and BMI was investigate. For the statistical analysis Mann–Whitney *U* test was used.
Results: The results showed no statistical difference between the 2 groups for FSH (U=614.0; $p = 0.475$), LH (U=496.0; $p = 0.665$), PRL (U=600.5; $p = 0.418$), P (U=620.5; $p = 0.503$) as well, as for BMI and the age when women entered PPOI.
Conclusion: The results showed that genetic mutation SOHLH2 as the reason for PPOI caused no influence on hormonal changes, BMI and the age entering the PPOI.

P47 Particular features of familial and sporadic premature ovarian failure

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Objective: Identify the differences between familial and sporadic premature ovarian failure.
Methods: The study was conducted on the basis of the Republican Specialized Scientific and Practical Medical Center of Endocrinology, in

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collaboration with the Centre for Medical Genetics of the Academy of Sciences of the Republic of Uzbekistan. A total of 121 women were examined during the study. Of these 47 subjects were included in Group 1 consisting of women with familial premature ovarian failure and 74 subjects were included in Group 2 consisting of women with sporadic forms of premature ovarian failure. The study included the following phases: medical and reproductive history; physical examination; hormonal status assessment, genetic analysis to determination of inhibin mutations

Results: the mean age of the surveyed women was 38.8 and 35.4 years respectively. When evaluating hormonal status in women of Group 1 we noted statistically significant decrease in estradiol and testosterone level: 47.82 ± 12.71 and 1.04 ± 0.41, respectively (p <0.001). Free androgen index was 1.23 ± 0.03 and 2.38 ± 0.9 (p <0.001), respectively. The level of antibodies to thyroid peroxidase was statistically higher in Group 2 subjects as compared to Group 1 and was equal to 17.3 ± 1.6 (p <0.001). Inhibin B gene mutation was observed in 14.8% of women in Group 1. The age of menopause before 40 years of age in mothers of Group 1 women was observed in 27 subjects.

Conclusions: There are no phenotypic differences between familial and sporadic forms of premature ovarian failure. The greatest prevalence of premature ovarian failure was observed in women whose mothers had menopause before 40 years of age. Genetic alterations were common in subjects with familial forms of premature ovarian failure, while sporadic forms of premature ovarian failure often were caused by autoimmune disorders.

P48 Ultrasonic characteristics of uterus and ovaries in women with hypogonadotropic hypogonadism before and after hormonal therapy

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There is a lack of specific data concerning uterus and ovarian characteristics in women with hypogonadotropic hypogonadism (HH). We prospectively evaluated pelvic ultrasounds in 74 women age 25 [21; 30] with HH (36 with isolated HH and 38 with hypopituitarism), 43 healthy women age 24 [23; 28] (HW) and 26 postmenopausal women age 56 [53; 58] (PM). Uterus volume (UV) was significantly lower in HH (17 [11; 24] cm^3) comparing with HW (42 [38; 56] cm^3, $p < 0.001$) and PM (28 [22; 40] cm^3, $p<0.001$). Also ovarian volume (OV) was lower in HH (2.2 [1.1; 4.6] cm^3) comparing with HW (9.1 [8.1; 9.6] cm^3, $p<0.001$) though it was higher than in PM (1.1 [0.5; 1.9] cm^3, $p=0.03$). UV and OV did not differ in isolated HH and hypopituitarism subgroups however were significantly lower in patients with amenorrhea I compared to amenorrhea II (UV 13 [10; 19] and 20 [14; 28] cm^3 $p<0.001$; OV 1.3 [0.5; 1.9] and 4.1 [2.1; 5.8] cm^3 $p<0.001$, respectively). OV in patients with amenorrhea I didn't differ from those in PM ($p = 0.75$). In women with HH ovarian volume correlated with duration of amenorrhea ($r = -0.37$ $p = 0.003$), FSH and LH levels ($r = 0.37$ $p = 0.002$; $r = 0.28$ $p = 0.002$). After treatment with estradiol 2 mg and didrogesterone 10 mg in cyclic manner (12–36 months) UV was 24.4 [15.9; 32.6] cm^3 ($p<0.001$ in comparison with HH before treatment) but these parameters were still lower than in HW ($p<0.001$). In women with initial amenorrhea I or II there were no difference in UV on treatment: 27.2 [13.7; 31.8] and 22.7 [18.4; 33.9] cm^3 ($p=0.21$). Uterus and ovarian characteristics in untreated women with HH differed from healthy women of comparable age and were similar by many criteria to those in postmenopausal women. Hormonal therapy increased uterus volume but could not restore it up to physiological level. Amenorrhea I was more important factor of genital hypoplasia than hypopituitarism.

P49 Ozone (O3)–oxygen mixture therapy inhibits endometrial implant growth

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Objective: The purpose of this study was to investigate the potential therapeutic efficiency of ozone therapy in the treatment of experimental endometriosis in rats.

Methods: Fifteen rats were divided into three groups, which were labeled as the (1) sham control, (2) the ozone (treated with intraperitoneal ozone-oxygen mixture) and (3) the GnRH-agonist (given single dose (1 mg) leuprolide acetate depot formulation) groups. Endometrial implant activity of superoxide dismutase (SOD), malondialdehyde (MDA), interleukin-1β (IL-1 β), IL-6, tumor necrosis factor-α (TNF- α), and vasculary endothelial growth factor (VEGF) were measured after ozone-therapy. Furthermore, peritoneal fluid activity of SOD, MDA, and TNF-α were also measured before and after ozone-therapy. Serum AMH levels of animals were given ozone-therapy and control groups were measured.

Results: Rats given ozone-therapy showed significantly reduced endometriotic implant volumes. After ozone-therapy, a significant increase in activity of SOD in peritoneal fluid was detected. Conversely, implant levels of SOD in rats given ozone therapy was found to be significantly decreased. Both peritoneal fluid and implant levels of MDA were significantly decreased after ozone-therapy. Implant levels of TNF-α, IL-1β, and IL-6 were significantly increased following ozone-therapy. VEGF levels of implant was found to be unchanged after ozone-therapy. Serum AMH levels of animals were given ozone-therapy and control groups were similar. The number of both primordial and preantral follicles were significantly decreased after ozone-therapy. However, the number of atretic follicles were similar in ozone-therapy and control groups.

Conclusions: Repeated administration of ozone-oxygen therapy in non-toxic doses inhibits growth of endometrial implants.

P50 Modern aspects of treatment for endometriosis and their pharmacological and economic assessment in the Caucasian region

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Purpose: Endometriosis is common in the Caucasian region. According to the official data,based on the birth rate in the region and its low social-economic status, we decided to study the therapeutic efficacy and safety of Dienogest for the treatment of endometriosis in women of reproductive age and to assess its pharmaco-economic effect in our region.

Methods: Open, randomised, multi-center trial in which patients are administered DNG orally at a daily dose 2mg or 4mg for a maximum period of 6 months. 72 patients (30±6years of age) with histologically confirmed endometriosis at stages I, II or III according to the rAFS score. Patients were randomised to one of two treatment groups via random selection. Endometriosis symptoms were recorded at baseline and after 4.16 and 24weeks of treatment. The effect of DNG on endometriotic lesions was assessed by transvaginal ultrasound. The final assessment of the effect was done via endoscopy after the end of the treatment. Adverse events were documented throughout the study.

Results: 34 patients were included in the 2mg group and 38-in the 4mg.group. After 24weeks of treatment,the rates for dysmenorrhea

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were reduced from 73% to 14% in the 2mg group and 12% in the 4mg group. Pre-menstrual pain was reported by 4% of patients out of 51% in both treatment groups,whereas the degree of dyspareunia was reduced from 63% to 9% in the 2mg group and 7% in the 4mg group according to VAS. The most common adverse events were mood swings – 12% in the 2mg group and 14.2% in the 4mg group; headache – 7.1% in the 2mg group and 9.7% in the 4mg group;acne – 7% in the 2mg group and 9.4% in the 4mg group,nausea – 5% in the 2mg group and 7.2% in the 4mg group.
Conclusions:In Caucasian women the 2mg/day dose of DNG has almost the same effect as the 4mg dose. Moreover, its more safe and comfortable for patients with less severe adverse sffects and thus has a clear economic advantage.

P51 Activated Hippo/YAP pathway promotes cell proliferation and anti-apoptosis in endometrial stromal cells of endometriosis

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Context: The imbalance in cell proliferation and apoptosis is considered as an important role in the pathogenesis of endometriosis, but the exact mechanisms remains unclear. A newly established signaling pathway– Hippo/YAP pathway plays a critical role in proliferation and apoptosis processes. However, the studies focus on Hippo/YAP pathway and endometriosis are lack.
Objective: The objective was to explore the function of Hippo/YAP pathway in endometriosis.
Setting and Design: The expression of YAP was firstly investigated in endometrium of women with or without endometriosis. The role of YAP in cell proliferation and apoptosis is identified by transfection of endometrial stromal cells (ESCs) *in vitro* and endometriosis animal model of nude mice and subsequent Verteporfin treatments *in vivo*.
Results: Our results revealed that increased expression of YAP and decreased expression of p-YAP in ectopic and eutopic endometrium, compared with normal endometrium. YAP knockdown in eutopic ESCs decreased cell proliferation and enhanced cell apoptosis companied with decreased expression of TEAD1, CTGF, and BCL-2; while overexpression of YAP resulted in increased proliferation and decreased apoptosis of normal ESCs with increased expression of TEAD1, CTGF, and BCL-2. By chromatin immunoprecipitation- quantitative PCR, CTGF and BCL-2 were identified as directly downstream target genes of YAP-TEAD1 active complex. In endometriosis animal model of nude mice treated with Verteporfin, the size of endometriotic lesions was significantly reduced.
Conclusions: Our study indicated that Hippo/YAP signaling pathway plays a critical role in the pathogenesis of endometriosis and should represent as a novel direction for therapeutic method against endometriosis.

P52 Hypoxia normalization prevents endometriosis development.

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Context: Induction and progression of endometriosis depends on endometrial tissue implantation, survival and angiogenesis. Formation of early implants is supported by local hypoxic milieu and it have been proven that partial oxygen pressure is important factor in pathogenesis of endometriosis. Myo-inositol trispyrophospate (ITPP) is a potent allosteric effector of hematoglobin that reduces tissue hypoxia.
Objective: The aim of the study was to investigate the impact of hypoxia normalization on endometriosis development in murine model.
Methods: Endometriosis was surgically induced in C57BL/6 female mice by autotransplantation of uterine horn fragments to parietal peritoneum. Mice were injected intraperitonealy by ITPP solution or vehicle.
Main Outcome Measure: Number of induced lesions, growth dynamic and lesion size was measured.
Result(s): Hypoxia normalization remarkably inhibits endometrial lesion growth and reduces lesion number.
Conclusions: The results confirm that hypoxia impact on pathogenesis of endometriosis. Hypoxia normalization seems to be a promising therapeutic approach for endometriosis.

P53 Clinico-morphological and molecular mechanisms of the pathogenesis of pelvic pain associated with external genital endometriosis

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Context: 80% in women with pelvic pain have endometriosis. The pathogenetic mechanisms of pain in endometriosis remains unclear.
Objective: Research the neurogenic mechanisms of pain syndrome pathogenesis in external genital endometriosis (EGE).
Methods: Pain intensity was assessed with VAS. The immunohistochemical study was performed with use of antibodies for neuromarkers (PGP9.5, NF, NGF; NGFRp75).
Materials: The study included 52 women with external genital endometriosis, with pain syndrome (I group) and without pain syndrome (II group).
Interventions: All patients underwent organ-preserving laparoscopic surgery by resection and/or coagulation of the EGE foci.
Main Outcome Measure(s): Patients in group I had recurrent (54.5%) or persistent (45.4%) pelvic pain. By VAS score, moderate pain was experienced by 45.5%, and severe pain by 54.5% of women. In group I, there were higher levels of depression, situational and personal anxiety, significantly reduced state of health, activity, mood and the main categories of quality of life ($p < 0.05$).
Results: The endometrial tissue had mostly a perivascular and intravascular, as well as a perineural growth pattern with signs of destruction of nerve fibers and the formation of ''amputation neuroma.'' In both groups neuromarkers expressions were observed in the nerve fibers of endometrial stromal heterotopias, as well as in the nerve fibers of surrounding tissue. It was established that a significantly higher expression of neuromarkers was observed in patients with the painful form of EGE ($p < 0.05$).
Conclusion: Painful form of EGE is characterized by a more specific and severe clinical course, which is associated with a high expression of neuromarkers and its receptor in the foci of endometriosis and the surrounding tissue, as well as with the molecular features that provide new growth of nerve fibers and formation of pain.

P54 Determination of angiogenesis markers in ovary endometriomas.

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Endometriosis is a high-spread disease but despite of the extensive research some lines of its pathogenesis are still uncertain. The

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objective of the study was to determine the level of endothelin-1 and collagen type IV in basal membranes of ovary endometrioma blood vessels. In the study 122 women with ovary endometriomas who underwent surgical removal of ovarian endometriosis lesions were involved. Women were divided into the groups according to the stages of r-AFS classification. Immune hystochemical test, determination of endothelin-1 and IV type collagens were conducted. In women with I–II stage of ovary endometriosis in the samples was evaluated mild intensiveness of IV type collagen lightning in basal membranes of ectopic endometrioid lesion vessels. Due to the presence of this type of collagens basal membranes are characterized with mechanic stability. Hystochemical evaluation of productive activity of endothelial lining showed uneven, majorly bright lightening. Optical density index (ODI) of endotheliocytes lightening was 0.27. In women with III–IV stage of the disease two different variants were observed. In first occasion significant contain of IV type collagen was observed, ODI of endotheliocytes lightening reached 0.32. Conducted study showed the decreased adhesive quality of endotheliocytes in ovarian endometriosis lesions in these women that can be a reason of endotheliocyte desquamation inside the vessel and intensification of hypoxia. Second variant was characterized by the mild lightening of IV type collagens in vessel wall basal membranes and the low ODI of endotheliocytes lightening level – 0.14. Described angiogenesis features allow to understand individual distinction in ovary endometriosis development and progression.

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P55 The effect of etonogestrel implant on endometriotic lesion: a pilot study.

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Context: Effect of etonogestrel on endometriotic lesions.
Objectives: The aim of this pilot study was to evaluate the effects on pain symptoms and the changes of ultrasound features and volumes of ovarian endometriomas after treatment with etonogestrel implant in patients with endometriosis.
Methods: Twelve patients affected by at least one endometrioma with the largest diameter <5 cm at transvaginal ultrasound scan (TVU), were enrolled in the study. All patients were then inserted an etonogestrel implant. Two patients had the implant removed for intense irregular bleeding during the study and were excluded from evaluation. Before treatment and after 3 and 6 months all the remaining patients underwent evaluation of the intensity of symptoms related to endometriosis by a Visual Analogic Scale (VAS) and TVUS evaluation of the volumes and the echogenicity of the cystic fluid.
Results: After six months all patients reported improvement of pain symptomst. The mean volume of endometriomas resulted significantly lower in comparison to baseline.
Conclusions: This study showed a new rational indication of etonogestrel implant in endometriotic patient for pain relief. Moreover, our results suggest that the etonogestrel implant maight significantly decrease the volume of endometriotic lesions.

P56 Expression of genes that encode the enzymes of local progesterone synthesis and progesterone receptors in ovarian endometriosis tissue

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Endometriosis is a complex gynecological disorder, associated with excessive estrogen action together with reduced protective effects of progesterone, which is due to lowered progesterone formation, accelerated progesterone metabolism, or decreased expression of the nuclear progesterone receptors. Membrane progesterone receptors could also be implicated in pathogenesis of endometriosis as in breast cancer, where they have been shown to be involved in the inhibition of cell apoptosis. In this study, we examined the expression of genes that encode the enzymes of local progesterone synthesis (STAR, CYP11A1, HSD3B1 and HSD3B2) and the genes that encode the progesterone receptors (PGR, PAQR7, PAQR8 and PAQR5) in tissue samples from patients with ovarian endometriosis and in control endometrium samples from healthy women. The genes involved in local progesterone synthesis were all statistically significantly up-regulated in the ovarian endometriosis tissue, compared to the control normal endometrial tissue. Likewise, the genes that encode the progesterone receptors were differentially expressed. We detected statistically significant down-regulation of PGR, while the expression of PAQR7 and PAQR8 was increased. The expression of PAQR5 was borderline statistically significantly upregulated. The phase of the menstrual cycle had no statistically significant effects on the expression of these genes. Our gene expression data suggest that in endometriosis, despite higher expression of the genes of local progesterone biosynthesis, due to the decreased levels of PGR, the protective actions of progesterone are likely to be reduced. As in breast cancer, increased expression of the PAQRs might contribute to lower apoptosis, and thus to the pathogenesis of the disease. Further studies at the protein levels are currently in progress.

P57 Evaluation of long-term results of treatment with aromatase inhibitors

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Context: Endometriosis (E) is a chronic disease. Till nowadays there has been lack of data concerning safety, efficiency and long-term results of aromatase inhibitors (AI) application in patients of reproductive age. Objective of the study was to examine long-term results of AI in therapy of E. 131 patients of reproductive age with E were examined. The diagnosis was stated during laparoscopy and was confirmed by histological examination. 88 (67.1%) women had chronic pelvic pain, 42 (32%) patients had dyspareunia and 73 (55.7%) women had infertility. According to the revised AFS classification, I stage of the disease was diagnosed in 2 patients (1.5%), II stage- in 8 females (6.1%), III stage – in 34 (26.0%) and IV stage was diagnosed in 87 patients (66.4%), respectively. After surgery patients were prescribed letrozole 5 mg/day in combination with orgametril 5 mg twice a day continuously for 6 months.
Results: During the course of treatment pain syndrome was absent in 98.5% of patients. None of the patients had symptoms and findings of recurrence of the disease. In 9 (6.9%) cases regression of endometriotic lesions was confirmed during second-look laparoscopies. The most common side-effects were spotting from genital tract (32.1% of patients), increase of body weight (22.1% of patients), and acne (13.8% of women). The duration of observation period was 3 years. After treatment 24 patients with infertility (32.9%) became pregnant. In 25% of patients pregnancy occurred spontaneously, in others – after ovulation induction or after IVF procedure. By now 14 patients (58.3%) delivered healthy babies on time. The rest of the pregnancies are still in progress. One patient had two deliveries during the observation period.
Conclusion: Therapy of E with the use of aromatase inhibitors appears to be effective.

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P58 Uterine myoma: new national guidelines (Russia) for the management of patients

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Context: The large expert group of gynecologists under the leadership of academician L.V.Adamyan developed national guidelines (Russia) for the management of patients with uterine myoma in 2015.
Objective: To develop recommendations for the management of patients with uterine myoma for the practitioner.
Methods: Articles relating to various aspects of uterine myoma were searched in PubMed Medline and The Cochrane Library and other important resources of data (from January 1999 to December 2014).
Interventions: The results of all available evidential studies in Russian and English, meta-analyzes and systematic reviews of randomized controlled trials were analyzed, which allowed to prepare recommendations for the treatment of uterine myoma based on the consensus opinion of experts.
Main Outcome Measures: Data about etiology, pathogenesis, symptoms, diagnosis (including ultrasound, spiral CT, MRI of the pelvic organs) as well as new surgery opportunities (laparoscopy, uterine artery embolisation, focused ultrasound-ablation), and the role of hormone therapy (GnRH agonists, ulipristal acetate, etc.) in the complex treatment of uterine myoma with confidence level of methods are presented in the recommendations.
Results: Special attention is paid to the specific issues – management of patients with myoma and infertility, women during pregnancy, during the perimenopause and the postmenopause, and also considering risk of cancer; a separate chapter is devoted to the myoma and cancer. Special algorithms of management of patients with submucosal uterine myoma, patients with multiple uterine myoma have been developed for the practitioners.
Conclusions: Clinical guidelines are intended for gynecologists, gynecologists-endoscopists, general surgeons, urologists, oncologists, family doctors, teachers of medical universities.

P59 Guiding the postoperative hormonal treatment in patients with endometriosis depending on the immunohistochemical profile of endometriosis implants

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Aim of the study: Evaluating the immunohistochemical profile of endometriosis implants in order to bring additional data regarding the adequate hormonal treatment, the evolution capacity of the endometriosis implants and the recall risk of the disease.
Material and Method: The study consisted in the histopathological examination and immunohistochemical analysis of the endometriosis tissue excised laparoscopically from 21 patients. The immunohistochemical analysis consisted in quantifying the expression of the hormonal receptors – ER, PR and the proliferation (ki-67) and anti-apoptotic (bcl-2) markers. The postoperative hormonal treatment applied, as well as its duration was decided depending on the expression of the immunohistochemical markers.
Results: The expression of the analyzed markers was different depending on the expansion of the endometriosis implants. In case of the marked expression of the ER and PR at the level of the endometriosis implants, the treatment prescribed was using estro-progestatives, while in case of marked expression of the PR we used progestatives (Visane). The intense expression of the anti-apoptotic marker bcl-2 and the cellular proliferation marker ki-67 demonstrate the evolution capacity of the disease and the risk of recall on short time, in these cases being necessary a long-term hormonal treatment.
Conclusion: Consolidation of the surgical treatment by prescribing a long-term medical treatment is essential, because endometriosis is a chronic relapsing disease. Although there are, as we have shown, a multitude of surgical and medical therapeutic options, the treatment of endometriosis must be individualized in each case, based also on the immunohistochemical analysis of the endometriosis implants.

P60 Effect of ATT on ovarian and pituitary function in female genital tuberculosis

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All India Institute of Medical Sciences

Context: Female genital tuberculosis (FGTB) is common in developing countries causing significant morbidity especially infertility through involvement of fallopian tube, endometrium, ovaries. Toxins of Mycobacterium Tuberculosis may have anti-gonadotrophic effect while FGTB can involve ovaries leading to their subnormal endocrinal function.
Objective: To evaluate the effect of FGTB on pituitary and ovarian endocrinal function.
Methods: Fifty infertile women with FGTB without tubo-ovarian masses diagnosed by positive AFB culture or epitheloid granuloma on endometrial aspirate or positive polymerase chain reaction with positive findings on laparoscopy or hysteroscopy were recruited. The ovarian function tests were performed on Day 2/3 as (FSH) serum follicle stimulating hormone levels, AMH (anti-mullerian hormone) levels, (AFC) antral follicle count.
Interventions: Transvaginal ultrasound was performed for ovarian volume, AFC, FSH, Luteinizing hormone (LH), AMH, estradiol (E2), progesterone were performed in all women of FGTB. All women were started on antitubercular therapy (ATT) for 6 months by DOTS. After completion of ATT, all the parameters were repeated.
Main Outcome Measures: Ovarian volume, AFC count, AMH, FSH levels.
Result: Ovarian volume was found to be reduced in FGTB patients. Significant increase in FSH (7.16 ± 7.26 mIU/ml) pre to post ATT, AMH (2.68 ± 0.97ng/ml) pre to post ATT, AFC count (7.40 ± 2.12) pre to post ATT.
Conclusion: FGTB affects ovarian function by either directly affecting them in direct process or through toxins of Mycobacterium Tuberculosis through antigonadotrophic and anti-gonadal effect.

P61 Hysteroscopic findings in female genital tuberculosis (FGTB)

Sona Dharmendra (IN), Jai Sharma (IN), Sneha J (IN)
All India Institute of Medical Sciences

Context: Female genital tuberculosis (FGTB) is common in developing countries causing significant morbidity especially infertility through involvement of fallopian tube, endometrium, ovaries. Toxins of Mycobacterium Tuberculosis may have anti-gonadotrophic effect while FGTB can involve ovaries leading to their subnormal endocrinal function.
Objective: To see the hysteroscopic findings in FGTB.
Methods: 50 infertile women with FGTB diagnosed by positive AFB on culture or epitheloid granuloma on endometrial aspirate or positive polymerase chain reaction with positive findings on laparoscopy or hysteroscopy were recruited.

Interventions: Hysteroscopic findings were performed in all women with FGTB by Resectoscope (Karl Store) to see the varying intra-uterine adhesions (European Society of Gynaecological Endoscopy classification [ESGE] of Intra-uterine adhesions 1995).
Main Outcome Measures: Pale endometrium, Grade I, Grade II, Grade III, Grade IV adhesions and grade V adhesions.
Result: Hysteroscopic findings shows pale endometrium in 20(42.5%), grade I adhesions in17(34.6%), grade II adhesions in 3 (6.3%), grade IIa adhesions in 2(4.2%), grade III adhesions in 1 (2.1%), grade IV adhesions in 2 (4.2%), grade Va adhesions in 2 (4.2%) and grade Vb adhesions in 4 (8.4%).
Conclusion: FGTB affects endometrium showing pale looking like cavity which is partially or completely obliterated by adhesions of varying grade (grade 1 to grade 5) often involving ostia causing infertility.

P62 Nature of pain syndrome in various forms of endometriosis

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Context: Endometriosis is the most common cause of chronic pelvic pain (CPP), affects 10% of women of reproductive age. So it is very significant scientific interest in studying the relationship of endometriosis severity, location, nature and intensity of pelvic pain. *Objective*: Determine the nature of pain in women with external genital endometriosis (EGE) various stages of distribution.
Materials and methods: The criteria for inclusion: age from 18 to 40 years; EGE confirmed with laparoscopy; the presence of pain lasting longer than 6 months; menstrual function. Exclusion criteria: uterine fibroids; varicose veins; inflammatory diseases of the pelvic organs; receiving hormonal therapy within the previous 6 months of the study. Patient(s): The study were examined 124 patients. In assessing the structure of pain was taken into account the nature of the pain, which was determined in accordance with pain questionnaire (Multidimensional Personality Questionnaire), to organize the symptoms of neuropathic pain and analyze their intensity rating scale was used neuropathic Pain – Pain Detect.
Results: For patients with superficial forms EGE characteristic nociceptive pain (74%), characterized by precise localisation and a good therapeutic effect of analgesics. Neuropathic pain is characterized by a lack of precise localisation longer than 6 months, no effect from the use of non-steroidal anti-inflammatory drugs, occurs 4.5 times more frequently in patients with infiltrative (70%), and combined forms of endometriosis (79%) compared with patients with uni- (17%) and bilateral endometrioid ovarian cysts (21%) and in women with superficial endometriosis.
Conclusions: The nature of the pain of endometriosis with surface forms predominate complaints characteristic nociceptive pain, neuropathic pain often occurs when combined and infiltrative forms of endometriosis.

P63 Dienogest in the treatment of endometriosis: a retrospective analysis of quality of life

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Introduction: Endometriosis is a common, chronic gynecological disease associated with a variety of symptoms, such as dysmenorrhea, dyspareunia, dyschezia, lower back pain, and chronic pelvic pain. Endometriosis affects quality of life (QoL) with impact on physical functioning, daily activities, work productivity and mental health. Dienogest is an innovative progestin that combines properties of both 19-nortestosterone and progesterone derivatives and caracterized by an anti-androgenic and anti-proliferative effects, a relatively moderate inhibition of gonadotropin secretion and a mainly peripheral mode of action.
Materials and methods: We performed a retrospective analysis in 80 women referred to our Endometriosis Centre with clinical/instrumental diagnosis of deep endometriosis and pelvic pain and/or endometrioma instrumentally documented, treated with dienogest 2 mg/daily. After 120 days of therapy all patients received a questionnaire and changes in QoL, pelvic pain, menstrual pain, dyspareunia, bleeding pattern and adverse events were recordered.
Results: All patients described improvement of quality of life, modification of menstrual pain, intermenstrual pain, dyspareunia. Treatment with dienogest significantly reduced the VAS score of dysmenorrhea. Only few minor adverse effects were described during treatment and quality of life improved, both in physical and psychological domains. Two patient discontinued therapy due to side effects and patients with ovarian endometriosis showed a reduction in the volume of ovarian endometrioma.
Conclusions: Dienogest 2 mg daily, improved symptoms of endometriosis and QoL and reduced endometriotic lesions with a favorable safety and tolerability profile in all patients. All patients experienced only few predictable adverse effects, with high patient compliance, and low withdrawal rates.

P64 Endometrial polyps and Levothyroxine-Treated Hypothyroidism: a retrospective study

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Context: Hypothyroidism is a common endocrine pathology, with increasing prevalence (4.6%, according to Golden, 2009), and endometrial polyps (EP) are equally common in women (prevalence 7.8%, Dreisler, 2009), independently from their menopausal or fertile status. Recent studies found a possible association between thyroid disorders and EP (Saccardi,2013.22 patients); moreover, levels of plasmatic TSH (Seebacher, 2013) and endometrial expression of TTF-1 (Ervine, 2014) are associated with poor prognosis in endometrial cancer patients.
Objective: To demonstrate the increased prevalence of Levothyroxine-Treated Hypothyroidism (LTH) in patients with EP compared to general population.
Patients: 837 women with EP who underwent diagnostic and operative Hysteroscopy (Hys) in 2009–2013. Mean age was 56 ±11.46 years, 350 fertile and 487 menopausal patients.
Interventions: All patients underwent diagnostic and operative Hys, with removal and histologic analysis of EP.
Main Outcome Measure: Increased prevalence of LTH in patients with EP. RESULTS We found a cumulative prevalence of 17.3% of LTH, (145 out of 837 women, OR 4.29), (startified prevalence: 20.5% in menopausal women and 12.8% in fertile women), while the reported prevalence of Hypothyroidism in the general population is around 4.6% (Golden, 2009). Of note, 8.2% of women with LTH had foci of endometrial cancer arising from EP surface, versus 2.4% of patients with EP and normal thyroid function.
Conclusions: The risk of Hypothyroidism for a woman with EP is enormously higher than the general population (OR 4.29). Patients with LTH and EP have a higher risk of endometrial cancer arising from EP (8.2% vs. 2.4%). Thyroid function should be studied in women with EP, especially if they are in menopause, and Hypothyroidism should be

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an indication for removal of EP. These data should be confirmed in randomized clinical studies.

P65 Comparative profile of cytokines, chemokines and growth factors in endometriosis: a multiplex analysis in peritoneal fluid

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Context: Endometriosis, a chronic estrogen-dependent inflammatory disorder is a leading cause of pain/infertility with unknown etiology. Cytokines, chemokines and growth factors play potential role in its causation and progression.
Objective: To assess the role of cytokines,chemokines and growth factors in endometriosis using multiplex assay in peritoneal fluid samples.
Methods: Patients ($n = 14$ endometriosis, $n = 25$ control) undergoing diagnostic/therapeutic laparoscopy in Dept.of Obs & Gynae, All India Institute of Medical Sciences, New Delhi were recruited.Regularly menstruating patients aged 23–41 yrs were included.Those with history of hormonal therapy for endometriosis or otherwise 3 months prior laparoscopy,other systemic immune disorder, malignancy and pregnancy were excluded.
Laparascopic retrival of peritoneal fluid was done after insertion of trocar & laparoscope before any surgical intervention. Samples were centrifuged and stored at -80°C. Eotaxin, GM-CSF, MCP-1, MIP-1β, VEGF, IL-6, G-CSF, FGF basic, RANTES & IP-10 were assayed in duplicate using BioplexPro™human cytokine panel(Bio-Rad, CA,USA). Protein estimated by Bradford assay and data expressed as pg/mg protein.
Results: IP-10 was significantly higher ($p = 0.023$) in patients with endometriosis (31.18±3.33 pg/mg) than that of patients without endometriosis (19.34±3.62 pg/mg). Eotaxin, GM-CSF, MCP-1, MIP-1β, VEGF, IL-6, G-CSF, FGF basic and RANTES were not significantly different between the groups. MIP-1α was significantly higher ($p = 0.014$) in moderate to severe (0.614 pg/mg) than minimal to mild endometriosis (0.308 pg/mg). Other factors were not significantly different among disease stages.
Conclusion: It is apparent from the study that IP-10 contributes to pathogenesis and MIP-1α might aid in progression of endometriosis. The findings need to be elucidated further in larger sample size study including fertile controls.

P66 Differential approaches to the treatment of various types of chronic endometritis

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Background: chronic endometritis (CE) is a clinical and morphological syndrome characterized by a complex of morphofunctional changes of endometrium of inflammatory genesis leading to disruption of normal cyclic transformation and receptivity of tissues. Incidence of chronic endometritis varies between 0.2 and 6.3%. It is a fact, that chronic endometritis is not only a medical problem, but also a social one, because CE is a reason of infertility, miscarriages, unsuccessful attempts of ART, complications during pregnancies and labors.
Aim: Study of morphological features of endometrium in patients with various types of chronic endometritis and production of differential approaches to the treatment of CE.
Method: Study was undertaken on 130 patients with chronic endometriris, which were divided into 2 groups: 1st – 69 women with hyperplastic variant of CE, 2nd- 61 patients with hypoplastic one. The study subgroup (54 in the 1st group and 46 in the 2nd one) were taking Poludanum and Diosmin 600. The patients of the control subgroup were taking antibacterial therapy, disaggregants and interferons. In the second step of the therapy dydrogesterone was given to the study subgroup as a pregravid preparation (10 mg twice a day from the 11 up to 25 day of menstrual cycle).
Findings and interpretation: using of immunocorrector Poludanum, venotonic drug Diosmin in treatment of CE leads to normalization of local immunity of endometrium, decreasing of inflammation, patients became pregnant during the year of observation. Results of treatment in patients wih hypoplastic variant of CE are not so positive because of the origin changes in local immunity and autoimmune character of the disorder and we can suppose that these women should be given hormone therapy, which contains both progestins and estrogens.

P67 Effects of dienogest for dysmenorrhea associated with endometriosis

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Context: Dysmenorrhea is the most common symptom in patients with endometriosis.
Objective: To evaluate the efficacy of dienogest for patients with dysmenorrhea associated with endometriosis.
Methods: All women received dienogest (2 mg once daily, orally) and changes in pelvic pain, bleeding pattern, adverse events were evaluated during and after treatment.
Patients: Eighty-nine patients with dysmenorrhea and pelvic pain associated with endometriosis under surgical diagnosis were included.
Interventions: Patients were assigned to receive dienogest and used their usual pain medications as needed during the trial.
Main Outcome Measures: After six months treatments, we used a zero- to three-point verbal rating scale(VRS) to measure the severity of disability because of dysmenorrhea in daily life, and the patients' use of analgesics.
Results: Total dysmenorrhea scores assessed by the VRS were significantly decreased at the end of treatment compared with pretreatment ($p = 0.000$). The mean(±SD) pain score for dysmenorrhea was 1.42 ± 1.1(pretreatment), 0.1 ± 0.3 (end of treatment). The mean nonmenstrual pelvic pain score(±SD) was 0.52 ± 0.6, 0.18 ± 0.3, respectively. It also shows significant difference ($p = 0.000$). The use of analgesics were significantly decreased at the end of treatment ($p = 0.000$). Most common side effect was irregular uterine bleeding (28/89. 31.5%), and only one patient was stopped because of severe bleeding. However, the incidence of uterine bleeding decreased with continued treatment and resolved after the end of treatment. There was another adverse event related to using dienogest, such as weight gains (pretreatment; 57.9 ± 9.7, end of treatment; 59.1 ± 12), but it was no statistical significance ($p = 0.090$).
Conclusions: The present study demonstrated that oral administration of dienogest could be used to effectively treat pain associated with endometriosis.

P68 Antibody arrays for discovery of novel biomarkers of endometriosis

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Endometriosis is an estrogen-dependent inflammatory disease which is characterized by the presence of endometrial tissue outside the

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uterine cavity. There are three types: ovarian, peritoneal and deep infiltrating endometriosis with different etiologies and pathogenesis. The gold standard for diagnosis of endometriosis is invasive laparoscopy that is combined with histological analysis. Since this is a surgical procedure reliable biological markers for non-invasive diagnosis remain of high interest. So far potential markers for noninvasive diagnosis of endometriosis have been searched for in different biological samples by targeted and global nontargeted approaches (1,2). Our research team has identified several panels of biomarkers in blood samples in previous transcriptomic, metabolomic and proteomic studies (3,4,5). Recently, we performed a proteomic study using antibody array platform to identify potential novel biomarkers for peritoneal endometriosis. In a discovery phase we analysed eight plasma samples in a dual-colour approach, targeting 900 different proteins. The samples were derived from women that underwent laparoscopy for evaluation of infertility of whom four were characterized by the presence of peritoneal endometriosis and four by the absence of it, respectively forming case and control group of this study. The bioinformatics analysis of this data is currently in progress. With this approach we aim to define a panel of biomarkers that could be clinically useful and might thus allow a non-invasive diagnosis of endometriosis.

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P69 Comparison of serum concentration of anti-mullerian hormone and follicle stimulating hormone with length of telomeres in women with premature ovarian insufficiency

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Context: Premature ovarian insufficiency(POI) is defined as hypergonadotropic amenorrhea caused by the cessation of ovarian activity in women before 40years of age, accompanied by a hypoestrogenism. POI affects 1% of women. The exact aetiology is unkown. Telomeres represent typical repeating nucleotide sequence at the end of linear chromosomes. The length of the telomeres in humans represents a biological marker of aging of cells.Irregularities in telomere length may be indicators of POI.
Objective: The purpose was to determine whether the length of telomeres in lymphocytes in women with POI differs from the length in women of the same age with normal functioning ovaries.We also determined whether there is a link between altered telomere length and the variation of serum AMH and FSH.
Methods and Patients: The study group included 27 women with POI, 20 to 39 years old. The control group included 32 randomly selected healthy women, same age. Interventions Reproductive history, gynaecological and ultrasound examination and measurements of AMH, FSH, LH, estradiol were performed. The length of telomeres were determined and calculated by two methods (Cawthon, Hanna).
Main outcome measures and Results: LH and FSH were significantly higher in group with POI than in control group (average 41.46 E/l, 96.46 E/l, $p < 0.001$). Estradiol and AMH were lower in group with POI (0.17nmol/l, $p = 0.01$, 0.1ug/l, $p < 0.001$). Antral follicle count was higher in controls (23.25, $p < 0.001$). Telomere length did not show any significant difference between the two groups ($p = 0.20$). There were no correlations between telomere length and FSH ($p = 0.16$) and AMH ($p = 0.63$).
Conclusions: The assessment of telomere length can not determine whether POI is an isolated biological process as a consequence of reduced initial stock of ovarian follicles or is it a generalized process of premature aging of the organism.

P70 Combination of Diane-35 with Metformin to reverse of endometrial atypical hyperplasia and early endometrial carcinoma with polycystic ovarian syndrome

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Objective: To explore the clinical efficacy and safety Diane-35 and metformin combination treatment for endometrial atypical hyperplasia(EAH) and Early endometrial carcinoma (EEC) in PCOS patients.
Methods: 42 PCOS patients with endometrium leision (30 EAH and12 EEC) were recurited. All patients were treated with Diane-35 (1 tablets per day, for 21 days one month) plus metformin (1000mg, qd) for 6 months. Endometrial biopsies and blood samples before,during,and after treatment were detected. Clinical parameters included BMI, serum FSH, LH, TT, SHBG, FAI, and HOMA-IR, and endometrial pathologies as well. After successful conversion of endometrial lesions, we continued to give patients with dydrogesterone(10mg per day, for 14 days per month) plus metformin .
Results: After 6-month treatment, in all PCOS patients (30 EAH, 12 EEC), the endometrium were confirmed by pathological evaluation to be reversed to normal epithelia with Diane-35 plus metformin treatment. By end of 6 months' treatment, mean BMI, TT, FAI, HOMA-IR were decreased respectively ($p < 0.05$), while SHBG were inceased ($p < 0.05$). The complete response (CR) rate was 100% (30/30 EAH, 12/12 EEC). During 6–18 months of follow-up, 2 EEC patients relapsed, and both of whom did not continue to use progesterone therapy monthly.
Conclusion: Diane 35, a low-dose oral contraceptives with anti-androgen activity, when used in combination with Metaformine can completely reverse the EEC and EAH to normal endometrium, even in those who has been failure to high-dose progestin treatment. Diane-35 with metformin combination treatment may be a good choice for the EAH and EEC in PCOS PCOS, which enables the patients to preserve the fertility.

P71 Elastosonografia transvaginale dei noduli endometriosici del retto-sigma: correlazione con sintomi e istologia

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Introduzione: L'obiettivo di questo studio prospettico è correlare le caratteristiche elastosonografiche dei noduli endometriosici del retto-sigma con i sintomi e l'istologia.
Materiali E Metodi: Le ecografie sono state eseguite con ecografo dotato di software per elastosonografia (Voluson E6). Gli elastogrammi sono stati classificati in 5 modelli seguendo il punteggio di elasticità: dal punteggio 1, scarsa rigidità (nodulo uniformemente ombreggiato di verde) al punto 5, intensa rigidità (nodulo uniformemente

ombreggiato di blu). É stato utilizzato un questionario standardizzato per valutare i sintomi gastrointestinali ed è stato calcolato un punteggio totale di tali sintomi. All'esame istologico sono state valutate: la profondità d'infiltrazione dell'endometriosi nella parete intestinale, il grado di fibrosi (da G0 a G4), la quantità di stroma endometriale e il disordine delle cellule muscolari (da D0 a D3).
Risultati: Lo studio ha incluso 24 pazienti sottoposte a resezione di retto-sigma per endometriosi. Il diametro massimo medio dei noduli endometriosici era 29 (± 7) mm; il volume medio era 8.4 (± 5.9) cm^3. In 7 pazienti il punteggio dell'elasticità era ≤ 3, in 8 pazienti era 4 e in 9 pazienti 5. Il punteggio di elasticità era significativamente correlato con l'intensità della dischezia (rho = 0.836; $p < 0.001$) e con lo score dei sintomi gastrointestinali (rho = 0.716; $p < 0.001$). La rigidità elastosonografica del nodulo era correlata con il grado di fibrosi (rho = 0.798; $p < 0.001$) e negativamente correlata con la quantità di stroma endometriale (rho = 0.656; $p < 0.001$). C'era una moderata correlazione tra rigidità elastosonografica e disordine delle cellule muscolari (rho = 0.446; $p = 0.029$).
Conclusioni: L'elastosonografia consente di predire le caratteristiche istologiche dei noduli endometriosici del retto-sigma e correla con la sintomatologia intestinale.

P72 Colonscopia virtuale nella diagnosi dell'endometriosi del retto-sigma: studio pilota

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Introduzione: La colonscopia virtuale (CV) è una tecnica di studio non-invasiva oggi di prima scelta per lo screening del cancro del colon-retto. L'obiettivo di questo studio è di valutare l'accuratezza della CV nella diagnosi dell'endometriosi del retto-sigma.
Materiali E Metodi: Sono state incluse nello studio pazienti con un forte sospetto clinico (sintomi ed esame obiettivo) di endometriosi intestinale. Sono state escluse le pazienti con una storia di chirurgia intestinale e le pazienti con controindicazioni a eseguire la preparazione intestinale e/o la CV. La CV è stata eseguita utilizzando una TAC a 16 strati. I dati sono stati analizzati con un software dedicato (General Eletric, ADW 4.2.5). Il lume intestinale è stato esaminato con navigazione virtuale.
Risultati: 53 Pazienti sono state arruolate nello studio, 42 sono state operate e sono state incluse nell'analisi finale. In 24 pazienti (57.1%) è stata diagnosticata l'endometriosi del retto-sigma durante l'intervento chirurgico. 10 noduli erano localizzati nel sigma, 9 nel retto e 5 nella giunzione retto-sigmoidea. Il diametro medio (±DS) dei noduli intestinali era 25.8 (±5.8) mm. La sensibilità, specificità, valore predittivo positivo e negativo, rapporto di verosimiglianza positivo e negativo della CV nella diagnosi dell'endometriosi del retto-sigma sono state rispettivamente: 95.8% (78.8%-99.3%), 88.9% (65.3%-98.3%), 92.0% (73.9%-98.8%), 94.1% (71.2%-99.0%), 8.62 (2.33–31.94) e 0.05 (0.01–0.32). In tutti i casi positivi è stata osservata una stenosi del colon. Non si sono verificati casi di reazioni vaso-vagali o perforazioni intestinali.
Conclusioni: La CV ha un'alta sensibilità e una specificità moderata nella diagnosi dell'endometriosi del retto-sigma; l'esame è stato ben tollerato dalle pazienti. Questi risultati dovranno essere confermati da studi futuri che includano un maggior numero di pazienti.

P73 Ultrasonoghrafic evaluation of the effect of dienogest on volume and features of ovarian endometriomas

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Context: Medical treatment and ultrasound scan in endometriosis
Objectives: The purpose of this prospective study was to evaluate the changes of ultrasound features and volumes of ovarian endometriomas after treatment with dienogest.
Methods: Twenty-seven premenopausal patients, diagnosed at transvaginal ultrasound scan (TVUS) with at least one ovarian cyst with the characteristics of endometrioma and the largest diameter between 2 and 5 cm, were included in this study. Three of the patients had previously undergone surgery for endometriosis. All the patients were revaluated by TVUS after six months' continuous treatment with dienogest 2 mg/day. The volumes and echogenicity of the cystic fluid were recorded in both occasions. Symptoms associated with endometriosis were also assessed (VAS score) and recorded prior and after the therapy.
Results: After six months of treatment a significant reduction of the mean volume of endometriomas was observed. The cystic fluid content showed changes in echogenicity, appearing more echogenic and with hyperechoic spots in 62% of the cases. Symptoms associated with endometriosis were also significantly reduced after treatment.
Conclusions: Treatment with dienogest, not only reduces the symptoms related to endometriosis but also the volume of endometriotic ovarian lesions.

P74 Are adiponectin and leptin related with insulin resistance and endometrial hyperplasia?

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Context: Epidemiologic and genetic evidence links between insulin resistance and endometrial cancer. Endometrial atypical hyperplasia is a precancerous stage of endometrial cancer.
Objective: To evaluate in rat animal model whether insulin resistance (IR) and endometrial hyperplasia (EH) affect adipokines and their receptors in plasma, adipose and uterus.
Methods: Female Sprague-Dawley (SD) rats were fed on a high-fat diet (HFD) and administered high-dose 17β-estradiol (E2) to establish an IR and EH model. ELISA, RT-PCR and western blot were carried to detect adipokines and their receptors.
Animals: 45 female SD rats (8 weeks old) were randomly divided into 5 groups ($n = 9$ for each group) of control (C), standard diet (StD) and ovariectomy (OVX) (NO), StD and E2 (NE), HFD and OVX (FO), HFD and E2 (FE). Following 48 weeks of feeding rats were subjected to OVX (except group C). NE and FE groups were administered E2 for 4 weeks.
Main Outcome Measures: Plasma and mRNA of adiponectin (Adipoq) and leptin (Lep). The mRNA of Adipoq and Lep in visceral adipose tissues and uterus, and protein and mRNA of adiponectin receptors (AdipoqRs) and leptin receptors (OB-Rs) in uterus.
Results: Plasma Adipoq and Lep is higher in groups without EH (NO and FO) than C group and EH groups (NE and FE) respectively. There is no difference of Adipoq and Lep mRNA expression in visceral adipose tissue. In uterus, compared to NO and FO groups, OB-R mRNA and protein expression are lower in NE and FE groups, and Adipoq mRNA and protein expression are lower in FE group than FO.
Conclusions: Insulin resistance induced by high-fat diet influences the expression of adiponectin, leptin and their receptors. The mutual

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effect of endometrial cell metabolism and adiponectin and leptin and their receptors indicates further findings are needed to gain greater insight into adipokines functions.

P75 Metabolism of progesterone in the endometriotic 12-Z cells and the control endometrial HIEEC cells

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Endometriosis is a chronic gynecological disease diagnosed in 30% to 50% of patients with fertility problems. It is an estrogen-dependent disease where the protective actions of progesterone are reduced. The aim of our study was to explore metabolism of progesterone at the gene expression and metabolite levels in the model cell line of peritoneal endometriosis 12-Z and in the cell line of normal proliferative endometrium HIEEC. Our results revealed increased expression of SRD5A1 and decreased expression AKR1C in 12-Z cells compared to HIEEC cells, which can lead to increased formation of 5α-pregnanes and lower formation of 4-pregnenes. The gene expression data were confirmed by identification of progesterone metabolites in the 12-Z and HIEEC cells by employing a recently established combined liquid chromatography-tandem mass spectrometry method [1]. These cell lines differed both in metabolic profiles and in the rate of metabolism, which was higher in HIEEC cells. In the 12-Z cells mostly 5α-pregnanes were formed, progesterone was reduced to 5α-pregnane-3.20-dione, 3β-hydroxy-5α-pregnane-20-one, and 3α-hydroxy-5α-pregnane-20-one. In the HIEEC cells progesterone was reduced to 20α-hydroxy-pregn-4-ene-3-one, 5α-pregnane-3.20-dione, 20α-hydroxy-5α-pregnane-3-one, 5α-pregnane-3β,20α-diol, and 5α-pregnane-3α,20α-diol. The si-RNA mediated gene silencing confirmed that in the 12-Z cells, 5α-reduction was catalyzed by SRD5A1, while 3-keto reduction was catalyzed by the AKR1C enzymes. The silencing of SRD5A1 in the 12-Z cells decreased the rate of progesterone metabolism and reduced the formation of 5α-pregnanes. Our data show that SRD5A1 represents a potential target for treatment of endometriosis.

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P76 Cambiamenti ecografici dei fibromi uterini dopo 3-mesi di terapia con ulipristal acetato (UPA)

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Introduzione: L'obiettivo di questo studio prospettico consiste nel valutare i cambiamenti ecografici dei fibromi uterini dopo 3 mesi di terapia con UPA.
Materiali E Metodi: Le pazienti reclutate hanno ricevuto un trattamento preoperatorio con UPA (5 mg/die per os) per tre mesi. Le ecografie sono state eseguite prima dell'inizio della terapia e al suo termine. Sono stati valutati i seguenti parametri: il numero dei fibromi, la loro posizione (in accordo con la classificazione FIGO), il loro diametro maggiore, il volume, il volume totale, la vascolarizzazione del fibroma di maggiori dimensioni e le caratteristiche elastografiche dei fibromi.
Risultati: 42 Pazienti hanno concluso lo studio. Dopo tre mesi di terapia con UPA il volume del fibroma più grande è significativamente diminuito ($p < 0.001$), la riduzione media percentuale è stata del 31.6%. Il volume totale dei fibromi si è significativamente ridotto dopo tre mesi di terapia ($p < 0.001$). La diminuzione del volume dei fibromi è stata maggiore per i fibromi di tipo 4 e 5 FIGO, rispetto ai tipi 0, 1 e 2 ($p < 0.05$). Lo spessore endometriale medio (± SD) al termine del trattamento era 7.7 (± 3.2) mm; solo una paziente ha riportato uno spessore endometriale >16 mm. La vascolarizzazione del fibroma più grande è significativamente diminuita dopo tre mesi di terapia ($p < 0.05$). Non-sono stati rilevati cambiamenti nelle caratteristiche elastografiche al termine della terapia.
Conclusioni: UPA causa la riduzione del volume dei fibromi; la riduzione in percentuale si è dimostrata maggiore nei fibromi intramurali. UPA diminuisce la vascolarizzazione dei fibromi ma non ne modifica le caratteristiche elastografiche.

P77 Diagnosis and management of POI – China's view

Jie Wu (CN)

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Primary ovarian insufficiency (POI) is a complex disorder characterized by cessation of ovarian-ovulation function in women before 40 years of age. The condition is defined as the absence of normal menses for at least 4 months, serum follicle-stimulating hormone (FSH) concentrations exceeding 40 IU/L at least one month apart, resulting in infertility, cardiovascular diseases, neurological disorders, and osteoporosis. POI affects 1% and 0.1% of women by the age of 40 and 30, respectively. Multiple causes contributing to POI include environmental factors, genetic background, autoimmunity, metabolism and iatrogenic factors. However, the cause of POI remains undetermined in most cases. Women with POI extremely rarely ovulate and achieve pregnancy spontaneously, so infertility is an important issue in POI patients in China. Numerous treatment protocols for follicular development and ovulation induction have been tested in patients with POI, none have been shown to be effective. Therefore, POI/POF remains a clinically challenging entity because IVF with donor oocytes is currently the only treatment known to be effective. Fortunately, the natural cycle IVF may be promising for the POI patients in the future. Importantly, the initial FSH and E2 levels should be monitored and follicle development and/or hormonal measurements are recommended for POI patients. Besides, POI patients, whether or not they desire pregnancy, should be treated with combination estrogen and progesterone hormone replacement therapy (HRT) to minimize bone loss and decrease the risk of cardiovascular events, relieve the vasomotor flushes and vaginal dryness.

P78 Clinical and laboratory indicators among phenotypes of polycystic ovary syndrome in Chinese Han nationality accoroding to the latest NIH recommendation

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Background: The diagnosis criteria of PCOS has always been controversial since PCOS was first described in 1935. Because of heterogeneity and ethnic difference, the prevalence rate and

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correlative indicators of different phenotypes have rarely been reported in Chinese people.
Objective: To investigate relevant indicators in PCOS with different phenotypes according to the National Institutes of Health (NIH, 2012) recommendations. Patients 647 women with PCOS and 60 controls.
Methods: Evaluation of clinical, endocrinic and metabolic parameters. All PCOS patients were divided into 4 subtypes. Group A defined as anovulation, hyperandrogenism and polycystic ovary(O+OA+P). Group B was O+HA. Group C was HA+P and Group D defined as HA+P. Correlation analysis of HOMA-Insulin Resistance in 4 phenotypes with other indicators respectively.
Main Outcome Measure(s): Blood levels of FSH, LH, total testosterone, fasting plasma glucose, fasting insulin, triglyceride, etc. Calculation of ferryman-Gallwey scoring and HOMA-IR. Results group A, the severe PCOS phenotype,was the most common phenotype in 63.2% of the patients. Only 9% of patients was seen in Group B. The two phenotypes had similar characteristics, but group A exhibited higher androgen level. The rate of Clinical and/or biochemical signs of hyperandrogenism was 87.8%, but hyperandrogenism, IR, TG were significant higher in group A than group B ($p < 0.05$). Group C (15.6%)and group D (12.9%) presented mild alterations, but LH and LH/FSH were significantly increased than controls ($p < 0.05$). Group D had similar Ferryman-Gallwey with the controls. IR was all positively correlated with ApoB/ApoA1, while only positively correlated with total testosterone in group A.
Conclusions: NIH typing can reflect the basic characteristics of PCOS. Although IR was not included into NIH criteria, it played a key role in the occurrence and development of PCOS.

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Gynecological Cancer

P79 Borderline ovarian tumor

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Borderline ovarian tumors are unusual among adolescents in comparison with adult women, only 14 cases have been reported in the literature. Their diagnosis is difficult, but have a better prognosis compared to invasive tumors. One of management's stake in these patients is to best preserve their subsequent fertility. Treatment for the early stages should be conservative, the first laparoscopic route being both referred to as diagnostic therapeutic aim. For more advanced stages uncertainties still persist. Staging, prognostic determinant element is needed in the management of patients. When it was not performed during the initial surgery, restaging be discussed. We draw your attention to a clinical case of mucinous borderline cystadenoma with a portion of ovarian adenocarcinoma in a girl of 15 years. On the occasion of this work and after a review of the literature, we will try to draw attention to this rare condition, to recall the main diagnostic aspects, but especially the multidisciplinary management and the preferred conservative treatment for the preservation of fertility in a context of eager young patient of pregnancy.

P80 An unusual presentation of granulosa cell tumor Case report

Merita Krasniqi (KO), Zeqir Dervishi (KO), Sahadete Shala (KO), Dardane Ukella (KO), Foljeta Kastrati (KO)
Kogj Prishtine

Granulosa cell tomours or granulosa theca cell tumours are tumours that arise from granulosa cells.These tumours are part of the sex cord gonadal stromal tumours or non-epithelial group of tumours. Granulosa cell tumours constitute less than 5% of all ovarian tumours. Ovarian granulose cell tumours are rare malignances,20% present of their have clinical picture of carcinoma.
Case presentation: Patient F.M,age 35,non-married,was hospitalizied due to the loss of apetite,loss of body weight,in mars 2015 in our hospital KOGj Prishtina.
Clinical examination: Laboratory analysis are were in accordance with reference values, tumor marker CA 125–8.61,CA 19.9–15.
Abdominal ultrasonography: Inside the abdomen a large mass (30×25 cm). In the tumor mass,there were necrotic changes. Inside the pelvis gynecological organs were not clerly differentiated.
Diagnosis: Tu cysticum ovari permagna lat sin.Status post laparatomiam aa V pp granulosa cell tumor sin.
Laparatomia transversalis sec Pfanenstiel: Extirpatio tumoris in toto (HP)
Patohistological report: Granulosa cell tumor(low grade). Two months after operationem, our patient not feelling well and with U/T was diagnosted same mass (25×25) in dexter ovary. A throught staging surgery was followed including total abdominal hysterectomy,retroperitoneal lymph node sampling. The patient then received six courses of postopartive adjuvant chemotherapy with CAP regiment.

Keywords

Granulosa cell tumor, low grade

P81 Leptin levels in serum and body mass index in patients with endometrial cancer

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Objectives: Obesity is a well-established risk factor for endometrial cancer. Leptin, a product of the ob gene, is involved in the regulation of body weight, energy balance, and reproductive function. The leptin secreted from adipose tissue, has been reported to play a role in such carcinogenic processes as cell proliferation, angiogenesis, and insulin regulation. The purpose of the current study is to investigate the relationships of the concentration of leptin with the endometrial cancer risk in postmenopausal female subjects.
Methods: This prospective study has been conducted in between January 2015 and June 2015 in the Obstetrics Gynecology Department of the University Hospital, Plovdiv, Bulgaria. A study includes 55 postmenopausal women – 32 obese women with histologically confirmed incident of endometrial cancer and 22 non-obese postmenopausal women with normal endometrium. The serum leptin levels were determined in fasting morning blood samples by commercial, double-antibody, sandwich enzyme-linked immunosorbent assay/ELISA/.
Results: Mean serum concentration of leptin in endometrial cancer was 21.11 ng/ml as opposed to 7.23 ng/ml in patients without endometrial pathology ($p < 0.0001$). Significantly, higher concentrations of leptin were noted in the BMI group of patients with endometrial cancer in comparison to controls ($p < 0.0001$). In univariate and multivariate logistic regression models, a positive association between EC and serum leptin and BMI ($p < 0.05$) exists.
Conclusions: In conclusion, the present results suggest that high serum levels of leptin ratio is independently associated with an increased risk for endometrial cancer. Serum leptin play important roles in the development of obesity-related endometrial cancer.

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P82 A diagnostic test evaluation of cervical cytology and HR-HPV screening for cervical lesions in Beijing

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Purpose: To study the incidence of cervical lesions through cytology and human papillomavirus (HPV) testing in Beijing, to evaluate the diagnostic accuracy of two different strategies used as the primary screening of such lesions and to provide a framework for more effective cervical cancer screening strategy as clinical guide.
Methods: Potential subjects (6185 women) were screened using two strategies. The first strategy used cytology as the sole screening test, and a positive cytology result was followed by colposcopy with biopsy. The other strategy used cytology, and a positive result was followed by HPV testing; a positive HPV result was followed by colposcopy with biopsy.
Results: The incidence of cervical lesions using the two different strategies was 6.01% (372/6185) and 3.02% (187/6185). A significant difference between the two strategies was found in the detection of chronic cervicitis and cervical intraepithelial neoplasia grade II and III (CIN II, CIN III) ($p < 0.005$). The sensitivity and specificity of the thinprep cytologic test (TCT) are 87.2% and 96.01%, respectively, and the TCT combined with hybrid capture 2 (HC2) are 74.29% and 98.85%, respectively.
Conclusions: The TCT and High Risk HPV (HR-HPV) test are the practical methods for detecting cervical lesions. The TCT is more sensitive and efficient and thus is superior to TCT combined with HR-HPV.

Keywords

Cytology, Cervical lesion, diagnosis, HR-HPV, sensitive

P83 H19 and MALAT1 lncRNAs expression level as prognostic factors in cervical oncogenesis

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Background: Cervical cancer is one of the most frequent cancers affecting women in Romania. Infection with high-risk human papillomaviruses (hrHPV) is the main cause for cervical neoplasia but there are other cofactors associated with cervical carcinogenesis. Currently accumulating evidence links the expression of long non-coding RNAs (lncRNAs) to neoplastic transformation, but little is known about their involvement in cervical cancer.
Objective: to investigate the expression levels of two lncRNAs (H19, MALAT1) in patients with HPV-induced cervical lesions and cancer.
Methods: 159 cervical specimens (20–77 years old, median: 36.7) from women with hrHPV-induced dysplastic cervical lesions (CIN1; CIN2+) and squamous cervical carcinoma (SCC) were investigated. All samples were tested for hrHPV DNA presence (Linear Array, Roche). 40 women (20–48 years old, median: 32) with negative cytological smears and HPV DNA negative were included as control group.Total RNA was isolated and lncRNAs expression levels were analysed by qRT-PCR.
Results: We found that both lncRNAs were significantly up-regulated in cervical samples. For H19 the highest levels were noted in SCC (mean n-fold: 1.264; $p < 0.0001$) and precancerous lesions (mean n-fold: 0.9194; $p = 0.0007$) compared with the control group. MALAT1 displayed an increased pattern of expression in SCC subjects (mean n-fold: 2.322; $p < 0.0001$) and precancerous lesions (mean n-fold: 1.202; $p = 0.0100$). Furthermore, for SCC patients H19 and MALAT1 higher levels were correlated with FIGO stage, lymph node metastasis ($p = 0.0136$, respectively $p = 0.049$). Also a strong correlation between HPV-positive samples and lncRNAs expression levels was observed ($p < 0.05$).
Conclusions: Our data indicate that both lncRNAs could represent novel factors involved in cervical carcinogenesis and underlines a potential oncogenic role for them in this pathology.

P84 Cervical cancer – knowledge, prevention and exposure to risk factors among students from various countries

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Context: Cervical cancer is one of the world's deadliest but most easily preventable forms of cancer among women.
Objectives: Incidence rates may vary immensely depending on a country: from 5.8 per 100 000 women in Austria to even 28.7 per 100 000 women in Romania. These differences should be analyzed as screening programmes and a wide range of treatment methods are available.
Methods: It was a cross-sectional study conducted by means of a questionnaire. The survey consisted of 4 parts including demographic information, short test of knowledge about HPV (Human papillomavirus) and cervical cancer, questions about applied prevention methods and possible risk factors among respondents.
Patients: The survey was conducted in France, Italy, Austria, the UK, Kosovo, Macedonia, Slovakia, Romania, Poland and Egypt. Answers from 5632 students were compared in accordance to incidence of cervical cancer in these countries presented by WHO International Agency for Research on Cancer.
Main Outcome Measures: There ere differences in level of knowledge and use of preventive methods.
Results: Students from countries with Age-world-standardized incidence rate lower than 10 had better knowledge concerning risk factors such as high number of sexual partners ($p < 0.001$), smoking ($p < 0.001$) or HPV infection ($p < 0.001$). Use of preventive methods was more frequent in countries with lower cervical cancer incidence: Pap smears [$p < 0.001$, $R^2 = 1.67$ (1.53–1.82)], HPV tests [$p < 0.001$, $R^2 = 3.77$ (3.03–4.60)] and HPV vaccines [$p < 0.001$, $R^2 = 2.43$ (2.14–2.75)]. There were no significant differences in family history of cervical cancer nor in immunosuppressive treatment.
Conclusions: It seems that the best method of decreasing cervical cancer incidence in countries with high morbidity could be improvement of educational levels concerning the disease, followed by facilitated access to preventive services.

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P85 Primary prevention of HPV infections among adolescents

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The incidence of infection increases with the sexual onset in puberty and adolescence.We made our educational programme for adolescents:''Knowlwdge is pleasure''. Adolescents are actively involved in the project. We made research during 3 years of the project (2007–2010), 51 high schools, 2295 students. 68% uses condoms (of which 40% at their first sexual intercourse), 12% hormonal contraception. 59% had first sexuall intercourse under the influence of alcohol, 13% under the influence of drugs. 39% have heard about HPV, 32% have heard that HPV presents a cancer risk factor. 70% estimate that their risk of contracting an STD is high. 85% know that condoms provide protection from both unwanted pregnancies as well as STD, 45% have no knowledge about the role of hormonal contraception. The key reasons for lack of implementation of HPV vaccination into the national immunization programme: High vaccine cost or inappropriate pricing policy,low level of awareness among public, negative public perception, low level of awarness among health care providers,not high on political agenda. Parents perceive the vaccine as risky.There are many reasons why people are not getting the HPV vaccine: one of the biggest reason is that physicians are hesitant to talk to 11- and 13-year-olds about vaccines when they feel compelled at the same time to talk about the sexual nature of the virus's transmission. I believe we should think of this vaccine as what it is: a cancer-preventing vaccine. Social media and text messaging can increase the amount of knowledge on the prevention of STDs. 80% of teens report using social networking sites. EDIT X

P86 The Role Of Genetic Polymorphism Gene TNF-α (G-308A) in the formation of cervical intraepithelial cervical neoplasia

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In recent years, several research groups have been studied polymorphism rs1800629 associative role in the formation of cervical CIN.
Objective: Molecular genetic analysis of polymorphism rs1800629 gene TNF-a in the formation of CIN in women of Uzbek nationality.
Materials and methods: The study included 91 women of Uzbek nationality with a diagnosis CIN (study group). Age patients studied ranged from 24 to 50 years. For a more precise assessment of the significance of polymorphic marker rs1800629 in the formation of CIN, a study group was divided into 2 sub-groups (comparison). The first subgroup of patients classified with endometrial hyperplasia had no cervical CIN ($n = 46$). Second group was formed from patients with CIN of cervix ($n = 45$). As a control group 95 healthy women were examined and they had no CIN signs and other gynecological problems. Also they had no relative bounds and matched to study group by their age. Analyses of genotype polymorphism allocation rs1800629 in 91 patients with CIN diagnoses revealed prevalence of homozygote G/G type (85.3% and 68.1%, respectively) above heterozygote G/A type (13.7% and 31.9%, respectively) and rare homozygote A/A genotype (1.0% and 0%, respectively). Homozygote condition – G/G of studied polymorphic type was more favorable for carriers than heterozygote type – G/A.
Conclusions: Presence of G/A genotype of polymorphism rs1800629 gene TNF-a in women may be considered as genetic factor of predisposition in CIN development.

P87 Hormone replacement therapy for a young woman with cervical sarcomatoid squamous cell carcinoma

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Cervical sarcomatoid squamous cell carcinoma (SSCC) is an extremely rare malignancy. We report the case of a young woman with cervical SSCC who experienced perimenopausal syndrome following treatment, and our evaluation of the considerations relating to hormone replacement therapy (HRT) in this case. A 24-year-old Chinese woman with SSCC underwent radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. Following surgery, she received radiation therapy, chemotherapy and lymphocyte immunotherapy, and developed severe menopausal symptoms. After assessing the pathological type of the carcinoma, hormone receptor status and disease stage, we performed HRT for this young woman. During two years of follow-up, she has remained cancer-free, without postmenopausal symptoms. We conclude that HRT following surgery may be appropriate in certain young women with cervical sarcomatoid carcinoma to enhance their quality of life.

P88 Association of BRCA2 N372H polymorphism with the risk of early onset of breast cancer in a cohort of Sri Lankan breast cancer patients

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Context: Several studies have been investigated the association of BRCA2 N372H (c.1114A>C) non-synonymous polymorphism with breast cancer risk, but the results were inconsistent. However, according to meta-analysis studies done in Northern European women have identified that HH genotype increased the risk of breast cancer by1.3-fold. In Sri Lanka, breast cancer is the leading cancer type among women and contributes to 25.2% of all cancers.
Objective: Current study is a preliminarily work to detect association of BRCA2 N372H polymorphism with breast cancer susceptibility in young breast cancer patients in Sri Lanka.
Methods: 21 young breast cancer patients (<40 years) with a strong family history of breast cancer and 10 healthy controls were analyzed for BRCA2 N372H polymorphism. Ethical approval and written informed consent obtained prior to the study. Genomic DNA was isolated from blood and PCR carried to amplify exon10. Direct sequencing was done using ABI 3500Dx Genetic Analyzer and sequences generated analyzed using Mutation Surveyor®, Alamut® and BioEdit® software.
Results: Eleven patients with NN genotype, seven patients with NH genotype and three patients with HH genotype were identified among young breast cancer patients. Allele frequency of ''A'' allele was higher among the young breast cancer patients (0.69) compared to ''C'' allele (0.31). Among healthy controls, ''A'' allele was (0.80) more frequent than the C allele (0.20).
Conclusion: Thus, no evidence was found to be significant to increase the breast cancer risk in young familial breast cancer patients by N372H polymorphism. Since this is a pilot study done on BRCA2 N372H polymorphism, it is necessary to expand the sample size to establish the association.

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P89 Impact of age on knowledge, attitude and behaviour with respect to breast cancer in women living in Albania

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Context: Breast cancer numbers are climbing high. During our practice,unfortunately more than half the cases of breast cancer diagnosed were at advanced stages.
Objective: This study aimed to determine if there is a link between knowledge and behavior towards breast cancer in different age groups of women, taking into consideration guidelines for those group targets.
Materials and methods: This study was designed as a survey over internet, through a questioner. A total of 642 women, aged 40–73 years old completed the questioner.
Patients Interventions: All answers from patients were revised. There was no interaction with them whatsoever.
Main Outcome: Evaluation of knowledge, attitudes and behavior with respect to breast cancer by age groups
Results:Age as a risk factor was identified in fewer women after the age of 50 compared to the younger ones ($p = 0.01$), as was having a relative with breast cancer ($p = 0.001$). Younger women were more aware of the fact that 1 in 8 women in their lifetime risk to have breast cancer. ($p < 0.001$). Women over 60 were less likely to undergo a mammogram as a reassurance compared to those under 60 ($p = 0.04$). Other health issues seemed to have their attention compared to the risk of breast cancer ($p < 0.001$). On contrary, women in their 40s were more likely to plan to undergo mammograms ($p < 0.001$). Although about 80% of women reported to practice breast self examination, only 30% had it done at the appropriate frequency
Conclusions: October is not enough to ''think pink''. Women starting at a young age need to be taught how to self-exam their breasts and when to see a doctor. Older women should be referred by their GPs for regular mammograms despite any underlying disease. As age increased, knowledge and positive behaviour and attitude decreased when it came to breast cancer risk.

P90 The influence of reproductive history on histopathological features and prognosis of breast cancer in young women

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Mauriziano Hospital

Context: Pregnancy seems to have a dual effect on breast cancer, with an increased risk early after delivery followed by a long-term protective effect.
Objective: We investigated the association between reproductive factors and pathological characteristics of breast cancer and the impact on prognosis in a population of breast cancer patients.
Methods: Clinical and pathological data were collected from our database.
pATIENTS: 444 women aged $\leq$40 years with diagnosis of breast cancer treated at the Gynecologic Oncology Division of the University of Turin (1987–2014) were included. Patients were classified into 4 group according to their reproductive history: nulliparous, women who gave birth within the previous 2 years, 2–5 years and >5 years.
Interventions And Main Outcome Measures: The analysis focused on the comparison of pathological features of breast cancer in patients stratified on the basis of their reproductive history, and the differences in survival.
Results: Patients who gave birth recently before breast cancer had larger tumor size, higher number of positive lymph nodes and higher grade. These patients showed lower expression of ER and PgR and a trend toward higher amplification of HER2 gene. The negative impact of pregnancy on survival is more evident when breast cancer was diagnosed early after delivery. The 10-years overall survival was 80% for the nulliparous group, 86% for the parous group >5years, 72% for the parous group 2–5 years and 77% for the parous group <2 years. Similar results were reported for disease-free survival.
Conclusions: The group of women who gave birth early before breast cancer have more aggressive tumors and a worse prognosis compared with women who had a pregnancy more than 5 years before diagnosis. This subgroup of patients have better prognosis also than nulliparous women, confirming the long-life protective effect of pregnancy.

P91 Subject: testicular feminism – Morison syndrome

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QKUK-KOGJ

Objective: Stands to the challenges encountered in the diagnosis and treatment of a rare case, in front of a few gynecologists experience with such cases.
Case interpretation: Female Patient T.A 31 years old,married,came to the O&G-Clinic on date:12.12.2014 in the endocrinology department with complains of abdominal pain in the lower quadrants accompanied with urinary discomfort, constipation and absence of menstrual cycle.
In the examination: Patient is tall, with secondary characteristics to female type but very poorly developed, external genital organs hypoplastic, with low pilosity. Ultrasonography in the pelvic cavity detected two tumefactions with irregular forms calcificated with dimension 9.2×7.8 cm in Douglas cavity with low quantity of fluid. LH and FSH are high, testosterone values in the upper limit The tumor markers are normal except CEA-6.0ng/mL. on MRI of head there are no pathologic findings, in Pelvic MRI two solid calcificatetd formations detected which they make presion to the urinary bladder.
Results: On date 08.02.2015 the Kariogram shows 46,XY which explains a Testicular Feminism.On date 23.02.2015,the patient get the surgical treatment, which two tumor masses are removed they are histopathologically diagnosed with Seminoma testis, and the histology of free fluid shows Maligne germinative cells. After this treatment patient is ordinated to oncologic institute for further treatment.
Conclusion: Diagnostic difficulties faced, kariogram he who determined that we are dealing with testicular feminism, while surgical treatment and histopathology of material removed, were those who put the final diagnosis. From this case we have concluded that patients with primary amenore be diagnostfikuar earlier to have good prognosis.

P92 Case review: rare cases of malignant tumors with acute abdomen in pregnancy

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Objective: To review the presentation and managements of acute abdomen cases in pregnancy caused by malignant tumors.
Methods: Cases of acute abdomen in pregnancy caused by Malignant tumors were reviewed within a year duration. The presentation and managements were compared.
Outcome and result: Two cases were reviewed. The first case was a 36 year-old, Gravida 2 para 1 with one previous scar presented with acute

lower abdominal pain and vomiting at 9 weeks gestation. perabdomen was a mobile and tender 26 weeks size mass. Emergency laparotomy was done with the impression of twisted ovarian cyst. Intraoperatively revealed normal uterus corresponded to dates with normal ovaries. There was a twisted pedunculated mass measuring 10 x 15 cm in size with a small stalk attached to the greater curvature of stomach. The histopathological examination revealed as malignant 3b Sarcomatoid epithelioid gastrointestinal stromal tumour (GIST). Oesophago-gastric-duodeno-scopy and computed tomography asessment done post delivery shows no evidence of local disease or distant metastasis. The second case was a 30 yearold Gravida 5 Para 3 + 1 presented with preterm labour at 35 weeks gestation. There was no changes in bowel habits nor significant loss of weight. She complained of severe persistent abdominal pain in active phase of labour. Examination revealed tense abdomen above the uterus. We proceeded with emergency cesarean section for acute abdomen. Intraoperative finding was a huge intraluminal mass obstructing the sigmoid colon. She underwent large bowel resection and colostomy. Histopatholgy report came back as well differentiated Adenocarcinoma of the colon. She was planned for chemotherapy and panproctocolectomy.

Discussion and Conclusion: Malignant tumours with acute abdomen in pregnancy is rare. It is challenging to make the diagnoses as the signs and symptoms might not be obvious.

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P93 Fertility-sparing surgery in high risk ovarian cancer: time for overcome initial concerns

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Introduction: Fertility-sparing surgery (FSS) is a strategy often considered in young patients with low-grade (G1–2) early-stage epithelial ovarian cancer (eEOC), whilst it is still controversial in high-risk patients. We investigated the role of FSS in low and high-risk (IAG3 and upper stages) eEOC patients undergoing comprehensive surgical staging.

Materials and methods: We analyzed data from 430 patients operated for eEOC from 1975 to 2015, focusing on patients submitted to FSS. Patients underwent FSS were compared with patients underwent radical-comprehensive-staging (RCS) in the same study period. Propensity-score was used to compare two homogenous groups of patients and avoid possible allocation bias. Disease-free (DFS) and overall survival (OS) outcomes were assessed using Kaplan-Meier and Cox models

Results: Overall, 71 (17%) and 359 (83%) patients had FSS and RCS, respectively. At univariate analysis, FSS did not influence the DFS (HR: 1.05 (95%CI: 0.55–2.02); $p = 0.80$) and OS (HR: 1.94 (95%CI: 0.75–4.99); $p = 0.18$). Independently, increased age and high-risk disease correlated with worse OS ($p > 0.01$). Focusing on high-risk patients, we observed that type of surgery (FSS vs. RCS) did not influence DFS and OS, even after balancing our population using a propensity-score matching ($p > 0.1$).

Conclusions: FSS upholds oncologic effectiveness of RCS, preserving reproductive and hormonal functions. Although high-risk eEOC patients experience worse survival outcomes than low-risk eEOC, FSS per se does not influence the risk of recurrence and should not be denied even in this group of patients.

P94 Peri-operative blood transfusions worsens survival of locally-advanced cervical cancer patients undergoing neoadjuvant chemotherapy

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Introduction: Transfusions represent one of the main progresses of modern medicine. However, accumulating evidence supports that transfusions correlate with worse survival outcomes in patients affected by solid cancers. In the present study we aimed to investigate the effects of peri-operative blood transfusion in locally advanced cervical cancer (LACC).

Methods: Data of consecutive patients affected by LACC scheduled to undergo neoadjuvant chemotherapy plus radical surgery were retrospectively searched in order to the test the impact of peri-operative transfusions on survival outcomes. Five-year survival outcomes were evaluated using Kaplan–Meir and Cox models.

Results: The study included 275 patients. Overall, 170 (62%) patients had blood transfusion. Five-year disease-free and overall survivals were 86% and 88%, respectively. Via univariate analysis we observed that transfusion correlated with an increased risk of developing recurrence ($p = 0.02$). Other factors associated with 5-year disease-free survival were clinical ($p = 0.06$) and pathological ($p = 0.03$) responses at neoadjuvant chemotherapy as well as parametrial ($p = 0.004$), vaginal ($p < 0.001$) and lymph node ($p = 0.002$) involvements. However, via multivariate analysis only vaginal ($p = 0.01$) and lymph node involvements ($p = 0.05$) correlate with worse disease-free survival. Interestingly a trend towards worse outcomes was observed for patients undergoing blood transfusion ($p = 0.07$). Looking at factors influencing overall survival we observed that lymph node status ($p = 0.01$) and vaginal involvement ($p = 0.06$) were independently associated with survival.

Conclusions: Blood transfusions seem potentially related to a slightly increased risk of developing recurrence. Further evidence is needed; however, on the light of the current evidence, appropriate transfusional measures are necessary to avoid unnecessary transfusions.

P95 Sex hormonal and metabolic profiles in endometrial hyperplasia and cancer patients

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Context: Endometrial cancer, especially Type I EC, is regarded as a stepwise disease. Unopposed estrogen exposure is thought to be the key factor stimulating the development of EH and EC. But it is unknown whether hormonal or metabolic disorders occur at the very early stages of abnormal endometrial proliferation.

Objective and Main Outcome Measure: To investigate the possible relationship between serum endocrine change and development of EC.

Methods and Patients: We conducted a prospective cross-sectional study. 628 patients (101 DPE, 200 SH, 128 CH, 94 EAH, 105 EC) and 124 healthy women were enrolled. All of them signed informed consent forms. General information was collected; sex hormones, SHBG, glucose metabolic profiles and serum lipids were examined. Statistical analysis was performed using SPSS 20.0 and 0.05 was chosen as the significance test level.

Intervention: Observational study.

Results: We did not find increased E2 among premenopausal women and it showed a tendency to decline as the aggravation of endometrial lesions, while it increased among postmenopausal women ($p < 0.05$). In a menopausal age paired mode, higher E2 level was found in EC

groups ($p < 0.01$). SHBG showed a downward trend in premenopausal women ($p < 0.01$), while it had no statistical difference in postmenopausal women. No statistically significant difference in E2/SHBG, P, FSH, LH and T was found among all groups. Increased PBG, FINS and HOMA-IR index were all related to development of endometrial lesions. Blood lipids level showed no significant correlation.
Conclusions: In our study, E2 level showed contrary tendency in subjects. Insulin resistance (IR) happened at DPE, which is the earliest stage of endometrial hyperplasia, and IR is associated with development of endometrial lesions. Increased local estrogen sensitivity might be the key mechanism involved in development of EC.

P96 PKN1 overexpression as a predictor of poor survival in endometrial cancer

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Context: Endometrial cancer (EC) is among the commonest gynaecological tumours with steadily increasing share in reproductive age women. Currently is fairly impossible to predict tumor behavior on early stages. It requires the biomarkers search for tumor's molecular profiling. The protein kinase 1(PKN1) inhibits cell migration, proliferation and invasiveness. Its overexpression was observed in different cancers.
Outcomes: To evaluate the PKN1 expression in primary EC; discover correlation with tumor characteristics and patient's survival.
Methods: Immunohistochemical analysis of 200 stained FFPE tissue samples (1 sample of tumour, 1 sample of adjacent benign tissue from each patient). 2 authors independently performed staining evaluation(4 levels) with light microscope. Results standardized in favour of weaker expression. Statistical analysis performed in SPSS.
Patients: 100 Women (age 36–92), who undergone hysterectomy due to primary EC in Karolinska University Hospital,Sweden. Follow-up data was taken from the medical records.
MOM: Correlation between PKN1 expression and following variables:patient's age, weight, BMI, tumour stage (FIGO), grade, ploidy, invasive depth, p53, estrogen (ER) and progesterone (PR) receptors expression.
Results: Cytoplasmic PKN1 expression was significantly higher in tumor tissue comparatively to adjacent normal tissue ($p < 0.0001$). Overexpression was significantly connected with worse survival of aged patients in multivariate analysis. Disease specific survival analysis showed significant correlation with PKN1 expression,age,depth of tumor invasion,ploidy,ER and PR expression. No correlation observed with stage, grade, and intensity of adjuvant treatment.
Conclusion: PKN1 is considered as future predictor of EC patient's survival. It was firstly demonstrated that, PKN1 cytoplasmic overexpression evidences poor survival in aged patients with deep-invasive ER+ and PR+ endometroid tumours.

P97 Preoperative sonovue contrast color Doppler evaluation of patients with cervical cancer

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Context: Tumor angiogenesis has gained much attention in oncology in recent years.
Objective: The purpose of the study was to determine whether Color Doppler ultrasound examination with intravenous contrast is superior for preoperative discrimination of FIGO stages of cervical cancer.
Patients: This is a prospective observational study. The study included fifteen patients with proven cervical cancer.
Interventions and Methods: Preoperative the patients were investigated with transvaginal Color Doppler ultrasonography and with SonoVue contrast Color Doppler.
Results: Contrast Doppler US after the SonoVue injection gave a good picture of the intense intralesional tumor angiogenesis. Of the 18 patients with clinically FIGO stage Ib1 Contrast-sonography showed 15 patients stage Ib1, 1-stage Ib2, 1-stage IIb and 1-stage IVa at final diagnosis. The gold standard was the histological diagnosis of the surgically removed tumors.
Conclusions: Contrast Doppler Ultrasound gave a better definition of the margins of the neoplastic lesions in the cervical cancer. Because contrast agents increase the sensitivity of detection of parametrial invasion and lymph node metastases, they could pay an important role in the evaluation of uterine cervical cancer.

P98 The Management of Cervical Pre invasive Disease

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Screening for cervical cancer with PAP smear and the evaluation of all abnormal results with colposcopy and biopsy are now a major public health challenge in Albania.The convectional PAP smear is a routine method in Albania screening women for cervical cancer.When a cytological abnormality is encountered on screening, it has to be confirmed with the help of a conclusive test .Colposcopy and directed biopsy is an accepted management technique for a selected cohort of patients with abnormal cytology.
Objective: The main goal of secondary cervical screening is to identify women with abnormal PAP smear, than to follow-up in colposcopy and,depending of these results, to do directed biopsy.
Methods: Colposcopy and directed biopsy was done. Histological prediction of colposcopic findings done according to the Reid's modified colposcopic index. Colposcopic guided biopsy taken from the most suspicious areas. The result of the biopsy correlated with the predicted diagnosis of Pap smear.
Patients – The stady involved recruitment of 436 women who took part in routine cervical screening at UH O-G ''K. Gliozheni'', were retrospectively reviewed and analysed.
Results: Total of 436 pap smear were taken from 1st January 2014 to 30th December 2014, which is the time period of our study. Out of these 60 patients had abnormal pap smear (ASCUS, LSIL, HSIL) . Colposcopy and directed biopsy was done in all patients and histopathology report was collected. The results were analysed statistically. Correlation between cytology and histopathology was considered to be 'fair', Kappa= 0.427. But the correlation was good for severe dysplastic lesions.
Conclusion: Pap smear is just a screening test and is subjected to limitations. Abnormal Pap smear should be further evaluated in order to get a correct histological diagnosis. The challenge is to enhance it with high cost-effective approaches.

P99 Do women with increased susceptibility to breast cancer have lower bone mineral density?

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Context: Data from the Womeńs Health Initiative (WHI) study show that women with breast cancer have lower bone mineral density (BMD).

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There is no data on whether that difference presents also in women with susceptibility to that cancer.
Objective: The objective of this study was to discuss whether women who were positive to BRCA1 and BRCA2 genes had lower BMD than a match group of standard risk women.
Methods: The results of spine and hip densitometries (T-score, DXA), were compared in both groups by using Student's t-test for independent samples, after testing its normal distribution by Kolmogorov–Smirnov statistical test. SPSS 20.0 was used for the analysis, considering a p value <0.05 as statistical significant.
Patients: An observational analytical unicenter study was performed including premenopausal women who underwent salpingo-oophorectomy between 1975 and 2014. Women exposed to treatments affecting bone metabolism were excluded. We included 71 that were divided into two groups: 29 BRCA carriers (mean age 41 ± 9) and 42 non-BRCA carriers (mean age 66 ± 9 years).
Interventions: BMD assessments were performed by hip and spine densitometries (T-score, DXA) within the year after the surgery.
Main Outcome Measures: BMD by DXA.
Results: Results of bone densitometry at both hip and spine were not statistically different between groups. (hip: IC 95% -0.49 to 0.42, $p=0.891$; spine: IC 95% -0.28 to 0.9, $p=0.3$).
Conclusions: We did not find statistically significant difference between BMD at either hip or spine between BRCA carriers and women at standard risk for that cancer. Possibly, the small sample may have affected the results. Further studies are required to clarify this hypothesis.

P100 Sociodemographic determinants of knowledge and attitude related to human papillomavirus (HPV) vaccination in the primary prevention of cervical cancer among University Tunku Abdul Rahman (UTAR) students

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Introduction: Cervical cancer is the third most common cancer among women globally and HPV is a recognized causative agent in 70% of all cases. The Malaysian government had officially implemented the HPV immunisation program in secondary school children in 2010.
Objective: To identify the sociodemographic determinants of knowledge and attitude towards HPV vaccination in the primary prevention of cervical cancer among UTAR students.
Methods: A cross-sectional study was conducted using self-administered questionnaires, recruiting 374 UTAR's students as respondents by using convenience sampling method. Respondents were categorized into good/poor level of knowledge and positive/negative attitude towards HPV vaccination.
Results: More than half of the respondents were female (64.5%) and majority were 20 years old and below (55.8%). Generally, 54.7% of the total respondents had high level of knowledge towards HPV vaccine and 57.5% of the total respondents showed negative attitude towards HPV vaccine. Female respondents age 20 years old and below showed good knowledge (56.4%) and more positive attitude (55.8%) towards HPV vaccine. Students from Faculty of Medicine and Health Sciences (FMHS) exhibited both good knowledge (67.3%) and positive attitude (62.4%) towards HPV vaccine as compare to Faculty of Accountancy and Management (FAM).
Conclusion: Majority of UTAR students have a good knowledge towards HPV vaccination; contrary exhibited negative attitude towards HPV vaccination depicting the necessity to impart and further intensify the sense of health awareness among all students especially among male students. The judicious use of social media apart from the conventional mass media should be an advantage as to enhance the practice of HPV vaccination among them and thereafter minimise the health and economic burden of cervical cancer.

P101 La prevenzione del tumore della mammella in gravidanza: progetto pilota

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Introduzione: Il carcinoma della mammella è la neoplasia più comune nelle donne in gravidanza con un'incidenza di 1 caso ogni 1000–3000 gravidanze (età media alla diagnosi 32–38 anni) (3; 4; 5) in progressivo incremento a causa dell'aumento dell'età delle donne alla prima gravidanza (età media al primo figlio: >31 anni)(6) e all'aumento di incidenza del tumore della mammella nelle donne giovani. In questo gruppo di pazienti si è osservato un ritardo diagnostico variabile da 1.5 a 6 mesi, dovuto sia alle difficoltà dell'esame obbiettivo per i cambiamenti fisiologici della mammella in gravidanza, sia alla scarsa attenzione al problema da parte degli specialisti che seguono la gravidanza (5). Circa il 90% dei casi il primo sintomo della neoplasia mammaria in gravidanza (nodulo palpabile, retrazione cutanea) è stato rilevato dalla paziente stessa, nonostante le ripetute visite cliniche alle quali si era sottoposta per monitorare la gravidanza. Si è deciso, quindi, di progettare uno studio pilota finalizzato alla prevenzione senologica per le donne in gravidanza. Gli obbiettivi del progetto sono la diagnosi precoce del carcinoma mammario in gravidanza, la sensibilizzazione delle donne e dei ginecologi al problema e la sensibilizzazione delle donne alla prevenzione senologica.
Materiali e metodi: Il progetto, che ha coinvolto i senologi dell'Ospedale Moriggia-Pelascini di Gravedona che operano anche presso gli ambulatori della Lega Italiana per la Lotta contro i Tumori e i ginecologi del medesimo Ospedale, consiste nell'offrire una visita senologica specialistica ed un'ecografia mammaria gratuite a tutte le donne gravide durante il primo trimestre quando le mammelle sono più facilmente indagabili. Il progetto è iniziato nel marzo 2013 e ha coinvolto i senologi dell'Ospedale Moriggia-Pelascini di Gravedona, che operano anche presso gli ambulatori della Lega Italiana per la Lotta contro i Tumori e i ginecologi del medesimo Ospedale. Per favorire l'adesione delle donne al progetto, si è deciso di offrire il controllo senologico gratuitamente; questo è stato possibile grazie al supporto economico del gruppo volontario di giovani donne operate alla mammella ''Giovani Marmotte Alto Lario''. E' stato predisposto un modulo che il ginecologo compila e consegna alla donna gravida al momento della visita sul quale sono riportati i dati anagrafici della donna, la nazionalità, l'età gestazionale, il numero di gravidanze e il numero telefonico da chiamare per prenotare la visita e l'ecografia mammaria. La seconda parte del modulo che è compilata dal senologo al momento della visita riportata la diagnosi e i consigli relativi alla visita eseguita. Il modulo è ritirato dal senologo al momento della visita e i dati sono inseriti in un database per le valutazioni statistiche, da una data-manager della Delegazione Alto Lario della LILT.
Risultati: L'analisi dei dati, dopo 2 anni e 6 mesi, hanno dimostrato una buona compliance (tasso di adesione) da parte delle donne. In particolare il 33.5% delle donne che hanno aderito al progetto non si era mai sottoposta ad un controllo senologico (età media 30 anni). Le criticità emerse sono due:
1.le donne non-italiane che hanno partecipato al progetto sono l' 8.2%
2.solo il 48% delle donne che hanno partecipato al progetto è stata inviata dai ginecologi dell'ospedale; questo ha evidenziato una scarsa attenzione al controllo senologico da parte dei ginecologi coinvolti, pur considerando che alcune donne non-vogliono sottoporsi al controllo senologico proposto. In particolare è stata evidenziata la perdita di attenzione dei ginecologi al progetto con il passare del tempo.
Per superare questo punto, i senologi hanno tenuto incontri informativi a cadenza bimestrale con i ginecologi, producendo dei reports con i dati di monitoraggio del progetto stesso.
Conclusioni: Il progetto si è mostrato fattibile e pertanto può essere riproposto in altri centri.

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Per implementare il progetto, da giugno 2015 si è deciso di coinvolgere le ostetriche, che prestano assistenza alla donna gravida (per la gravidanza fisiologica). Per questo sono state organizzate riunioni per informare e sensibilizzare le ostetriche e si è deciso inoltre di organizzare un corso di senologia indirizzato a loro, per aumentare le loro conoscenze senologiche.

Surgery

P102 Diagnostic and operative hysteroscopy before IVF

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Context: Hysteroscopy is the gold standard test for assessing the uterine cavity. There is evidence that performing hysteroscopy before starting IVF treatment could increase the chance of pregnancy in the subsequent IVF cycle in women who had one or more failed IVF attempts.
Objective: to evaluate the safety and diagnostic value of hysteroscopy before IVF.
Methods: diagnostic or operative hysteroscopy was performed in all patients.
Patients: 600 patients seeking treatment for subfertility
Main Outcome Measures: the presence of minor and major pathology of the endometrium in infertile patients
Results: Seventy-eight percent of all procedures were done under intravenous anesthesia. Diagnostic hysteroscopy was performed successfully in all women. The most common operative procedure was polypectomy and the most complicated one was myomectomy. The combination of mechanical instrument and bipolar energy were used in most of the cases, while the percentage of complications was extremely low. Diagnostic hysteroscopy was performed successfully in all women. 53.7% had a history of ART failures. In 36% findings at hysteroscopy were normal, whereas in 64%, hysteroscopy revealed intrauterine lesions (polyps, septa, submucosal leiomyomas, or synechiae) that led to operative hysteroscopy. The total percentage of abnormal intrauterine findings was higher in women with a history of repeated ART failures in comparison with those with no history of ART attempts.
Conclusion: Hysteroscopy is a safe, highly sensitive, precise diagnostic and operative endoscopic procedure. Diagnostic hysteroscopy should be performed after all IVF failure and maybe before IVF in all patients, because a significant percentage of them have undiagnosed uterine disease that may impair the success of fertility treatment.

P103 Role of laparoscopy and hysteroscopy in the evaluation of uterine scar after cesarean section and its surgical correction

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Study *Objective*: At present time there is a stable tendency to increase in frequency of Cesarean section that's why evaluation of the uterine scar condition is actual.
Design: 29 Patients with the uterine scar incompetence were enrolled in the study. Patients were divided in 3 groups: 1st – diagnostic hysteroscopy and laparoscopy (7), 2nd – hysteroscopy, Laparoscopic repair of incompetence scar (8), 3 – hysteroscopy, Laparoscopic excision of incompetence scar margins and its repair.
Setting: Dept. Operative Gynecology of the Research Centre for Obst., Gyn., & Perinatology.
Intervention: hysteroscopy, Laparoscopic excision of incompetence scar margins and its repair.
Measurements and Main Results: mean age of patients was 28.4±3.8 years. All patients had history of urgent cesarean section (acute hypoxia, secondary weakness of labor, clinically narrow pelvis). The thickness of the scar by ultrasound and MRI to 4 mm, the presence of niches was in all cases. 23 patients had menorrhagia, metrorrhagia, pain, dyspareunia, infertility. Mean operative time was 52±15; 106±38; 143±32 min, respectively. 7 patients had intrauterine synechia. Intaoperative blood loss was extremely low (50 ml). No complications were observed. One patient of the 3 group had reoperation. After operation all patients of 2 and 3 groups had thickness of the scar up to 6 mm. At present time 8 patients are pregnant.
Conclusion: Laparoscopic repair of incompetence scar is minimally invasive and effective treatment. But this issue requires further study: development of criteria for the evaluation of the scar incompetence with the use of ultrasound and MRI, indications for incompetence scar repair, the choice of surgical method of surgical treatment, evaluation of results

P104 Laparoscopic excision of benign ovarian cysts: outcome in 100 consecutive patients

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Context: Surgical excision of ovarian cysts has the possibility to result in damage to ovarian function and affect fertility.
Objective: To evaluate patients undergoing laparoscopic excision of ovarian cysts and to assess their future fertility.
Design: Retrospective clinical study
Methods: Patients who underwent laparoscopic excision of ovarian cysts between March 1993 and November 2014 were included in the study. A prospective follow-up was conducted. Operative course and reproductive outcomes were investigated.
Results: During the 14-year period, 100 consecutive women (mean age: 30.4±6.2 years, parity: 0.5±0.7) with ovarian cysts (endometrioma $n=84$, dermoid $n=12$, serous cysts $n=4$) were included in the study. Median duration of follow-up was 8.5 years (range 2–17 years). Average size of ovarian cysts was 5.3±1.9 cm and cysts were more common on right side ($n=53$). Spillage was observed in three patients. No significant intraoperative or postoperative complications were seen. Ninety two women were keen on future pregnancy and 79 conceived following surgery ($n=52$ spontaneous; $n=27$ artificial). Mean duration for conception following cystectomy was 12 months. Overall recurrence rate after 12 months of 6%. In total, 85.9% patients seeking fertility became pregnant and 68 carried their conception to term (86.1%). Cesarean section was done in a majority ($n=60$, 75.9%).
Conclusion: Laparoscopic ovarian cystectomy is a safe procedure with low surgical complications and good fertility outcome.

P105 Laparoscopic management of interstitial ectopic pregnancy

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Context: To illustrate the successful management of interstitial ectopic pregnancies with laparoscopic excision.

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Objective: To describe the detection and evaluation of a interstitial ectopic gestation and its subsequent treatment with laparoscopic excision.
Patient(s): Three women (mean age: 28 yrs, range: 24–32 yrs) underwent laparoscopic excision for interstitial ectopic gestation at our institution.
Measure(s): Mean operative time, blood loss, complications, fertility outcome
Result(s): Mean operative time was 49.4 ± 8.4 minutes (range:41–69 mins). Average estimated blood loss was 50 ±4 mL (range: 48–52 mL). There were no intraoperative or postoperative complications. Average duration of hospital stay was 24 ± 3 hours. All patients are currently doing well on followup visits.
Conclusion: The authors demonstrate the role of laparoscopic excision and conclude that this operative technique, when performed by an experienced surgeon, allows for improved surgical dexterity and can be considered a safe and effective method in the management of interstitial ectopic pregnancy.

P106 AMH changes following laparoscopic tubal sterilization

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Context: Tubal sterilization is a commonly practiced contraceptive method. However, this intervention has been proposed as cause of ovarian damage and early menopause due to reducing utero-ovarian blood flow.
Objective: To investigate whether ovarian reserve estimated by Anti-Müllerian Hormone (AMH) levels, is affected by laparoscopic tubal sterilization
Methods: Prospective controlled cohort study. AMH levels were measured pre-operatively and as 3- and 6- months post-operatively
Patient(s): Thirteen women (age 18–44 years) undergoing laparoscopic tubal ligation at Södersjukhuset, Stockholm Sweden (cases) and twelve women undergoing a diagnostic laparoscopy (control group). The choice of contraceptive method had already been made by the patients at the time of recruitment.
Intervention(s): Laparoscopic tubal ligation by bipolar coagulation in the cases' study group.
Main Outcome Measure(s): Differences in changes in AMH levels between the cases' and controls' groups.
Result(s): The serum concentrations of AMH were maintained within normal ranges and did not change significantly over time in any of the groups. In the sterilization group median AMH showed a small increase from baseline levels (1.2 μg/L to 1.3 μg/L at 3-months and to 1.9 μg/L at 6-months, $p = 0.161$ and $p = 0.093$, respectively). Similar non-significant changes were observed in the control group.
Conclusions: This study does not support that laparoscopic tubal ligation leads to a decreased ovarian reserve on the short-term, estimated by serum AMH concentrations. We found a trend towards increasing AMH after laparoscopic tubal ligation, which was not explained by the previous use of hormonal contraceptives.

P107 Laparoscopy in treatment of adnexal masses during pregnancy

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Context: Comparison of laparoscopy (Ls) and laparotomy (Lt) in treatment of adnexal masses during pregnancy
Objective: To evaluate main surgery parameters and obstetrical outcomes
Methods: Retrospective and prospective analysis
Patients: 123 Pregnant women underwent surgery for adnexal masses during pregnancy
Interventions: 41-Lt, 82-Ls during pregnancy
Main outcomes: operative time, bloodloss, length of hospital stay, gestational age, birth weight, Apgar score, rates of low birth weight, miscarriage and preterm labor
Results: The Ls group had shorter operative time (63.2±2.8 min vs. 86.1±2.5 min, $p < 0.05$), less bloodloss during surgery (99.5±10.7 ml vs. 245.4±55.0 ml, $p < 0.05$), less frequency of administration of narcotic analgetics (1.7±0.3 ml of 2% promedol vs. 3.9±0.4 ml), shorter length of hospital stay (8.6±0.4 days vs. 10.9±0.5 days, $p < 0.05$) than the Lt group. There were no significant differences for mean gestational age, mean birth weight, mean Apgar score, rates of low birth weight or miscarriage. Preterm labour was the single outcome that was significantly different between groups (6.1% in Ls group vs. 17.1% in Lt group, $p < 0.05$). Lt surgery had a significantly higher risk of preterm labour than Ls (OR 7.8; 95% CI 1.98–30.78; $p = 0.003$). Gestational age at surgery over 24 weeks also had a higher risk of preterm labour (OR 4.17; 95% CI 0.94–18.52; $p = 0.061$). Surgery performed in 3rd trimester had a significantly higher risk of preterm labour than in 2nd trimester (OR 10.6; 95% CI 1.35–83.54; $p = 0.025$). Women with adnexal mass and fetoplacental insufficiency had a significantly higher risk of preterm labour compared with those with adnexal mass alone (OR 17.5; 95% CI 3.33–92.09; $p = 0.001$).
Conclusions: Laparoscopy has obvious benefits in pregnancy. Performing laparoscopic surgery in mid-second trimester of pregnancy would minimize the risk of preterm labor.

P108 Subtotal and total laparoscopic hysterectomy (SLH and TLH) with prevention of pelvic floor dysfunction

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Context: In gynaecologic endoscopic surgery, endoscopic hysterectomies are performed since 1990 and have reached as well with single port entry as well as with multiple port entry or with robotic assistance an acceptable success rate with few side effects. NESA has established an advice for the absolutely necessary surgical steps.
Objective: Laparoscopic Total Hysterectomy (TLH) in benign cases consists of 4 steps:
1. Recognition of anatomy and separation of the uterus from the pelvic side wall and from its vascular supply
2. Intrafascial dissection out of the vagina by conservation of pelvic fascial compartments, like sacro-uterine ligaments.
3. Prevention of descent of pelvic floor and douglascele by fixation of the sacro-uterine ligaments to the vaginal stump
4. Vaginal extraction and closing of vagina by a continuous suture.

Methods: Laparoscopic Subtotal Hysterectomy (LSH) in benign cases, with specific indications, consists of 3 steps:
1. Intrafascial resection of the uterus from the cervix
2. Uterine contained morcellation and resection
3. Peritonealisation of the cervical stump

The correct indication for the selected procedure of hysterectomy in accordance with the wish of the patient depends on the knowledge of the individual surgeon and his current possibilities. We should never insist on one technology but always have a panel for discussion.
Patients and Results: In 1014 patients (2008–2015) no uterine sarcoma was detected at pathohistolgoy. As complications one serious infection and one haemorrhage requiring a second laparoscopy occurred.
Conclusion: TLH and SLH resulted to be save techniques preventing pelvic floor dysfunction and descent if performed in the correct way.

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P109 The impact of ovarian surgery on ovarian reserve in patients with endometriosis

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Background: We investigate the impact of previous ovarian surgery on ovarian reserve in patients with endometriosis.
Methods: We have investigate a total of 60 female patients who had been diagnosticated with ovarian endometriosis. We further divided these patients into two groups. Group 1: endometriosis group without previous surgery; Group 2: endometriosis group with previous surgery. The parameters for comparison included age, body mass index, serum estradiol, follicle-stimulating hormone, luteinizing hormone, cancer antigen 125, and anti-Müllerian hormone (AMH) level, AFC (antral follicles count), ovarian volume.
Results: The level of serum AMH was highest in group 1 and lowest in group 2. The decline was significant between group 1 and group 2.Ovarian volume and AFC was lowest in group 2
Conclusions: Performing repeated ovarian surgery in patients with recurrent endometriosis needs careful consideration and adequate patient counselling because of the predictable deteriorating ovarian reserve.

P110 Biocompatible porcine dermis graft to treat severe cystocele: impact on quality of life and sexuality

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Context: The increase in the average age of survival and the growing attention on quality of life resulted in a growing demand of health care by women with urinary incontinence and pelvic organ prolapse, first lived with shame and resignation.
Objective: To investigate changes in quality of life, sexual activity and clitoral flow after repairing of severe cystocele using biocompatible porcine dermis graft.
Methods: Patient underwent a complete urogynecological workup at baseline. Baden–Walker halfway system was used to asses vaginal support. The Short Form-36 questionnaire and the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) were administrated at baseline and 12 months after surgical treatment. Each woman underwent translabial color Doppler ultrasonography before and 12 months after surgical treatment.
Patients: We examinated 20 sexually active women, ranging from 47 to 71 years (mean age 58.7 $\pm$ 5.4), with mean parity 2.65 $\pm$ 0.99.
Interventions: Surgical restoration of Cystocele using porcine dermis acellular collagen matrix BioMesh technique (PelviSoft BioMesh, CR Bard, Cranston, R.I., USA).
Main Outcome Measures: Operation and hospitalization mean time were respectively 77.5 min and three days. No major surgical complications were recorded. Minor complications such urinary infection, gluteal pains were observed.
Results: Women reported a definitely improvement in QoL and PISQ-12 scores at 12- months follow-up (p <0.001). A significant reduction of dyspareunia was observed in eleven women (11/12 = 91.7%). Color Doppler measurement showed not significative change in clitoral flow (p = NS).
Conclusions: The impact of surgery on vaginal anatomy, quality of life, sexual and urinary function, might be influenced by the surgical approach, the associated procedures, as well as by the type of mesh.

P111 Clinical management issues in percutaneous breast biopsy

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Context: Minimally invasive biopsy should be a standard practice in the non-operative diagnosis of breast lesions that are suspicious for or highly suggestive of malignancy. There has been steady development in percutaneous biopsy.
Objectives: We review the different types of breast biopsy devices currently available.
Results: Percutaneous core biopsy is most often used for evaluation of BI-RADS category 4 (suspicious) and 5 lesions (highly suspicious of malignancy). The automated core biopsy needle is performed for mass lesions to characterize the lesion histologically and obtain information that is important in planning overall oncological management. Vacuum-assisted biopsy (11, 10, 8 G) addresses the need for larger volumes of tissue for histological examination and allows biopsy of lesions that are difficult to sample: small lesions that may require placement of a localizing clip; complex lesions (cystic and solid components) and architectural distorsion that may be underestimated with core biopsy. It also has a role in therapeutic excision of some breast lesions, such as fibroadenomas, papillomas and radial scars. The accuracy of diagnosis of breast lesions depends on the correlation of clinical findings, imaging features of a breast lesion, and the results of sampling. Repeat biopsy is warranted if histologic findings and imaging findings are discordant. Surgical excision is warranted for lesions yielding a percutaneous diagnosis of ductal atypia, lobular carcinoma in situ or possible phyllodes tumor. Decisions regarding further management can be discussed at multidisciplinary team meetings.
Conclusion: It is necessary to optimize criteria for patient selection, develop and define the role of new technologies for tissue acquisition, refine protocols for management after percutaneous breast biopsy, and assess long-term outcome.

P112 Therapeutic approach of periductal recurrent mastitis

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Context: Periductal recurrent mastitis is a chronic inflammatory disease of the breast caused by inflammation of one or more breast ducts outside the lactation. The terms of subareolar abscess, squamous metaplasia of lactifere ducts or Zuska's disease are sinonims. *Objective*: To present our expetize regarding the treatment of recurrent periductal mastistis.
Methods: Between 2006 and 2011 we performed surgery on 15 cases of periductal recurrent mastitis.
Patients: General characteristics of the lot: mean age 37 years, mean parity 1.6 births (births 0–4) – 2 patients were nulliparous. All cases had a history of previous surgery performed in other centers, interventions that consisted in the incision and drainage of the abscess. 11 cases

(73.3%) had one previous surgery, the remaining 4 cases underwent two surgical operations.
Inteventions: Treatment consisted in the broad excision of the fistulous tract and the ductal ectasia with the surrounding breast tissue untill the pectoralis major muscle fascia. Periareolar incision was practiced (approximately 50% of the circumference of the areola), extended radially to the fistulous tract, which was is excised untill healthy skin. Fistulous tract and affected breast duct was identified by methylene blue injection.
Main outcome measure: No intraoperative or postoperative complications were recorded immediately.
Results: Patients were discharged 24 hours after surgery. Relapse after treatment was 13.3% (2 cases) and consisted of the emergence of a green discharge through the nipple by affecting other breast duct.
Conclusion: Periductal recurrent mastitis treatment is exclusively surgical and consists in the excision of secretory ductal orifice and fistulous tract with periductal breast tissue. Conservative treatment with antibiotics and NSAID is used exclusively for first inflammation, followed when appropriate by surgery.

P113 Optimal surgical approaches for hysterectomy in patients with large uterine myoma

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Study Objective: The aim of this work was to improve the tactics of radical surgical treatment and surgery techniques in patients with large uterine myoma by utilizing various surgical approaches.
Design: Level II Scientific Evidence.
Patients: Patients with large uterine fibroids who underwent surgery in two of the above institutions.
Intervention: Total laparoscopic hysterectomy, total abdominal hysterectomy, and vaginal hysterectomy.
Measurements and Main Results: The study included 369 patients with large uterine fibroids: 213 (57%) patients underwent total laparoscopic hysterectomy (TLH), 99 (27%) patients – total abdominal hysterectomy (TAH) and 57 (16%) patients – total vaginal hysterectomy (TVH) with the age range between 30 and 62 years. Mean operative time in the TLH group was 114.93 minutes and in groups AH and VH 108.18 and 112.89 minutes respectively. Uterine weight in the TLH group ranged from 300 to 2470 g, in AH – from 300 to 7300 g and in the VH group-from 300 to 1240 g. The intraoperative blood loss was 164.44 ml; 377.27 +- 324.07 ml; and 222.37 +- 81.78 ml respectively. Intraoperative injuries of the bladder, ureter, intestines were observed in 3 patients (1.4%) during TLH, 4 patients (4%) during AH, in 1 (1.75%) during VH. Bleeding over 500 mL was observed in 4 patients undergoing AH (4%). In groups TLH and VH no conversion to laparotomy occured. Conversion to laparoscopy occured in 1 (1.75%) patient in VH group.
Conclusion: Thus, the laparoscopic approach is a relaible alternative to laparotomy in patients undergoing hysterectomy for uterine myoma of large size. The vaginal access in some patients with large uterine fibroids is possible under favorable conditions (wide pubic arch, capacious vagina, theuterus is moving, the lack of severity of adhesions in the pelvis, etc.).

P114 Differences of post operation treatment based on operation's weekdays

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Brief Introduction Background: It is important to attend the patients in post operation period. The doctor is changing the treatment everyday based on patients' conditions. It is very important to reduce the treatment by days if the section cesarea is uncomplicated. Midwives are very important in the follow up process of uncomplicated section caesarean.
Materials and methods: We included in this study all uncomplicated section caesarean for the period Jan 2012 to Dec 2014 performed in Tirana University ''Queen Geraldine'' Hospital. This group of operated patients is divided in two subgroups: operated in weekend and operated in weekdays.
Results: If we will calculate the intravenous liquids administered in two groups resulted to be increased with 28%. It is very important the difference between two groups in administration of antibiotics that resulted 23% higher in the group operated in weekend compared with the other group operated in weekdays. Oxytocin administration resulted to be 14% higher in the weekend group of operated patients. Administration of analgesics is increased by 9% in weekend groups. The patients satisfaction was much more higher in weekdays compared with weekend because the frequency of midwives visits to the patients is lower in weekends as well as blood pressure measured by midwives is in frequency difference by 48 minutes. The same difference is for fever measure, respiratory frequency and pulse rate. The hospital stay is higher in weekend other than weekdays.
Conclusions: Comparison between two groups operated in weekend and operated in weekdays shows differences in overtreatment and lower attention for patients from their doctors and midwives. Days off influenced directly the consultations of operated patients. The individual treatment cost for the hospital will be increased in weekend compared with weekdays.

P115 Synergy of genital prolapse and varicose veins of pelvis

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Context: Literature review analysis demonstrates that genital prolapsed (GP) and varicose veins of pelvis (VVP) in women are the result of a connective tissue dysplasia, as a manifestation of systemic connective tissue disorders at the level of the pelvic complex. It should be developed an optimal algorithm of diagnosing of VVP in women who seek the help of a gynecologist due to GP.
Objective: The purpose of the study was to evaluate the synergy effect of these pathologies on the amount of blood loss during reconstructive surgery on vagina.
Methods: The study was conducted on the basis of 2 Maternity Hospital of the Tashkent Medical Academy Clinics. The basis of this study made a retrospective study of 223 case hystories of patients who underwent anterior and posterior colporrhaphy for the period 2008–2012, next step was clinical and laboratory studies of 60 women with prolapse of the vaginal walls II and III degree admitted to gynecology unit in 2012 to 2014 period.To all patients were performed following algorithm of preoperative examination: laboratory tests, ultrasound and Doppler-mapping of pelvic venous system. Complex treatment was prescribed to patients of main group.
Results: According on pathogenesis of PVV, following tasks were chosen for its treatment: normalization of venous tone, improvement of pelvic venous hemodynamics, blood – and lymph flow, improving of trophic processes flow in pelvic tissues, stabilization and normalization of connective tissue metabolism.

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Conclusions: Blood loss in main group was significantly less than in comparison 200±100 ml and 500±150 ml respectively, which signs on positive effect of complex treatment before surgery neither of traditional.

P116 Intraoperative transrectal ultrasonography for hysteroscopic metroplasty of septate uterus: a case report

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OORR Foggia

Introduction: Evaluation of the uterine cavity is a basic step in female infertility workup. Hysteroscopy is considered the gold standard for diagnosis of intrauterine lesions. Three-dimensional ultrasound (3D US) has recently become available in gynecological practice. Hysteroscopic metroplasty (HM) in women with septate uterus and unexplained infertility improve clinical pregnancy rate and live birth rate. After HM a residual septum or adhesions occurr with an incidence of 8–38%. We evaluated the efficacy of intraoperative 3D Transrectal Ultrasonography (3D TRUS) combined with hysteroscopy during uterine metroplasty in preventing residual septum.
Case Report: We performed a preoperatory 3D US examination in a 37 years old woman, with a diagnosis of uterus septum and primitive infertility. Septum was defined according to the ESGE ESHRE classification (2013): the uterus showed a smooth external profile and an internal profile with a notch of 17.53 mm, an intertubaric distance of 29.1 mm, an intertubaric angle of 78.87°. At the hysteroscopic examination, the uterine cavity appeared divided by a septum extending until its upper third, the tubal ostia were displayed bilaterally. The resection began from the lower margin of the septum with 5 Charr scissors and continued with a progressive horizontal incision in the midline of the uterine cavity. During the procedure an ultrasound probe in 3D mode was inserted in the rectum in order to obtain a intraoperatory visualization of the uterus (3D TRUS). The procedure was considered complete when the intraoperatory 3D TRUS confirmed the complete resection of the septum and the presence of muscolar fibers. At the follow up 5 months later, the 3D US showed the absence of residual septum.
Conclusion: Intraoperative TRUS can be performed safely during HM and may increase the likelihood of complete resection of the uterine septum.

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Metabolic Syndrome/ PCOS/Sex/Sport/ Hyperandrogenism

P117 The prevalence of non-classic adrenal hyperplasia among women with hyperandrogenism

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Aim: To detect the incidence of non-classical congenital adrenal hyperplasia (NCAH) associated with 21-hydroxylase insufficiency among female residents of the Republic of Uzbekistan with hirsutisim and hyperandrogenemia.

Materials and methods: To conduct the study 97 hirsutic and hyperandrogenemic women referred to the Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Health Ministry undergoing diagnostic testing and clinical ultrasound of the ovaries and uterus were selected. Presence/absence of acne, alopecia and menstrual dysfunction were among the parameters to be registered. The modified Ferriman-Galloway system was used for assessment of hirsutism, the participants having scores above 8. Blood samples were taken to measure fasting glucose, prolactin, FSH, LH, testosterone, 17OHP and the molecular-genetic CYP21 test.
Results: 1 NCAH associated with 21-hydroxylase insufficiency was found in 11 women (11.4%), PCOS being registered in the rest ($n = 86$, 88.6%). 2 The clinical picture of women with NCAH is not differ from women's PCOS. 3 The findings indicate the need for a genetic research for differential diagnosis of NCAH in patients with hyperandrogenism.

P118 Hyperandrogenism impact on reproductive age

María Varela Belzarena (UY)

It is the most common edocrinological disorder in reproductive age, which has recently aroused a growing concern in the scientific community and has important consequences en womeńs lives and their descendants with posible high psychoemotional and economic costs not only for the individual but also for the population. The scientific research on this matter is fairly recent and promising. From the first works of Stein and Leventhal at the beginning of the XX century until the present works of Baron-Cohen, we have advanced a lot in the topic and every time there are more pathologies linked to this disorder. The reach of the hyperandrogenism goes from cosmetic and psycological problems, infertility, even sports decisions.The purpose of this work is to look over the available bibliography about hyperandrogenism in reproductive age. A blbliographic search was done in pubmed articles within a period of 5 years (2010–2014), mesh terms suchs as androgens and women; hyperandrogenism and women; hyperandrogenism and cardiovascular risk were used. In the last one it was limited to metaanalisis or reviews. We found 75 articles plus 2 text books, and after the review 55 articles were included. There are pathologies where we cańt doubt anymore that it is linked, such as infertility, cardiovascular risk and metabolic syndrome. There are others which deserve more research such as recurrent premature miscarriage, hyperemesis gravydarum, ovary cancer and vascular breast cancer. In epigenetics it is important to continue the research in the field of the PPD, ontogeny and epigenetics of the PCOS and Metabolic Syndrome. The incidence of metabolic syndrome increases notoriously with the menopause which means that as soon as it can be indentified during the reproductive age the better we can improve and focus on prevention where it is really justified.

P119 Effects of hyperandrogenism on metabolic disorder in patients with PCOS: a systematic review and meta-analysis

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Context: Hyperandrogenism (HA) is a feature of polycystic ovary syndrome (PCOS). There was inconsistent for the effect of HA in PCOS on metabolic parameters.

Objective: we conducted a systematic review and meta-analysis to evaluate the effect of HA in PCOS on metabolic parameters.
Methods: We searched PubMed, EMBASE, Cochrane, Web of Science, Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), WanFang data and VIP for clinical observational studies, which were published in Chinese or English from Jan, 1980 to Nov, 2014. The study evaluated PCOS patients with or without HA on metabolic parameters was included. The main outcomes were prevalence of metabolic syndrome, indexes of IR including homeostasis model assessment IR index (HOMA-IR), incidence of IR, biomarkers of serum lipid metabolism such as total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL). Egger's test was performed for publication bias analysis.
Result(s): Of 4457 identified trials, 32 observational studies were included for the final analysis comprising 9556 female with PCOS. 6482 cases were having HA, and the others were negative. Results showed that there were significant differences in the incidence of metabolic syndrome, HOMA-IR, rate of IR, TC level and HDL level between PCOS patients with or without HA, except for LDL level. No significant publication bias was found as P value of Egger's test was 0.82.
Conclusions: HA may play an important role in metabolic disorders in PCOS patients. The incidence of metabolic syndrome, IR indexes, and most biomarkers of serum lipid metabolism were significantly different between patients with and without HA. However, these results should be carefully consulted as the limited number and poor quality of included studies.

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P120 Melatonin and sleep disorders in polycystic ovary syndrome

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Endocrinology Research Centre

Context: Melatonin regulates the sleep cycle and reproductive function. It is one of the main components of the antioxidant system that neutralizes free radicals. However, limiting its synthesis caused by disorders or sleep deprivation may worsen the balance of the antioxidant system, and as a result disrupt the normal growth and maturation of follicles in women with polycystic ovary syndrome (PCOS), which have proven high concentration of lipid peroxidation products, causing damage to the oocyte.
Objective: To study the relationship of sleep disorders with the severity of PCOS depending on the age and body mass index (BMI).
Methods: The survey through questionnaires scoring subjective sleep characteristics, the STOP Questionnaire and Hospital Anxiety and Depression Scale.
Patients: Two groups of patients with PCOS aged from 17 to 35 years (mean age 25.8 $\pm$ 4.3 years), 27 patients with a BMI$>$ 25 kg/m^2 and 32 patients with BMI $<$25 kg/m^2.
Interventions: PCOS was diagnosed on the basis of ESHRE/ASR (2007) criteria. The control group: 45 healthy women without menstrual disorders.
Results: Patients with PCOS have more frequent sleep disorders and depression compared to the control group (absolute risk in the ''case'' group was 0.574, in the control group – 0.387, R*R* = 1.48). The presence of PCOS increased the probability of sleep and mental health disorders by 18.7%. The presence of overweight increased the probability of sleep abnormalities and depression by 12.2%. Disorders were more common in younger patients.
Conclusions: The results allow us to conclude that patients with PCOS and a higher BMI have a higher risk of sleep disorders and depression compared to the control group and patients with normal BMI.

P121 There are differences in the correlations between fat distribution and hemostatic parameters in women with polycystic ovary syndrome and healthy controls matched for age and body mass index

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Context: Android fat distribution in polycystic ovary syndrome (PCOS) is associated with different comorbidities; however, its correlation with hemostatic parameters remains unclear.*Objective*: To correlate hemostatic parameters with clinical markers of fat distribution and laboratory variables in women with PCOS compared to healthy controls.
Methods: A cross-sectional study was conducted in a tertiary teaching hospital.Patient(s): Forty-five women with PCOS and 45 controls matched for age and body mass index (BMI).*Intervention(s)*: Clinical evaluation and venipuncture.
Main Outcome Measure(s): Age, BMI, waist circumference (WC), hip circumference(HC), waist-hip ratio (WHR), Ferriman-Gallwey index, fasting glucose and insulin, total testosterone, free testosterone (FT), thrombin-activatable fibrinolysis inhibitor (TAFI), D-dimer, plasminogen activator inhibitor (PAI-1), and the thrombin generation test parameters: lag time (Tlag), time to peak thrombin generation (Tmax), peak concentration (Cmax) and the area under the thrombin generation curve (TAUC).
Result(s): In the PCOS group, BMI and WC correlated positively with TAFI, D-dimer, PAI-1, Cmax and TAUC; HC with D-dimer and PAI-1; WHR with TAFI, D-dimer and PAI-1; glucose with TAFI; insulin and homeostasis-model assessment of insulin resistance with PAI-1; and FT with Cmax and TAUC. Age correlated positively with D-dimer and PAI-1, and negatively with Tlag and Tmax. In the controls, no correlations were found between any clinical markers of fat distribution and hemostatic parameters; however, age and fasting glucose correlated positively with PAI-1, and FT with Tmax and TAUC.
Conclusion(s): Although groups were paired for age and BMI, android fat distribution in PCOS directly affected hemostatic parameters. Further studies may identify correlations between these findings and increased thromboembolic risk.

P122 Effects of Diane-35 and Marvelon in women with polycystic ovary syndrome: a randomized, controlled trial

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Context: Polycystic ovary syndrome(PCOS) is more than just a reproductive disorder, and is currently considered a syndrome with metabolic consequences that could affect women's health during different stages of life. Therefore, lifelong individualized management should be considered. The choice of therapy is multiplex. Pharmacological agents commonly used to manage the symptoms are metformin and oral contraceptives(OCPs). An important issue is the best choices of therapy tailored to heterogeneous individuals, since the distinct variability among PCOS women could significantly influence the efficacy and clinical response of agents used.
Objectives: Investigating effects and differences between Diane-35 and Marvelon in the treatment of PCOS.

Method: A randomized, controlled trial.
Patients: PCOS patients.
Intervention: Diane-35 or Marvelon, with a combination of metformin were randomizedly administered.
Main Outcome Measures: BMI, WHR, HOMA-IRI, ovarian volume and metabolic index.
Results: All patients recovered regular menstrual cycle after 6 months. In IR groups, Diane-35 and Marvelon decreased BMI and WHR significantly, while not significantly in HOMA-IRI. Both decreased LH/FSH, serum testerone, score of acne, ovarian volume, and number of follicles with no statistically significance, while fasting TG, TCh, LDL, HDL and AIP increased significantly, especially for Diane-35. In non-IR groups, both medicines increased BMI, WHR and HOMA-IRI but not significantly. Both decreased acne score and AIP.
Conclusion: Diane-35 or Marvelon could relieve symptom of PCOS; but might reduce insulin sensitivity and interfere with lipid metabolism when used alone. Metformin could improve glucose metabolism and lower BMI in PCOS-IR patients.

Supported by National Natural Science Fund (81270665) and Scientific Research Projects of Dept. of Health in Sichuan Province (No.2012SZ0031)

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P123 Should subclinical hypothyroidism be an exclusion criterion? Shedding some light on PCOS diagnosis

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Objective: To examine whether patients with subclinical hypothyroidism (SCH) should be initially excluded from PCOS group or not.
Methods: Cross-sectional comparative study.
Patients: Seven hundred third four patients were enrolled: 462 with true PCOS, 31 with PCOS-like-subclinical hypothyroidism (PCOS-like-SCH), and 241 normal cycling women.
Intervention(s): None
Main Outcome Measure(s): Comparisons of clinical, metabolic, and hormonal parameters among PCOS, PCOS-like-SCH, and normal cycling controls were performed.
Results: True PCOS and PCOS-like-SCH presented similar signs of hyperandrogenism and anthropometrical parameters. Fasting insulin and C-peptide concentrations were higher in PCOS than in PCOS-like-SCH patients ($p < 0.05$). Glucose intolerance and insulin resistance presented similar prevalence in PCOS and PCOS-like-SCH patients ($p = 0.186$ and $p = 0.293$, respectively). Estradiol levels and free estrogen index (FEI) were higher in PCOS patients than in other groups ($p < 0.05$). TSH levels showed positive correlation with lean body mass (LBM) either after simple or multiple correlations ($p = 0.014$ and $p = 0.010$, respectively).
Conclusions: There seems to be no difference in clinical and most metabolic parameters between true PCOS and PCOS-like-SCH patients. If the normal upper limit cutoff is used to excluded thyroid disorders from PCOS subjects, many true PCOS patients with associated SCH would be unnecessarily excluded.

P124 Clinical, ultrasound and hormonal correlation in PCOS patients treated at the Gynecology Department of Hospital Cesar Amador Kühl from January to July 2015

German Fernandez Lopez (NI)
Clinica Médica de Infertilidad

Context: The diagnosis of the PCOS syndrome yet still under discussion. The importance of the diagnosis lies in the complications in the short, medium and long term related to the syndrome, especially after it was discovered that education, changes in lifestyle, exercise and diet, play an important role in prevention, management and monitoring.
Objective: This research aimed to describe the association between clinical and hormonal parameters, ultrasound in the diagnosis of PCOS by conducting a correlational study.
Methods: The sample was selected using the formula of multivariate correlations, the sample was obtained from the patients who met the criteria of Rotterdam and attended spontaneously to Hospital César Amador Kühl.
Interventions: patients selected were performed a clinical history, physical examination, imaging studies (transvaginal ultrasound) as well as hormonal profile diseases including differential diagnosis.
Main Outcome Measures: The variables studied were divided into clinical, clinical, hormonal and ultrasonographic. For the analysis of these variables they were divided into continuous and discrete to the association of discrete contingency tables were used to determine the association between discrete variables with continuous variables the Student *t* test (ANOVA) was used and to determine the association of the Continuous variables the statistical method of linear regression was used. A statistically significant association with a value of $p < 0.05$ was determined.
Results: An association between the presence of hirsutism and elevated total testosterone was found.
Conclusions: It was not possible to find association between clinical and hormonal parameters, ultrasound.

P125 Quantification of visceral adipose tissue in women with polycystic ovary syndrome: dual-energy X-ray absorptiometry (DXA) vs. MRI

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Context: Visceral adipose tissue (VAT) is related to the metabolic syndrome (MS). Polycystic Ovary Syndrome (PCOS) is closely related to MS as 40–70% of PCOS-women are obese. VAT is quantitated directly by CT, ultra sound and MRI. VAT measurement in PCOS-patients can be a tool to assess their metabolic risk and monitor effect of lifestyle and medical intervention. MRI is gold standard, without radiation, however, time consuming, expensive and complicated. In contrast, Dual-energy X-ray absorptiometry (DXA) is fast, easy to perform, and widely accessible in a clinical setting. Recently, new software enables DXA to measure VAT.
Objective: To compare VAT measurements by DXA and MRI in PCOS.
Method: DXA-software (APEX 4.0 Hologic, Bedford, USA) calculated VAT as SAT (subcutaneous AT) subtracted from TAAT (total abdominal AT). TAAT measured in a 5 cm transverse slice at L4/L5-level between the inner abdominal muscle, and SAT estimated from the subcutaneous fat between the skin and outer abdominal wall on both flanks. MRI (Achieva 3.0 T, Philips Medical Systems, Best, NL) measured VAT in a 1 cm thick transverse slice at the L3-level.
Patients: 68 women with PCOS.
Main outcome measure: Difference in MRI- and DXA-VAT volume.
Results: (Mean (range)): Age 29.4 years (19–44); Weight 92.9 kg (59.1–132.0); BMI 33.2 kg/m2 (23.4–45.4); DXA-VAT 432.9 cm^3 (72.1–971.0); MRI-VAT 116.6 cm^3 (28.0–242.0).Linear regression between MRI-VAT and DXA-VAT: $\beta = 0.22$, $R = 0.81$, $p < 0.001$. DXA-VAT CV 6.5%, Inter correlation coefficient (ICC) 0.96.
Conclusion: Due to difference in anatomical location of the measures area, DXA- and MRI-VAT volumes were considerably different. However, the two methods correlated closely and DXA reproducibility was acceptable making DXA-VAT suitable for repeated measurements in the same patient.

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P126 Vitamin D deficiency in women with polycystic ovary syndrome

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Context: Many studies have investigated vitamin D status in women with polycystic ovary syndrome (PCOS), but there is no consensus on whether or not its serum levels are different between women with and without PCOS. Current evidence suggests an inverse association between vitamin D status and metabolic disturbances in PCOS.
Objective: To evaluate prevalence of vitamin D deficiency in women with PCOS.
Methods: Serum vitamin D concentrations less than 30 ng/mL were classified as its frank deficiency and compared in reproductive age women with PCOS according the Rotterdam criteria and body mass index and age matched controls. Correlations between metabolic parameters and vitamin D status were analyzed separately in patients and controls.
Patient(s): 58 PCOS women and 28 healthy controls were recruited in observational, cross-sectional study.
Main Outcome Measure: Serum vitamin D concentrations
Result(s): No significant differences were observed in serum vitamin D levels or prevalence of its deficiency between PCOS and healthy women (43.1% in patients vs. 42.9% in controls, respectively). There were no correlation between vitamin D levels and indices of glucose or lipid metabolism in both groups. In PCOS women we found significantly negative correlations of vitamin D levels with body mass index and dehydroepiandrosterone sulfate serum concentrations.
Conclusions: Although we found no differences in the level of serum vitamin D in PCOS and healthy women, the potential relationship between it and PCOS requires further investigation. Since vitamin D deficiency prevalence is high, large intervention trials are warranted to evaluate the effect of vitamin D supplementation in PCOS women. Modest sample size, the presence of other potential confounding factors, such as outdoor times or dietary patterns which could affect the serum vitamin D levels.

P127 Vitamin D levels in Turkish adolescent girls with polycystic ovary syndrome and correlation with clinical and biochemical parameters

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Context: To determine the relationship between serum vitamin D status and metabolic or clinical profiles of PCOs.
Objective: Polycystic ovary syndrome (PCOs) is a common endocrinopathy among the female adolescents and young women, characterized by chronic anovulation, hirsutism and metabolic abnormalities . The aim of this study is to investigate the relationship between vitamin–D with metabolic parameters and other characteristics of the PCOs.
Methods: We analyzed 31 girls with PCOs using the Rotterdam criteria and 35 girls were non – PCOs controls. Serum 25 –hydroxy vitamin D level was measured. Anthropometric, clinical, endocrine, metabolic components were determined in both groups.
Patients: The study included 66 Turkısh girls, of whom 31 girls had PCOs and 35 girls were non- PCOs controls.
Interventions: Morning venous samples were obtained after a 12-hour overnight fasting from the participants 2nd or 3th day of a menstruel cycle. 25(OH) D levels were determined by chemiluminescence immunoassay system (CLIA) . The serum concentration of glucose, lipid profiles was measured using standard methods.
Main Outcome Measures: The mean differences between groups were compared by Student's t test. Nominal data were analyzed by Pearson's chi-square test with 95% confidence interval.
Results: The group with PCOs showed no differences in the level of 25-hydroxy vitamin D (14.58 ± 6.15 vs. 16.02 ± 7.87, $p = 0.414$). In addition to this, significant correlations not found between 25 (OH) D levels and endocrine or metabolic parameters in either PCOs patients or controls.
Conclusion: There was no difference in the level of serum Vitamin D between PCOs patients and matched controls. Vitamin D deficiency was common both patients and controls. Also we didn't find any relationship between serum vitamin D levels and clinical or metabolic profiles.

P128 Frequency of thyroid dysfunctions in patients with polycystic ovary syndrome in child-bearing age

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Bearing age, with prevalence of 6–15%. Some studies have found PCOS association with thyroid dysfunction in the range of 4–26%. The disorder associated most frequently with POS is the autoimmune hypothyroidism and the subclinical hypothyroidism.
Objective: Determine the frequency of thyroid dysfunctions in polycystic ovary syndrome patients in child-bearing stage.
Methods: An ambispective, descriptive, observational, and cross-sectional study was performed. The data collected was assessed using descriptive statistics methods, with Spearman correlation.
Patients: 61 Patients with PCOS, based on the 2003 Rotterdam criteria, between 20 and 40 years of age, in the Hospital Juárez of México.
Interventions: Complete thyroid profile was requested with antithyroid antibodies.
Main Outcome Measures: Ferriman–Gallwey scale, baseline transvaginal ultrasound, androgen profile (free testosterone, total testosterone, androstenedione, DHEA, DHEAS, 17α hydroxyprogesterone, and cortisol) and thyroid profile with antithyroid antibody.
Results: A sample was obtained of 61 patients with age range from 20 to 40 years; the average age 23 years. The 28% has some thyroid dysfunction ($n = 17$) and seventy-two percent ($n = 44$) were euthyroid. The most frequent dysfunctions were autoimmune hypothyroidism in 7.9% ($n = 6$), primary hypothyroidism with negative antithyroid antibodies in 6.12% ($n = 5$), subclinical hypothyroid-dism in 3.12% ($n = 2$), primary hyperthyroidism in 3.12% ($n = 2$), and euthyroid with positive antithyroid antibodies in 3.12% ($n = 2$). The most common phenotype was A 46.1% ($n = 28$).
Conclusions: In our study, the thyroid dysfunction frequency in patients with PCOS amounted to 28%, being the autoimmune hypothyroidism the most frequent condition.

P129 The prevalence and effect of PCOS among women with GDM in China

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Context: Women with polycystic ovary syndrome (PCOS) are prone to developing gestational diabetes mellitus (GDM). Few studies evaluated women with GDM to determine the frequency and effect of PCOS among them.

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Objective: To evaluate the prevalence and effect of PCOS among GDM women by analyzing pre-conception characteristics, pregnancy and neonatal outcomes.
Methods: Pre-conception characteristics, pregnancy and neonatal outcomes of 998 GDM women who gave live birth in Department of Obstetrics, West China Second University Hospital, Sichuan University between Jan 1 and Dec 31, 2014 were reviewed retrospectively. They were divided into 3 groups: PCOS group (diagnosis of PCOS pre-conception), uncertain PCOS group (suspicious of PCOS due to their symptoms), non-PCOS group(without PCOS or symptoms of PCOS). One-way ANOVA, t test and Chi-square test were used for analysis.
Patient: See above
Intervention: None
Main Outcome Measures: Age, pre-conception BMI, fertilization way, weight gain during gestation, blood glucose, metabolic disease during pregnancy, delivery mode, neonatal weight and Apgar score.
Results: 998 Women were included. 91 were not accessible and 36 refused to participate. Remaining 871 were analyzed. Prevalence rate of PCOS was 4.82% (42/871). Pre-conception BMI of PCOS group (22.44±3.30) was higher than uncertain PCOS group (21.10±2.65, $p = 0.003$) and non-PCOS group (21.33±2.80, $p = 0.014$). Natural pregnancy rate of PCOS group (59.52%, 25/42) was lower than other groups (84.12%, 233/277 and 90.04%, 497/552) ($p < 0.01$). There was no significant difference in other data.
Conclusions: PCOS occurs in a normal rate among GDM women. GDM women with PCOS have higher pre-conception BMI and lower natural pregnancy rate than those without PCOS. Early diagnosis and management to PCOS women pre-conception and during gestation could contribute to maternal and fetal outcome.

P130 Identification and analysis of potential serum biomarkers for polycystic ovary syndrome in patients with insulin resistance

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Objective: To analyze and identify the clinical and metabolic characteristics and differentially expressed proteins in polycystic ovary syndrome patients with insulin resistance (PCOS-IR) group and polycystic ovary syndrome patients without insulin resistance (PCOS-NIR) group.
Method: Two hundred and eighteen reproductive women with PCOS were divided into two groups: PCOS-IR group ($N = 84$) and PCOS-NIR group ($N = 134$) in this case-control study.
Main Outcome Measure(s): The metabolic parameters were compared between the two groups. The differentially expressed proteins were identified by differential in-gel electrophoresis and matrix-assisted laser desorption ionization/time-of-flight MS. Some of the differentially expressed proteins were also identified by Western blot and ELISA.
Results: The levels of total cholesterol, triglyceride, low-density lipoprotein, fasting blood glucose, 3-hour blood glucose, and uric acid in the PCOS-IR group were higher than those in the PCOS-NIR group ($p < 0.05$). Twenty differential protein spots were screened. Four differentially expressed proteins, namely afamin, serotransferrin, complement C3, and apolipoprotein C-III (APOC3), were distinguished between the two groups. APOC3 was expressed more in the PCOS-IR group than those in the PCOS-NIR group, which was validated by Western blot and ELISA. The results of ELISA for APOC3 were used to generate the receiver operator characteristic curve; the area under the curve was 0.624.
Conclusion: The metabolic disorder in the blood glucose, blood lipid, and uric acid was more severe in the PCOS-IR group. Four upregulated proteins were differentially expressed between the two groups. APOC3 might help in the diagnosis of women with PCOS-IR.

P131 Hormonal and immunological state of women with polycystic ovary syndrome

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The purpose of our research was to study hormonal and immunological state of women with polycystic ovary syndrome before and after laparoscopic treatment. There were examined 175 patients with polycystic ovary syndrome and 20 healthy women (control group) at the age 18–30 years. The number of patients according to treatment methods was divided by random selection. 34 women from examined ones were examined 3 months before and after laparoscopy. Hormonal investigation was held 3 months before and after laparoscopy to reveal (LH, FSH, testosterone, sex-steroid binding globulin (SSBG)) and cytokines concentration: interleukin-6(IL-6) and tumor necrosis factor-a (TNFα). Amount of hormones in blood serum in women with polycystic ovary syndrome before and after laparoscopy was: LH lowered from 11.5±1.3 to 7.4±0.7 IU/l, FSH (IU/l) did not changed authentically, and the ratio LH/FSH lowered to 1.4±0.15. Testosterone levels lowered from 2.7±0.2 to 2.2±0.1 ng/ml, at the same time concentration of SSBG increased 1.6 times. As the results of few research works that describe cytokine state condition in women with polycystic ovary syndrome are controversary, we determined in this comparative study that in blood serum in polycystic ovary syndrome there were significantly larger amount of IL-6 and TNF. We revealed a relation between TNF and IL-6 levels drop and menstrual cycle disorders frequency. 3 months after laparoscopy IL-6 and TNF levels lowered to 28.8±2.2 pg/ml and 30.6±2.1 pg/ml respectively. After treatment frequency of olygomenorrhea decreased nearly 2.5 times, cases of amenorrhea were not observed. Received data confirm expediency of cytokine state investigation in women with polycystic ovary syndrome for further correction on this level.

P132 Serum antimüllerian hormone levels in the diagnosis and phenotypic characterization of polycystic ovary syndrome

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Context: PCOS may be diagnosed by the presence of different combinations of hyperandrogenism, oligo-anovulation and polycystic morphology of the ovary. Measurement of AMH serum levels, which correlate with the number of ovarian follicles, has been recently proposed as a new diagnostic criterion, as an alternative to the ovarian morphology.
Objective: To compare the performance of AMH assay and the ultrasonographic assessment of the ovaries in the diagnosis of PCOS, and to explore which factors are associated with AMH levels in these patients.
Patients And Methods: 83 Well-characterized PCOS patients and 28healthy women were included in the study. Serum AMH was

measured by the ELISA Gen2 assay, whereas ovarian US assessment was carried out by an experienced sonographer. In addition, serum androgens were assayed by liquid chromatography/mass spectrometry and equilibrium dialysis, and insulin sensitivity (only in PCOS women) by the hyperinsulinemic euglycemic clamp.
Main Outcome Measures: AMH levels in PCOS patients and controls.
Results: Serum AMH levels were higher in PCOS patients than in controls (12.0±1.0 vs. 5.1±0.7 ug/L, $p<0.001$), and in the classic phenotype than in the other clinical phenotypes. AMH levels correlated positively with follicle number and ovarian volume.They correlated positively with serum LH and ovarian androgen levels, as well as with insulin sensitivity. In women in which diagnosis of PCOS was made independently of the US criteria and controls, ROC curves analysis showed that performance of AMH assay in diagnosing PCOS was significantly lower than performance of ovarian follicles count.
Conclusion: Serum AMH levels are increased in PCOS women, particularly in the classic phenotype, and are associated with several characteristics of these subjects. AMH performance in diagnosing PCOS appears to be lower than performance of ovarian US.

P133 The role of prostate specific antigen (PSA) in diagnosis of polycystic ovary syndrome

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Context: PCOS is the commonest endocrine disorder in women of a reproductive age and commonest cause of androgen excess in this population. Many authors suggest that PSA could be a new marker of hiperandrogenism in PCOS.
Objective: To assess the role of PSA in PCOS diagnosis and PSA concentration in PCOS women vs. healthy women. To determine if there is a correlation between PSA and hormonal parameters.
Methods: PCOS was diagnosed based on Rotterdam criteria. PSA and fPSA serum concentration, free andogen index(FAI) and hormonal parameters were assessed. A cut-off level of total PSA(TPSA), total testosterone(tT), and free androgen index(FAI) was established for the sensitivity, specificity, area under curve, diagnostic accuracy and positive and negative predictive values of diagnosis of PCOS.
Patients: 165 Women with PCOS and 40 healthy women.
Interventions: Blood samples were taken. TVUs examination was evaluated.
Main Outcome Measures: The median levels of TPSA, tT and androstendione were significantly higher in PCOS women vs. control group. The median value of FAI was significantly higher in PCOS women vs. control group (4.31 vs. 1.79, $p<0.001$). There was a significant correlation of TPSA and tT($r=0.173$, $p=0.027$) and TPSA and FAI($r=0.2603$, $p=0.001$).
Results: For FAI AUC 82.1%, threshold 2.56 nmol/l, specificity 77.57%, sensitivity 82.14%, positive LR 3.66, negative LR 0.230, for tT AUC 80.5%, threshold 0.54 ng/ml, specificity 59.03%, sensitivity 92.87%, positive LR 2.26, negative LR 0.12, for TPSA AUC 66.3%, threshold 0.005 ng/ml, specificity 63.03%, sensitivity 68.96%, positive LR 1.86, negative LR 0.49.
Conclusions: Women with PCOS have significantly higher serum concentration of TPSA vs. healthy women. TPSA positively correlate with tT and FAI. FAI is the best marker for hyperandrogenism and has better accuracy than tT and total PSA serum levels in diagnosis of PCOS.

P134 Increased risk of psychiatric disorders in PCOS women in southwest China

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Background: Polycystic Ovary Syndrome (PCOS) and its characteristic symptoms have been bothering reproductive aged women substantially. Apart from the physical effects, this disease also brings with psychological problems. This survey is conducted in response to lack of systematic study of the psychological state and HRQoL of PCOS patients in Southwestern China, and to determinate if they are more likely to be anxious and/or depression.
Methods: A total of 120 PCOS outpatients were enrolled into the study as PCOS group, and 100 age-matched healthy women chosen as controls. Their basic information (age, menstruation, education degree, fertility demand, and body weight and height) was collected. Several standardized questionnaires as General Health Questionnaire-12-item version (GHQ-12), State-Trait Anxiety Inventory (STAI), Beck-Depression Inventory (BDI), and Hospital Anxiety and Depression Scale and General Health Questionnaire (HADS) were applied to assess general mental health condition, and Health-Related Quality of Life (HRQoL) by 36-item Short-Form health survey (SF-36).
Results: The prevalence of anxiety (17% vs. 2%)and depression (27.5% vs. 3%) in PCOS group were higher than controls ($p<0.001$). HRQoL of PCOS group was significantly lower than controls (496.7±135.1 vs. 572.4±157.7, $p<0.001$). Among PCOS patients, women desire conception within 1 year were more likely to be anxious and depressed than those without fertile desire.
Conclusions: PCOS patients were more likely to be depressed and anxious. The mental health of those patients should be concerned and psychological therapy should take into consideration.

P135 The effects of combination therapy with oral contraceptives and metformin on the concentration of anti-Müllerian hormone in polycystic ovary syndrome

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Context: Polycystic ovary syndrome (PCOS) has been considered to be common endocrine disorders in women of reproductive age.Anti-Müllerian hormone (AMH) concentrations have been found to be increased in PCOS patients compared to women with normal ovaries.
Objective: to evaluate the effects of the contraceptive and metformin on endocrine, metabolic parameters and AMH in PCOS women and discuss the relationship between changed AMH and evaluations of PCOS therapy.
Methods:Prospective self-control study.
Patients:71 PCOS patients. *Interventions*: Oral contraceptives and metformin (500mg tid) for six month.
Main Outcome Measures: Their blood pressure, body mass index (BMI), waist circumference and waist to hip ratio (WHR), fasting insulin (FIN), fasting plasma glucose (FPG) and blood serum sex hormone and blood lipid were measured before and after treatment. Serum AMH was measured by ELISA.
Results: After six month treatment, their median F-G, GAGS scores, waist circumference, LH, T, and LH/FSH significantly were lower ($p<0.05$). Metabolic parameters such as FPG, HOMA-IR, TC/HDL and LDL/HDL were significantly higher in the before treatment group than in the after treatment group ($p<0.05$). Both sides ovarian volume were significantly decreased after treatment. Serum levels of AMH were significantly different before and after treatment group ($p<0.001$). Meanwhile, in before and after treatment PCOS women, Serum AMH levels were positively correlated with T ($r=0.513$, $p<0.001$) and with T ($r=0.643$, $p<0.001$), respectively.

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Conclusion: Combination therapy with oral contraceptives and metformin is a suitable method for PCOS. Serum AMH levels are decreased in PCOS women after oral contraceptives and metformin treatment. AMH could be a new parameter to evaluate the treatment of PCOS, the exact standard need further studies.

P136 Metabolic risks at different phenotypes of patients with polycystic ovary syndrome

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Context: Polycystic ovary syndrome (PCOS) is a disease characterized by the presence of chronic oligo- and/or anovulation (AN), hyperandrogenism (HA) and polycystic ovaries. PCOS is regarded as one of the components of the metabolic syndrome. According to ESHRE/ASRM (2007) phenotypes of PCOS were identified: Classic (HA + ultrasound polycystic + AN), Ovulatory (HA + ultrasound polycystic), Nonandrogenic (AN + ultrasound polycystic), Anovulatory (HA + AN).
Objective: Evaluation of metabolic risks in women with different phenotypes of PCOS.
Methods: Examination of BMI, total cholesterol, LDL-C, HDL-C, triglycerides, oral glucose tolerance test, insulin. Re-examination of these parameters was performed at a mean of 5.8 years.
Patients: 150 Patients, aged 29–38 years.
Interventions: Patients received treatment: group A (32 patients) – metformin (MF) (1700–2000mg/d); Group B (38 patients) – combined oral contraceptives (COC); Group C (79 patients) – MF and/or COC and/or progestogen and/or ovarian drilling.
Results: Classic phenotype was identified in 46% of patients, Ovulatory – in 23%, Nonandrogenic – in 18% and Anovulatory – in 13%. Percentages ratio of phenotypes during the observed period (5.8 years) did not changed. It was established that regardless of the phenotype patients are overweight (87%), have carbohydrate metabolism disorders (31%), and dyslipidemia (100%). Metabolic risks are maximally expressed in patients with classical and ovulatory phenotypes. It is proved that combination therapy is the most effective for the treatment of PCOS. The maximum statistically significant effect is achieved in patients with classic phenotype (significant reduction in triglycerides, total cholesterol, insulin).
Conclusion: Considering the chronic course of PCOS and metabolic risks multidisciplinary approach is needed in the treatment and management of patients.

P137 Insulin resistance and acromegaly: about 15 cases

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Context: Acromegaly is a rare disease,usually caused by hypersecretion of growth hormone by a pituitary adenoma and very rarely by ectopic secretion of GHRH.It remains a serious disease reduces life expectancy because of its cardiovascular and metabolic impact.
Objective: The objective of this study is to report the glycemic profile in patients followed for acromegaly in CHU Med VI of Marrakech.
Patient – Intervention: We performed a retrospective study over a period of 2 years. Fifteen cases were identified.
Intervention: In terms of methodology,we studied a family history of diabetes,hypertension and dyslipidemia; Girth, body mass index (BMI), hypertension, diabetes mellitus or impaired glucose tolerance and dyslipidemia in these patients.
Main outcome measure: Glucose intolerance and diabetes with insulin resistance are commonly encountered complications acromegaly. Some studies have shown a direct correlation between the rate of GH and the degree of glucose intolerance. The hyperinsulinemia and insulin resistance may play an important role in the cardiovascular risk of these patients.
Result: The average age was 43 years (20–63) with a sex ratio (M/F) = 0.33. The duration of the disease at diagnosis was on average 7 years (3–14). Family history were 13.3% diabetes mellitus and heart disease.Pathological BMI was objectified in 52% of cases; 46.6% of these patients were pre-diabetes, 40% diabetic (a total of 84.6% of carbohydrate anomalies)and 46.7% have dyslipidemia. Moreover, 26.6% of our patients are hypertensive.
Conclusion: Approximately 84.6% in our series of cases had carbohydrate abnormalities. Diagnostic and therapeutic delay can worsen or even cause the patient's death. After surgical recovery, the evolution of diabetes and/or glucose intolerance is usually favorable.

P138 Clinical study diamel therapy in polycystic ovary syndrome, reduces hyperinsulinaemia, insulin resistance and hyperandrogenaemia

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Objectives: To determine the effect of Diamel on the insulin resistance, insulin sensitivity, and sexual hormones results in women with polycystic ovary syndrome (PCOS). A study was carried out on 37 patients with this disorder. A triple-blind clinical trial was designed in which the Diamel food supplement was compared with a placebo. The women with reproductive ages were randomly distributed in two groups, with 18 and 19 women respectively, and they took Diamel or placebo and were followed up during 6 months with clinical and biochemical evaluation.
Main Outcome Measures: We aimed at identifying the response of women with the PCOS in treatment with Diamel for to evaluate insulin sensitivity and sexual hormones.
Results: A significant decrease in the HOMA-IR from the initial value at six months was observed in the group with Diamel. The insulin sensitivity improved considerably in this group. The rate of menstrual recovery was higher in the group with Diamel, and two patients from this group obtained pregnancy. The hormone levels shows a significant decrease in testosterone at 3 months in the group with Diamel compared with the control group. The LH also decreases in the same group when comparing the start with 6 months.
Conclusions: We concluded that the Diamel decreases insulin resistance and improves sensitivity to this hormone in women with PCOS, with improvement in the levels of LH and testosterone.

P139 Metabolic endocrine correlation of the dermatological manifestations in the polycystic ovary syndrome

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Context: The main dermatological manifestations of the polycystic ovary syndrome include hirsutism, acne, seborrhea, alopecia, and acanthosis nigricans
Objective: Determine the association of the dermatological manifestations with biochemical and metabolic markers in women with polycystic ovary syndrome.
Methods: Descriptive, observational, cross-sectional, prospective study; the estimated sample size was of 97 women

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Patients: Women of child-bearing age, with polycystic ovary syndrome diagnosed with the Rotterdam criteria and with no prior treatment for three months at least
Interventions: None
Main Outcome Measures: Assessment of the presence of acne, hirsutism, alopecia, seborrhea y acanthosis nigricans, serum glucose, insulin, total testosterone, free testosterone, androstenedione, DHEA, DHEAS, 17αhydroxyprogesterone, total cholesterol, c-LDL, c-HDL, triglycerides, baseline transvaginal ultrasound
Results: Hirsutism was observed in 82.5%, acanthosis nigricans 75.3%, acne 74.2%, seborrhea 52.6%, and androgenic alopecia 9.3%. Positive association of hirsutism with high levels of total testosterone, free testosterone, androstenedione, and DHEA-S. Acne association with high levels of free testosterone and DHEA-S, total testosterone, HOMA, total cholesterol and triglycerides. Positive association of acanthosis nigricans with high levels of free testosterone, DHEA, DHEA-S, HOMA, and triglycerides
Conclusions: Hirsutism, acne, and seborrhea were associated with elevation of total testosterone, free testosterone, androstenedine, and DHEAS, as well as total cholesterol, triglycerides, c-LDL, c-HDL, similar to the reports of the studies of Chanukvadze et al. and Ozdemir et al., all of them atherogenic dyslipidemia markers. Thus, the importance of assessing them in the search for alterations of these variables to reduce cardiometabolic risk.

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P140 D-Chiro-inositol and PCOS

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Context: D-chiro-inositol and ovary.
Objective: In the present study we aim to further study the role played by D-chiro-inositol at ovarian level.
Methods: This is a cohort study, conducted on women who referred to our gynecologic clinic in ''Mbreteresha Geraldine'' Hospital, Albania, in the time period between 2014–2015.
Patients: A total of 80 women, aged <40 years and diagnosed with PCOS were enrolled in this study.
Interventions: All the subjects were selected among patients undergoing ICSI procedure. In particular, insulin resistance was assessed by calculating the HOMA index.
Main Outcome: Insulin resistance was present in 34 subjects (A) and absent in 46 (B). Patients were randomly divided into 5 groups ($n = 16$): a placebo group, and 4 groups (A-D) that received 300–600–1200–2400 mg of DCI daily respectively. All treatments were carried out for 8 weeks before follicle stimulating hormone (rFSH) administration.
Results: Patients matching the inclusion criteria were randomized into five groups by a computer program. Total r-FSH units and number of days of stimulation differed between the groups. In particular, compared to the placebo group, the FSH IU administered were increased significantly in the two groups that received the higher doses of DCI. Estradiol levels at hCG administration were significantly different only in the group D. The total number of oocytes retrieved were similar between the groups, and number of MII oocytes significantly similar. Total r-FSH units increased significantly in the two groups that received the higher doses of DCI.
Conclusions: Indeed, increasing DCI dosage progressively doesn't improve oocyte quality and ovarian response. Because of the small number of patients in this study, the statistical data are insufficient.

P141 Insuline resistence index value in patients with NAFLD compared to the healthy individuals

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Context: HOMA-IR has been known for good correlation to glycemic clamp. Although values have shown large variability, nevertheless, different attempts have been to show the best values with best impact on NAFLD.
Objective: We aimed to identify the HOMA-IR cut off value that best distinguishes NAFLD from a control group (healthy individuals).
Materials And Methods: We studied a group of 58 patients diagnosed with NAFLD through abdominal ultrasound and blood work, and a group of 44 healthy individuals, with no underlying disorders, no liver disease, normal values from OGT, negative ultrasound for liver disease. Blood work for insulin and glycemic levels were provided and HOMA-IR was calculated.
Patients Interventions: All patients were screened through abdominal ultrasound and blood work for both NAFLD and glicemic-insulin levels. Careful anamnesis was taken from doctors questions regarding drinking habits, smoking, OC, other conditions-diseases.
Main Outcome: Identification of HOMA-IR, value that can best discern NAFLD patients and otherwise healthy individuals in Tirana, Albania.
Results: Patients diagnosed with NAFLD, had also higher levels of insulin and glycemia, as well as higher HOMA-IR values. HOMA-IR 75th percentile for healthy individuals group was 1.78: the best area under the curve index was acquired for values of 2.0 [AUC= 0.840 (0.781–0.899 CI 95%), sensitivity was found to be 85%, specificity: 83%] while value 2.5 manifested best specificity lacking prime loss in sensitivity [AUC=0.831 (0.773–0.888) Se = 72%, Sp = 94%].
Conclusion: HOMA-IR values from 2.0 or 2.5 and above demonstrate increased diagnostic value in differentiating NAFLD carriers from otherwise healthy individuals.

P142 Association with increased serum leptin, insulin and prolactin levels in obese infertile women

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Background and Objectives: Obesity appears to be associated with female reproductive dysfunction and infertility in women of reproductive age. This study was done in order to understand the relationship between serum insulin, prolactin, leptin levels and infertility in obese childbearing age women.
Methods and Results: There were two groups of infertile obese women ($n = 75$) compared with control obese fertile women ($n = 30$) with same ages to find the contribution of serum insulin, prolactin and leptin levels in causation of fertility. The results showed that serum insulin, prolactin and leptin, and also BMI parameters were significantly raised in infertile women ($p < 0.001$). It was found that the correlation between serum insulin and BMI, serum leptin and BMI, also serum prolactin and BMI are statistically significant ($r = 0.3–0.4–0.6$ $p < 0.01$-<0.05).
Conclusions: This study has shown that obesity is associated with infertility in women of reproductive age.The reproductive dysfunction and other sex hormonal imbalance may also be associated with BMI and serum leptin, prolactin, insulin resistance in infertility. The mechanisms associated with these findings require further investigations.

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P143 Relationship between severity of polycystic ovary syndrome phenotype (PCOS) and quality of life (QoL) and sexual self-esteem

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Context: PCOS is a common disease which manifests itself as a oligo-/anovulation, hyperandrogenism and characteristic ovarian morphology in ultrasound. The presence of PCOS affects QoL, but each components have different influence on it.
Objective: The aim of the study was to find correlations between measurable biological parameters such as hormonal serum levels, BMI, hirsutism and psychological parameters such as global and sexual self-esteem and finally QoL.
Patients and Methods: Sixty patients admitted to the Department of Gynecological Endocrinology of Poznań Univeristy of Medical Sciences were investigated. All of them were between 19 to 39 years old and were diagnosed with PCOS. Serum levels of LH, FSH, estradiol and androgens were measured and BMI had been calculated. The modified Ferriman- Gallwey Scale had been used to assess hirsutism.
Main Outcome Measures: The patients underwent three questionnaire surveys: Rosenberg Self- Esteem Scale (SES), Sexual Self- Esteem Inventory (SSEI-W) and SF-36 Health Survey.
Results: Several important correlations had been found. QoL correlates negatively with the intensity of hirsutism. Moreover there was significant positive correlation between general and sexual self-esteem and QoL. We did not find any correlations between BMI and QoL. Otherwise, there was a significant correlation between BMI and sexual self-esteem. The higher the BMI the worse sexual self-esteem. There were significant positive correlations between estradiol levels and social functioning (as a component of QoL). There was also negative correlation between testosterone levels and general health (QoL component).
Conclusions: The study proved the influence of biological and psychological features on PCOS patients QoL. The obesity in PCOS interfere with sexual self-esteem. Estrogens and androgens concentrations correlate with QoL in PCOS.

P144 A two purpose use of Orlistat in obese women with polycystic ovary syndrome: weight loss and androgen reduction

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Context: Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in young women. PCOS affects 6% and 8% of women in reproductive age. Hyperandrogenism is the hallmark of PCOS. Excessive androgen has an important role in the pathophysiology of PCOS. The aim of this study was to appoint evidence based and clinically applicable advises effect of Orlistat on weight loss and serum anderogen levels reduction in obese women with PCOS.
Objective: 32 PCOS patients in the Gynecology clinic of Taleghani hospital were enrolled randomly.
Methods: The Sera of androgens (Testosterone, 17(OH) P, DHEAS, SHBG were measured before and after treatment of 12 weeks with orlistat. For all patients performed Rotterdam Criteria and transvaginal sonography for evaluation of ovarian patterns. In this study, $p < 0.05$ was considered to indicate statistical significance.
Results: The study included 32 patients. The mean age was 27.75 ± 6.22 and the mean body mass index was 32.69 ± 0.94 kg/m2. Comparing with baseline, treatment with orlistat resulted in a significant reduction in weight, BMI, and waist circumference ($p = 0.001$). We found a remarkable reduction in total Testosterone levels ($P < 0.001$). Treatment improved the SHBG plasma levels, but the difference was not significant. There was no reduction in other androgen levels. As an incidental finding we encountered with a 30 mm decreasing size of uterine leiomyoma.
Conclusion: This study showed a significant reduction on weight and total total Testosterone levels, as the most important anderogens in PCOS patients. Therefore controlling of weight and treatment by a short course of Orlistat can be useful in management of PCOS cases.

Keywords
PCOS, Orlistat, Androgen, Weight loss

P145 Prevalence of metabolic syndrome in Brazilian postmenopausal women with overwigth and obesity

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Context: Aging is associated with a weight gain, reduction on basic metabolic rate, and replacement of muscle tissue by adipose tissue. Cardiovascular diseases are the main cause of mortality of females and metabolic Syndrome (MetS) has been identified as a risk factor.
Objectives: to determine the prevalence of MetS in women with obesity and overweight in the postmenopausal period according to National Cholesterol Education Program (ATPIII NCEP) and the International Diabetes Federation (IDF), to compare the results and association between MetS and the weight according to the body mass index (BMI).
Methods and Patients: Cross-sectional study in 1537 postmenopausal women attending at Santa Casa de São Paulo – may 2014 to may 2015.
Interventions: Inclusion criteria (amenorrhea > one year; FSH>30mIU/mL; BMI>25kg/m^2), 686 patients were suitable according to the MetS ATPIII NCEP and to IDF criteria. A bivariate analysis was performed using the chi-square test (statistically significant <0.05).
Results: The prevalence of MetS was 52.76% (ATP III) and 61.80% (IDF). Overweight were 58.89% and the prevalence of MetS was 45.80% (ATPIII) and 56.68% (IDF). 28.57% had grade 1 obesity and the prevalence of MetS was 57.14% (ATP III) and 64.79% (IDF. 9.91%). In women which obesity grade 2 the prevalence of MetS was 76.47% (ATPIII) and 80.88% (IDF). Obesity grade 3 was present in 2.63% with MetS prevalence of 72.22% in both criteria. The association between MetS and the weight BMI in both was $p < 0.00001$ (ATP III) and $p = 0.00087$ (IDF).
Conclusions: There is high prevalence of MetS in women with obesity and overweight during the postmenopausal period and this is higher by the IDF. In addition, there is association between MetS and weight according to the BMI.

P146 Prevalence of the metabolic syndrome in women with polycystic ovary syndrome in R. Macedonia

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Metabolic and endocrine dysfunctions that occur in polycystic ovary syndrome (PCOS) can be associated with future co-morbidities such as diabetes, cardiovascular disease, and endometrial cancer. Generally polycystic ovary syndrome and the metabolic syndrome have many features in common and may share the same pathogenesis. This study

was performed to determine the prevalence and predictors of the metabolic syndrome among women with PCOS and different ethnic groups living in R. Macedonia.
Design: The clinical, hormonal, and oral glucose tolerance test results were analyzed in 116 PCOS women.
Main Outcome Measures: Waist circumference, fasting glucose, high-density lipoprotein cholesterol and triglyceride concentrations, and blood pressure were the main outcome measures. *Results*: The prevalence for individual components comprising the metabolic syndrome were: waist circumference greater than 80 cm in 88%, high-density lipoprotein cholesterol less than 1.3mmol/l in 65.5%, triglycerides greater than or equal to 1.7 mmol/l in 10.4%, blood pressure greater than or equal to 130/85 mm Hg in 7%, and fasting glucose concentrations greater than or equal to 5.6 mmol/l in 7.8%. Mean fasting insulin was 8.6 μIU/ml, and HOMA IR greater than 2.5 in 30%. The prevalence of the metabolic syndrome did not differ significantly between ethnic groups.
Conclusions: The metabolic syndrome and its individual components are common in PCOS, particularly among women with the highest insulin levels and BMI. Hyperinsulinemia is a likely common pathogenetic factor for both PCOS and the metabolic syndrome.

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P147 Factors affecting the prevalence of depressive symptoms in women with PCOS

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Context: PCOS is a common endocrinopathy characterized by hyperandrogenism, chronic anovulation, infertility, obesity and is associated with insulin resistance. Reports show high prevalence of depressive symptoms among women with PCOS.
Objective: The aim of the study is to investigate the prevalence and severity of symptoms of mood disorders among women with PCOS and to explore factors increase the risk of their occurrence.
Methods: We examined the relationship between the level of depressive symptoms measured by Beck Depression Inventory and factors such as infertility treatment, testosterone and hiperinsulinemia. We analyzed the internal structure of answers of patients in Beck Depression Scale
Patient(s): Women ($n = 55$), ages 19–37 with PCOS, examined between 2012 and 2015.
Interventions: Physical examinations, serum testing, completion of Beck Depression Inventory (BDI) and questionnaire, in which patients responded to the question whether they were undergoing infertility treatment.
Main Outcome Measures: Scores >9 indicated a positive screen for depression – mild 10–20, moderate 20–27, and severe >28.
Results: 28 Received a positive result on the onset of symptoms of depression. Among these, 22 patients received the result of mild, depressive disorders, 3 moderate and 3 severe. There was no correlation between the level of depression in BDS and testosterone, hiperinsulinemia or infertility treatment. Analysis shows that PCOS women frequently experience negative emotions in connection with the assessment of their appearance, as well as anxiety about the future and their own health.
Conclusions: Hyperinsulinemia, hyperandrogenism and infertility were found not to be associated with depression symptoms in PCOS in the tested sample that is inconsistent with the results of other published studies. Hence it indicates the complexity of factors influencing depression in PCOS women.

P148 Common sexual myths in Turkey

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Myths are thoughts people think they are true. Sexual myths are mostly exaggerated and false beliefs which have no scientific. Lack of sexual knowledge and education, when combined with society's strict behavior, taboos and restrictions about sexuality can lead to several sexual problems and sexual dysfunctions. Marital status, educational level, region lived until adolescence (sub-district and village or province and district), first source for sexual information and result of the first sexual relationship influence rates of belief for sexual myths are ımportan factors for having myths. In Turkey, sexuality can not spoken easily between couples and in society. There are some common myths which are ''people believe that men desire the sexual intercourse all the time and they are always ready for this'', ''sexuality is instinctive and it cannot be learned'', ''masturbation is harmful and sinful'', ''blood must come in first sexual intercourse because of hymen'', ''virginity is important'', ''sexual activity must be initiated by a man'', ''sexual fantasies are shameful and sinful'', ''all physical convergences must end with intercourse'', ''foreplay is a waste of time'', ''woman's body is her best weapon'', ''women who initiate sex are immoral'', ''men with larger sexual organs are more virile''. Sexual myths and prejudices affect people's expectations negatively, and can cause feelings of guilt and inadequacy, and especially in men's fear of failure. So that myths cause sexual dysfunction in couples. There are also no more researh about sexuality because of permission and ethic procedure difficulty. Starting education at a very early age is shown as the most effective method of preventing sexual myths. This education should start with parents, and continuing it in a structured way during school ages is ideal.

P149 Relationship between hyperandrogenism, obesity, inflammation and polycystic ovary syndrome

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Context: PCOS is a metabolic and reproductive disorder, associated with obesity and hyperandrogenism.
Objective: To determine the status of circulating levels of CRP, TNF-α, IL-27, IL-35, IL-37, α-1 acid glycoprotein in patients with PCOS compared with controls and to evaluate their relation with hyperandrogenism and obesity.
Methods: Prospective design in an university hospital setting.
Patients: 48 Patients with PCOS (29 obese, 19 lean) and 40 healthy controls (20 obese, 20 lean).
Interventions: CRP, TNF-α, IL-27, IL-35, IL-37 and α-1 acid glycoprotein levels were measured using commercially available ELISA kits. TT, androstenedione A4, SHBG and DHEA-S levels were measured using ECL.
Main Outcome Measures: CRP, TNF-α, IL-27, IL-35, IL-37 and α-1 acid glycoprotein blood levels.
Results: Levels of TT, A4, DHEA-S were significantly higher in patients with PCOS than in controls both in the obese and lean groups, while levels of SHBG were significantly lower in all patients with PCOS (all $p < 0.05$). FAI values were significantly higher in all patients with PCOS

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than in all controls (all $p < 0.05$). Levels of CRP, TNF-α, α-1 acid glycoprotein were significantly increased in all patients with PCOS compared with all controls (all $p < 0.001$). FAI had a positive correlation with CRP, TNF-α, α-1 acid glycoprotein, a negative correlation with IL-27, IL-25, IL-37 (all $p < 0.01$). Binary logistic regression analyses revealed that IL-35, IL-37, TT, SHBG, DHEA-S were significant single predictors of PCOS ($p < 0.001$). AUC values showed that the predictive performance of performance of IL-35, IL-37, SHBG and DHEA-S were excellent (AUC 0.971, 0.991, 0.968, 0.994, respectively; all $p < 0.001$).
Conclusions: The findings of the present study further confirm the proinflammatory state of PCOS. Moreover, obesity along with PCOS significantly elevates the inflammatory status and hyperandrogenism.

P150 Severe rapid onset hirsutism: description of three cases

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Introduction: Hirsutism is a common disorder affecting between 5% and 10% of women of reproductive age in the general population; it's a sign of increased circulating levels of androgens (endogenous or exogenous) or increased sensitivity of hair follicles. Ovarian tumors producing androgens is rare and characterized by a rapid onset of hirsutism.
Case description: A 54-year-old postmenopausal women and a 23-years-old with secondary amenorrhea showed hirsutism with elevated values of serum androgens. Pelvic ultrasound scan and abdomen MRI revealed ovarian mass with a solid and a fluid component. The postmenopausal women underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy while in the second case an enucleoresection of the mass was performed. Both histological examination deposed for Sertoli-Leydig cell tumor. After surgery serum androgens became normal and hirsutism improved. After 20 days of surgery the young woman had spontaneously menstrual cycle. We also describe a case of a 69-year-old women with a rapid onset severe hirsutism with elevated serum testosterone and an enlargement of both ovaries. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed and histological examination of them deposed for steroid cell tumor. After surgery serum androgens became undetectable and hirsutism improved significantly.
Conclusion: Hirsutism, especially with rapid onset, should be investigated hormonally and with an imagine study through pelvic ultrasound and if necessary abdomen MRI. Sertoli-Leydig cell tumor and steroid cell tumor are rare; the half of these tumors show rapid onset hirsutism and ovarian masses. In the presence of ovarian masses or a suspect enlargement of them surgery is the treatment of choice; chemioterapy is reserved to metastatic patient, in poorly differentiated ones or in presence of heterologous elements. The 5-year survival for well differentiated forms was 100%. Recurrence is rare and generally within one year.

P151 Detection of glucose metabolism disorders using OGTT with insulin, in reproductive-aged patients

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Context: High prevalence of glucose metabolism disorders (GMD) such as glucose intolerance (GI) and insulin resistance (IR) exist in women with reproductive diseases. Diagnosis of GMD is generally done through the HOMA index, Oral Glucose Tolerance Test with insulin (OGTT-I) with two points (0 and 120 min) or five points (0, 30, 60, 90, and 120 min).
Objective: To compare the detection of GMD through Homa index, two and five points OGTT-I.
Methods: Five-points OGTT I conducted after 10 hour fasting.
Patients: 430 women with reproductive disorders.
Intervention: Five-points OGTT-I.
Main Outcome Measures: Glucose and insulin obtained from blood samples. Subjects were classified regarding the presence/absence of GMD according to the HOMA index, and interpretation of two- and five points OGTT-I.
Results: HOMA index estimates less altered subjects (4.9%; $p < 0.01$) than two points OGTT-I (33.7%), which are lower than estimates from five points OGTT I (48.6%; $p < 0.01$). Regarding IR, five points OGTT-I estimates the highest percentage (31.6%), followed by two points OGTT-I (25.6%), and the HOMA index (4.8%). Regarding GI, five points OGTT-I estimated a higher percentage of altered subjects (31.8%) than two points OGTT-I (17.4%).
Conclusions: The use of five points OGTT-I detects 14.9% more GMD altered subjects than two points OGTT-I ($p < 0.01$) and 43.7% more than the HOMA index ($p < 0.01$). Also, five points OGTT-I detects 6% more subjects with IR than two points OGTT-I ($p < 0.10$) and 26.7% more than the HOMA index ($p < 0.01$). Two points OGTT-I can detect 20.7% more IR subjects than the HOMA index ($p < 0.01$). With respect to GI five points OGTT-I detects 14.4% more altered subjects than two points OGTT-I. The analysis of glucose and insulin from the five points OGTT-I allow better distinction of different GMD (IR, IG or IR+IG) than two points OGTT-I or the HOMA index.

P152 The prevalence and risk factors of sexual dysfunction in young Chinese women according to FSFI: an internet-based survey

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Objectives: Female sexual dysfunction (FSD) is a very common disease around the world. However, the prevalence of FSD in Chinese women is unknown. This is the first study investigating a large number of young women all over China using the internet to assess the prevalence and types of FSD and to identify the risk factors of FSD.
Methods: Primary study endpoint was the Female Sexual Function Index (FSFI), with additional questions on contraception, sexual activity, partnership stability, pregnancy and other factors which may influence sexual function. The online questionnaires were completed by women from 31 of the 34 provinces of China.
Main Outcome Measure: The FSFI with additional questions on different factors that may influence sexual function.
Results: A total of 1.784 completed questionnaires were received, and 1.161 were included in the analyses after screening (65.08%). The mean age of women was 25.68±4.63 years. The mean total FSFI score was 25.09±4.61. According to FSFI definitions (setting the cutoff score as 26.55), 58.57% of women were at risk of FSD. Based on domain scores, 53 were considered at high risk of pain dysfunction (4.57%), 42 for desire (3.62%), 37 for orgasm (3.19%), 27 for arousal (2.33%), 11 for satisfaction (0.95%) and 2 for lubrication dysfunction (0.17%).
Conclusions: Our results indicate that the prevalence of FSFI scores indicating the risk of sexual dysfunction was 58.57% in chinese women and that unstable partnership, pressure from wish for children, no contraception, negative self-evaluation on appearance, and increasing age are significantly associated with FSD for young women investigated across all over China.

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P153 Urinary excretion of IL-1β, TGF-β1 and MCP-1 in pregnant women with type 1 diabetes with different stages of diabetic nephropathy

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Objective: To study the level of urinary excretion of interleukin-1β (IL-1β), monocyte chemoattractant protein-1 (MCP-1) and transforming growth factor (TGF-β1) in pregnant women with diabetes mellitus (DM) type 1, depending on the level of albumin excretion in daily urine in different trimesters of pregnancy.
Methods: The study included 48 pregnant women with type 1 diabetes, from 19 to 36 years old [25 (22.0, 27.0)] and the duration of diabetes from 1 year to 26 years [10 (5.0; 12.0)]. All the patients were divided on 3 groups: with normoalbuminuria (NAU), microalbuminuria (MAU) and proteinuria (PU). The level of urinary IL-1β, MCP-1 and TGF-β1 in the daily urine was measured by enzyme-linked immunosorbent assay (ELISA) in different trimesters of pregnancy.
Results: In pregnant women with type 1 diabetes in 1 trimester there was statistically significant increase in urinary excretion of TGF-β1 in the group of women with the MAU ($p = 0.003$) and PU ($p = 0.01$) compared to the level of excretion of TGF-β1 in pregnant women the NAU. The level of the daily urinary excretion of MCP-1 ($p = 0.018$) and IL-1β ($p = 0.017$) is higher in pregnant women with PU compared with their excretion in pregnant women with the NAU. In the 2 and 3 trimesters in pregnant women with type 1 diabetes in group with PU the level of urinary excretion of IL-1β, MCP-1 and TGF-β1 2–3 times higher than the value of their urinary excretion in group of pregnant women with the NAU. We found a positive correlation between the level of albuminuria and excretion of TGF-β1, IL-1β and MCP-1 in the urine ($p<0.05$).

P154 Mood disorders and hyperandrogenism in women with polycystic ovary syndrome

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Context: There is evidence of significantly higher prevalence of mental disorders in women with polycystic ovary syndrome (PCOS) compared with healthy women. The presented data on the relationships of mental status and manifestations of PCOS are very heterogeneous.
Objective: The aim of this study was to determine the frequency of anxiety and depression in Russian patients with PCOS and to examine whether mental problems could be associated with hyperandrogenism.
Methods: This was a single center observational study. PCOS was diagnosed according ESHRE/ASRM criteria. All participants were also examined by a psychiatrist. International Neuropsychiatric Interview (M.I.N.I. 6.0) and Hospital Anxiety and Depression Scale (HADS) were used.
Patients: The study involved 78 women aged 18–39 years (median age 26 years). All participants were divided into 2 groups: 26 patients in Group 1 (normoandrogenic) and 52 women in Group 2 (with hyperandrogenism).
Results: According to the M.I.N.I. 6.0 criteria 40 patients (51.28%) had suffered from at least one depressive episode by the time of examination with 15 women (19.23%) corresponding to the current depressive episode category among them. 22 patients (28.21%) had symptoms of generalized anxiety. 12 (15.38%) and 28 women (35.89%) showed abnormal results (≥8 points, HADS) for depression and anxiety respectively. 2 (2.64%) and 8 (10.26%) patients showed clinically significant symptoms (≥11 points) of depression and anxiety respectively. The Mann–Whitney *U*-test showed significant difference between the Groups 1 and 2 only in the level of anxiety (HADS) ($p<0.05$). Abnormal results were more frequent in Group 1 than in Group 2: 46.15% vs. 30.71%.
Conclusions: Women with PCOS are vulnerable to mood disorders, moreover anxiety is more frequent in women with non-androgenic phenotype in comparison with androgenic phenotypes.

P155 Adipokines, metabolic and atherogenic parameters in insulin resistant and non-insulin resistant women with polycystic ovary syndrome

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Objective: To investigate leptin, adiponectin and vaspin levels and their relationship with other clinical, metabolic and atherogenic parameters in insulin resistant and non-insulin resistant women with polycystic ovary syndrome (PCOS).
Patients and Methods: The study included 67 PCOS women (28 insulin resistant and 39 non-insulin resistant) and 20 age-matched healthy women. The following parameters were determined: weight, height, waist and hip circumferences, basal levels of plasma glucose, immunoreactive insulin (IRI), total cholesterol (TC), HDL-cholesterol (HDL-C), triglycerides (TG), LH, FSH, oestradiol (E2), testosterone, leptin, adiponectin, vaspin. Body mass index (BMI), waist-hip ratio (WHR), homeostasis model assessment insulin resistance index (HOMA-IR), LDL-cholesterol (LDL-C), atherogenic index of plasma (AIP), LH/FSH ratio, and leptin/adiponectin ratio (L/A) were calculated.
Results: Similar leptin levels were found in the PCOS group and the control group. Non-insulin resistant PCOS women had significantly higher vaspin and adiponectin levels compared to the insulin resistant PCOS women and the controls. L/A and AIP were significantly higher in the insulin-resistant PCOS women compared to the non-insulin resistant PCOS women and the controls. Leptin showed significant positive correlation with BMI, WHR, IRI, HOMA-IR, TC, LDL-C, TG. Significant negative correlation between adiponectin and leptin, BMI, WHR, IRI, HOMA-IR, TG, AIP was found. Adiponectin correlated positively with E2 and vaspin correlated negatively with FSH.
Conclusion: PCOS women were at higher metabolic and atherogenic risk as compared to the healthy women that was more pronounced in the insulin-resistant group. The significantly higher levels of vaspin in the non-insulin resistant PCOS women suggest a novel mechanism by which vaspin potentially modulates insulin action.

P156 The diagnostic and predictive value of four blood lipid ratios in patients with polycystic ovary syndrome for metabolic syndrome: a cross-sectional study

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Context: Polycystic ovary syndrome (PCOS) is the most common endocrine disease and metabolic disorder affecting 5% ~10% in reproductive aged women. Some lipid ratios can identify individuals at increased risk for metabolic syndrome (MS).
Objective: To investigate and compare predictive and diagnostic value of the LDL-C/HDL-C, ApoB/ApoAI, TG/HDL-C, TC/HDL-C ratios for metabolic syndrome(MS) in PCOS patients. Patients 492 patients with PCOS were included in this study.

Methods: Clinical examination for anthropometric information, blood sample for metabolic parameters was collected. All patients were divided into two groups according to the international diabetes federation (IDF) diagnostic criteria: MS group and non-MS group. Divide all patients into 6 groups by the number of abnormal component, from 0 to 5 components. Correlations between the 4 ratios and parameters in MS diagnostic criteria were analyzed respectively. The diagnostic value of 4 ratios were determined and compared by ROC curves.
Main outcome measures: Differences between the two groups were compared, including blood pressure, waist circumference, fasting glucose, fasting insulin, LDL-C, HDL-C, ApoAI, ApoB, triglyceride, total cholesterol, etc.
Results: Mean values of the 4 blood lipid ratios increased with increasing in the number of abnormal components, and all ratios were significantly correlated to parameters in MS criteria. TG/HDL-C obtained the biggest area under the curve (AUC) of 0.936 determined by ROC curves, suggesting that TG/HDL-C has the greatest diagnostic value of MS. The cutoff value of TG/HDL-C was set at 1.088, with the sensitivity of 0.857 and the specificity of 0.883.
Conclusion: TG/HDL-C is the best diagnostic and predictive parameter of MS among 4 ratios. PCOS Patients whose TG/HDL-C ratio is over 1.088 should be noted the risk of MS, and take corresponding intervention to prevent MS.

P157 Androgen excess increases food intake through down-regulating hypothalamus insulin and leptin sensitivity in female rat

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Objective: Androgen excess in women is associated with obesity. The aim of the study was to investigate the mechanism through which androgen excess regulates food intake and obesity in female.
Materials and Methods: In this study, we used dihydrotestosterone (DHT) induced-rat model (DHT rat) to test the hypothesis that androgen excess regulates appetite through insulin and leptin signal in hypothalamus. We also use GT1–7 cell to study the direct effect of DHT on insulin and leptin signal through androgen receptor (AR).
Results: DHT rat show increased food intake, resulting in obesity and increased body fat. They also show decreased hypothalamus sensitivity to insulin and leptin, and increased expression of agouti-related peptide (AgRP) and neuropeptide Y (NPY). In GT1–7 cell, DHT reduced insulin and leptin signal and the androgen receptor antagonist flutamide can bock that effect.
Conclusion: In summary, these data indicate that androgen excess increase food intake resulting in obesity through down-regulating insulin and leptin signal in hypothalamus.

Keywords

Androgen excess, food intake, hypothalamus, insulin sensitivity, leptin sensitivity

P158 Cytotoxicity receptors' uNK cells in the endometrium of women with PCOS

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OORR Foggia

Introduction: Endometrium is characterized by a large component of immune cells. An abnormal percentage of endometrial lymphocyte subsets was found in patients with recurrent pregnancy loss and implantation failure. Also obesity and PCOS associated with insulin resistance is characterized by increased circulating inflammatory cytokines and increased expression of NK markers of cytotoxicity in the peripheral blood. The aim of the study is to analyzed the cytokines and the expression of activation markers of uterine NK cells in the endometrium of women with PCOS
Materials and methods: 19 Patients with PCOS and 9 healthy women (control group) were enrolled. In the secretory phase of the cycle the patients underwent endometrial biopsy. TNFα, IL 1β, IL-6, IL-12, IL-15, IL-18, and activation markers of NK cells NKp46, NKG2D, CD56 were evaluated.
Results: In the PCOS group we observed a significant increase of IL-18, TNFα, IL-12 ($p < 0.05$), IL-15 ($p < 0.01$) and an increase of CD56, NKp46, NKG2A, NKG2D ($p < 0.01$) in PCOS.
Conclusions: Increased expression of pro-inflammatory cytokines and activation markers of uNK cells found in the endometrium from patients whit PCOS may concur to explain the abnormal endometrial receptivity in these patients.

P159 Sexual attachment of anorgasmic women: role of Oxytocin

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Introduction: Oxytocin is known as the hormone of breastfeeding and childbirth. The study aims to evaluate Oxytocin serum levels before and after sexual activity in healthy orgasmic women and in women affected by anorgasmia.
Material and methods: The sample was constituted by 15 orgasmic women with 15 anorgasmic women. The McCoy Female Sexuality Questionnaire was administered and serum Oxytocin levels were measured during the follicular phase of the menstrual cycle, before sexual activity (T0) and 15 minutes after coital sexual activity with the partner (T1). Plasmatic measurement of Oxytocin was made through a enzyme-linked immunoassay test.
Results: At T0, anorgasmic women had lower levels of Oxytocin than orgasmic women ($p < 0.01$). At T1, Oxytocin levels did not change in anorgasmic women ($p = \text{NS}$). Contrarily orgasmic women has a statistically significant increase in hormone levels ($p < 0.001$).
Conclusions: The results of the study showed a correlation between Oxytocin levels and sexual activity: in anorgasmic women the experience is not metabolized and lived as pleasant, whereas orgasmic women are fully satisfied about their experience. Oxytocin peak during sexual arousal determines loss of bodily memory but not of emotions, activating repetitive processes which represent a survival behavior for maintenance of species.

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P160 The role of β-endorphins in the pathogenesis of polycystic ovary syndrome (PCOS) in lean women: comparison of β-endorphins levels in lean women with and without PCOS and association between endorphins concentration and other hormonal parameters in women with a BMI (body mass index) within a normal range

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Context: The aim of this study was to evaluate the **β**-endorphin plasma levels in lean women with polycystic ovary syndrome as well as in women without this disorder. The associations between **β**- endorphins and other laboratory parameters were also investigated.
Patients and Methods: 31 women lean, defined as women with normal range body mass index, 15 with polycystic ovary syndrome and 16 without this disorder were included to the study. In all the patients the level of **β**-endorphins was measured. Also the diagnostic laboratory profile including hormone assessment was made in all patients.
Results: There were significant differences in **β**-endorphin levels between the two groups. The **β**-endorphin level was higher in the polycystic ovary syndrome group compared to the healthy controls (15.5 pg/ml vs. 6.9 pg/ml, $p < 0.0001$). The **β**-endorphin levels positively correlated with cortisol at 8 am ($R = 0.632$, $p = 0.011$) and negatively correlated with sex hormone binding globuline ($R = 0.518$, $p = 0.0478$) in polycystic ovary syndrome group. Increase in **β**-endorphin level of 1 pg/ml was associated with an increase of cortisol at 8 am level of 1.134 μg/dl and decrease of sex hormone binding globuline of 0.948 nmol/l in polycystic ovary syndrome group.
Conclusion: Our study showed that the levels of **β**-endorphins were significantly higher in lean patients with polycystic ovary syndrome than in lean controls. Moreover, **β**-endorphins levels were found to be correlated with other hormonal parameters. In this respect, **β**-endorphins may play an important role in polycystic ovary syndrome pathophysiology and pathogenesis.

P161 Kisspeptin and galanin-like peptide (GALP) relationship in women with polycystic ovary syndrome (PCOS)

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Objective: To compare kisspeptin and GALP levels between women with and without PCOS and to analyze the correlation between kisspeptin, GALP and PCOS-related hormonal and metabolic disturbances.
Patients and Methods: The study included 40 PCOS women, and a control group of 16 normal weight women with regular menstrual pattern and no signs of hyperandrogenisms. PCOS women were divided into 2 groups, based on body mass index: overweight ($\geq 25\ kg/m^2$) and normal weight (18–25 kg/m^2). Circulating levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), sex-hormone binding globulin (SHBG), thyroid stimulating hormone (TSH), prolactin, fasting insulin, kisspeptin and GALP were measured.
Results: Kisspeptin ($p < 0.05$) was significantly higher in the overweight PCOS women than in the controls, and was not significantly different between the normal weight PCOS women and the controls ($p > 0.05$). GALP levels were significantly higher both in the overweight and normal weight PCOS women compared to the controls ($p < 0.01$, $p < 0.05$, resp.). In the normal weight PCOS women kisspeptin correlated positively with GALP ($p < 0.01$), waist circumference (WC) ($p < 0.05$) and free androgen index (FAI) ($p < 0.05$) and negatively with fasting glucose ($p < 0.05$) and GALP correlated positively with WC ($p < 0.05$) and kisspeptin ($p < 0.01$). In the overweight PCOS women kisspeptin correlated positively with insulin ($p < 0.05$), T ($p < 0.05$), SHBG ($p < 0.01$) and FAI ($p < 0.001$). In this group there was a significant positive correlation between GALP and LH ($p < 0.05$), LH/FSH ratio ($p < 0.05$), T ($p < 0.01$) and FAI ($p < 0.01$).
Conclusions: Our results showed that in the PCOS women kisspeptin levels were associated mainly with metabolic disturbances, while GALP was associated with both metabolic and hormonal disorders. We suggest that kisspeptin and GALP may be involved in the pathogenesis of PCOS.

P162 Ovarian morphology in PCOS – a comparison of 2D and 3D transvaginal ultrasound with MRI as gold standard

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Context: Polycystic ovarian syndrome (PCOS) is diagnosed by the presence of minimum two out of three Rotterdam criteria: oligo-/anovulation, hyperandrogenism and polycystic ovary morphology (PCOM). PCOM is defined as ≥12 follicles (2–9 mm) and/or volume >10 ml in at least one ovary, assessed by 2D transvaginal ultrasound (TVUS). Since PCOM is central in PCOS diagnostics, we are in need of accurate imaging methods as well as new thresholds for ovarian volume and antral follicle count when using up-to-date 2D scanners and new 3D modalities. Several studies have compared 2D and 3D TVUS with respect to ovarian morphology, mainly in non-PCOS populations and without a gold standard.
Objective: To describe PCOM assessed by 2D and 3D TVUS, with MRI as a gold standard.
Methods: 66 Women with PCOS where examined with 2D-, 3D TVUS, and MRI. Ovarian volume were calculated from 2D TVUS using the formula v=L*W*H*0.523 and from MRI by calculating volumes from 2mm sections. 3D data were analyzed using the VOCAL-tool, 4DView, GE Healthcare.
Main Outcome Measure: Difference in ovarian volume measured by 2D and 3D TVUS, as compared to MRI.
Results: Estimates for mean ovarian volume (±1.96SD) were: 2D TVUS: 9.40ml (2.30–16.50); 3D TVUS: 10.88ml (3.63–18.13); and MRI: 10.65 ml (2.62–18.67).
2D TVUS was 14.9% (10.1–19.4%, $p < 0.001$) lower than MRI, and 11.6% (6.0–17.0%, $p < 0.001$) lower than 3D TVUS, whereas 3D TVUS was similar to MRI.
Conclusion: When examining PCOM, 2D TVUS gives lower ovarian volume estimates than both MRI and 3D TVUS, whereas 3D TVUS estimates are closer to MRI estimates.

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P163 MYO-inositol in the treatment of women with polycystic ovary syndrome (PCOS)

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Context: PCOS is considered as a typical gender-specific representative of metabolic syndrome with insulin resistance and compensatory hyperinsulinaemia being the underlying mechanism. Recently there are some data on beneficial metabolic and clinical effects of myo-inositol combined with folic acid in the treatment of PCOS women.
Objective: To evaluate the effect of myo-inositol alone or in combination with metformin on some metabolic and hormonal disturbances in PCOS women.
Patients and Methods: The study comprised of 146 insulin resistant overweight women with PCOS diagnosed according to Rotterdam ESHRE-ASRM criteria treated up to 6 months with 2 g myo-inositol + 0.4 mg folic acid (Inofolic®, LO.LI Pharma, Rome, Italy) 2 x 1 sachet per day as monotherapy (Group 1) or added to metformin (1250–1500 mg/daily) (Group 2).
Main Outcome Measures: Anthromometric, clinical, biochemical and hormonal parameters were assessed before and after the treatment in all the participants.
Results: We found significant decrease in body weight, BMI, LH/FSH ratio; prolactin, androstendione, total testosterone, 17-OH-progesterone, HOMA-index, area under the curve (AUC) of insulin during an oral glucose tolerance test (OGTT) and amelioration of the lipid profile in all patients that were more pronounced in the group with combined treatment. Menstrual cyclicity was restored in a significant percent of women with initial menstrual irregularity in both groups starting from the third month.
Conclusion: Our data support beneficial effects of myo-inositol for metabolic/hormonal abnormalities and for improving menstrual irregularities in PCOS women. The effects could be explained to a greater extent by the significant weight reduction, improved insulin sensitivity and amelioration of ovarian function.

P164 Asymmetric dimethylarginine in women with polycystic ovary syndrome (PCOS)

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Objective: to determine the plasma levels of asymmetric dimethylarginine (ADMA) and assess its relationship with clinical, metabolic and hormonal parameters in women with PCOS.
Patients and Methods: The study comprised of 22 PCOS women (mean age – 26.64±3.96 years; mean body mass index (BMI) – 30.56±4.34kg/m^2) and 17 age and BMI matched clinically healthy women (mean age – 29.35±5.30 years; mean BMI – 32.20±7.39kg/m^2). The following measurements and laboratory tests were performed: weight, height, waist circumference, blood pressure (BP), basal levels of follicle stimulating hormone (FSH), lutheinizing hormone (LH), total testosterone (T), ADMA, plasma glucose, immunoreactive insulin (IRI), total and HDL-cholesterol, triglycerides, leptin, resistin, interleukin-6 (IL-6). BMI, waist-hip-ratio (WHR) and homeostasis model assessment insulin resistance index (HOMA-IR) were calculated.
Results: Significantly higher ADMA levels were found in the PCOS women than in the controls (0.80±0.31, resp. 0.55±0.28 μmol/l, $p < 0.05$). Significantly higher in the patients than in the controls were the basal levels of resistin (5.65±1.99 vs. 4.36±1.80 ng/ml), IRI (11.39±4.93 vs. 5.99±1.50 μIU/ml), HOMA-IR (2.74±1.31 vs. 1.29±0.38), systolic BP (119.77±10.74 vs. 113.24±9.83 mmHg), as well as T (0.68±0.16 vs. 0.46±0.15 ng/ml), and LH/FSH (1.24±0.85 vs. 0.58±0.34). All other parameters did not differ significantly between the two groups. In the PCOS women no significant correlation between ADMA and the other clinical, hormonal and metabolic parameters was found.
Conclusions: The higher levels of ADMA (a marker of endothelial dysfunction) as well as of IRI, HOMA-IR, and systolic BP in the PCOS women proved an increased cardiovascular risk. The elevated resistin levels suggest a possible pathophysiological role of this adipocytokine in the development of various metabolic disorders in PCOS.

Steroids/Stem Cells/ Basic science

P165 The effect of third generation aromatase inhibitors in bone metabolism and biomechanical assessment of femoral bone in ovariectomized rats

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Introduction: Aromatase inhibitors are widely used in the treatment of hormone sensitive breast cancer in postmenopausal women. The purpose of this study was to evaluate the strength of the bone by conducting a biomechanical study on the femoral bones and to access the levels of bone turnover markers in ovariectomized rats treated with anastrazole and letrozole.
Materials and methods: Fourty-five Wistar rats underwent ovariectomy and were randomized in three groups in order to receive no treatment, anastrazole or letrozole. At the time of the surgical procedure, two and four months after, serum levels of OPG and RANKL were determined. At the end of the 4-month period, ten control animals of similar age were added to the experiment. At this point, all animals were euthanized and the femoral bone was removed en block in order to perform the biomechanic study. The applied force, the deflection of the central section, the maximum load sustained by the bone specimen, the stiffness of the bone and the energy absorbed until fracture, were measured.
Results: Two months after the initiation of the experimental protocol, differences were observed in the mean levels of OPG and RANKL between control ovariectomized rats and animals that were treated with anastrazole and letrozole, Interestingly, these findings were not observed at the end of the experiment (4 months). On the other hand, the biomechanical study of the femoral bones revealed a decreased

value of stiffness among animals treated with aromatase inhibitors as compared to their control counterparts
Conclusion: Anastrazole and letrozole significantly affect bone metabolism and this effect seems to directly correlate with the biomechanical properties of bones.
Funding: IKY fellowships of excellence for postgraduate studies in Greece – Siemens Program.

P166 Outcomes following IVF procedure in unexplained, endometriosis-associated infertility and pcos in UKKMC

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Objective: To assess and compare possible differences in outcome after IVF procedure in unexplained, endometriosis-associated and PCOS infertility.
Method: This was a retrospective comparative study of women underwent in-vitro fertilization (IVF) from 1 January 2013 to 31 December 2013 in Medically Assisted Conception Unit, UKMMC. The IVF outcome from three subfertility groups – unexplained, endometriosis-associated and polycystic ovarian syndrome, were analysed.
Results: The total number of patient underwent first IVF treatment from the three subfertility groups were 131. However, only 80.1% ($n = 105$) proceeded with embryo transfer. There were 36 cases for unexplained, 40 cases for endometriosis, and 29 cases for PCOS. 73.3% of IVF cycles were induced gonadotropin agent alone (unexplained $n = 22$, endometriosis $n = 31$, PCOS $n = 31$). The PCOS group yielded the highest number of oocytes retrieved with mean 11.47± SD8.22), while endometriosis group had the lowest number of oocytes retrieved (mean 8.25 ±SD 5.61). The endometrial thickness was comparable among groups with overall mean 11.8 ± SD1.88 mm. The overall live birth rate per cycle in these populations was 15.3%. The live birth rate per first IVF cycle for unexplained, endometriosis and PCOS was 13.8%, 12.5% and 19.4% respectively. PCOS has the least number of miscarriage ($n = 2$, 5%). The mean birth weight was analogous in the three different subgroups, 2586 ± 561 g.
Conclusion: The overall pregnancy rate and the live birth rate of the three subgroups were comparable to each other, with good obstetric and fetal outcome.

Keywords
IVF treatment, outcome, unexplained, endometriosis-associated, PCOS

P167 Does nulliparity modulate the expression levels of main pro-angiogenic factors: VEGF, VEGFR2, Akt and ERK2, in the mouse ovary?

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Context: Nulliparity is considered a risk factor for ovarian cancer, while pregnancy and lactation have protective roles. Nulliparity represents a condition capable of affecting, in the ovaries of both young and aged mice, the expression levels of the pro-angiogenic factors VEGF and VEGFR2, and modulating the degree of phosphorylation of VEGFR2, ERK2, pAkt and PTEN, which are VEGFR2-activated downstream signals involved in endothelial cell proliferation, survival and permeability. VEGF and VEGFR2 expression levels increases during ageing and ovarian cancer.
Objective: This experimental animal study involved a total of 40 CD1 female mice, young (4-months-old) and old (15-months-old), both parous and nulliparous, where the expression levels of VEGF, VEGFR2, ERK2, Akt and PTEN proteins were determined.
Methods: Mice were maintained in the animal house; part of them, called Mothers (M), were mated with males and sacrificed after the first pregnancy and lactation (Young, Y, $n = 10$) or at 15 month (Old, O, $n = 10$) of age, when natural cyclicity was definitively lost. The same protocol was adopted for the group of nulliparous mice, called Virgins (V), sacrificed without mating either young (YV, $n = 10$) or old (OV, $n = 10$). Ovaries were collected and stored for western blot analysis.
Main Outcome Measures: The expression levels of VEGF, VEGFR2, ERK2, Akt and PTEN proteins were determined into the 4 groups.
Results: Results obtained in this study evidenced that: 1. VEGF content was always higher in V than in M, but no age-dependent increase of VEGF was recorded in V because of the high levels already present in the YV; 2. VEGFR2 content was higher in V than in M, and was accumulated in OV; 3. Akt and ERK2 were phosphorylated more efficiently in V than in M; 4. PTEN was under phosphorylated in OV.
Conclusion: The finding that in the ovaries of nulliparous (V) mice the expression levels of pro-angiogenic proteins are enhanced in comparison to parous (M) mice, contributes to explain epidemiological data by providing the first molecular explanation of the protective role of pregnancy on female health. Conversely, the over-expression of specific pro-angiogenic proteins and their over-activity provide favorable conditions for neo-angiogenesisand can contribute to explain the reason why the incidence of ovarian cancer in nulliparous women is higher than in parous women.

P168 Influence of statin therapy on steroids production in hypertensive older men

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Aim: Dehydroepiandrosteronesulfate is precursor of steroids synthesis. Cholesterol is basic substance for DHEAS synthesis. Positive effect of statin therapy can be masked by the negative effect of and decreased production of endogenous steroids.
Materials and Methods: 40 Male patients, age under 55, who had diagnosed hypertension more than one year processed. They were separated in two groups of 20. First group used statins, longer than 6 months, and other group was without statins. Exclusion criteria were diabetes mellitus and thyroid diseases. Total, free testosterone and DHEAS were compared. DHEAS was determined by imunohemiluminiscention, total and free testosterone by RIA method.
Results: Average age in statin group was 66.0 + _ 8.26, in other 64.85 + _7.48. Median total testosterone in statin group 13.45 (8.22 to 42.90) in other 16.85 (9.99 to 33.17). Median free testosterone in statin group 0.42 (0.09 to 1.83) in other 0.41 (0.13 to 1.75). Median DHEAS in statin group 1.19 (0.30 to 5.62) in other 3.16 (1.23 to 6.72). The conclusion was carried out at significance level 0.05. No statistically significant differences in total and free testosterone was found. Difference in DHEAS level between two groups is significant.
Conclusion: Statinotherapy had negative effect on DHEAS production and neutral on production of total and free testosterone. Compromising production DHEAS confirms that its main substrate is cholesterol, while the synthesis of testosterone compensates by alternative routes.

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P169 Are the inhibin beta A(βA) under influence of melatonin treatment in the ovary of pinealectomized rats?

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Objective: The study aims to identify the target genes of melatonin in the ovarian tissue of adult pinealectomized female rats after melatonin treatment rats.
Methods: Forty-five adult virgin female rats (Rattus norvegicus albinus) were randomized to three groups of 10 animals each: GSh – Sham (falsely pinealectomized) received vehicle; GPx – pinealectomized who received vehicle; GPxMe – pinealectomized with melatonin reposition (10μg/night, each animal) for 60 consecutive days. After treatment, the animals were euthanized by overdose of ketamine and xilazine, some ovaries were collected, kept in liquid nitrogen and stored at −80°C for posterior expression analyses by cDNA microarray (Kit GeneChip® Rat Genome 230 2.0 Array, Affymetrix) of genes related to ovarian functions. The microarray assay was carried out in triplicate for each group. Data were normalized and subjected to the GeneChip® Operating Software and later confirmed by the DNA-Chip Analyzer (dChip) software of secondary analyses. Gene expressions were considered significantly different when they were 2.0× over or low expressed, when compared to the control group. Some samples were appropriately kept for posterior qRT-PCR analyses and others were processed for paraffin embedding.
Results: We found the upregulation of inhibin beta A gene in the ovarian tissue of GPxMe compared to those of the group GSh and GPx. Based on these data, we later confirmed the overexpression of inhibin beta-A by qRT-PCR ($p = 0.0009$) and by immunohistochemistry, which showed higher immunoreactivity of Inhibin beta-A in GPxMe in the follicular cells compared to GSh and GPx.
Conclusion: Our data suggest that melatonin determined the over-expression of inhibin beta-A in the ovaries pinealectomized female rats.

P170 Does progesterone have protective effects on ovarian I/R injury?

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Context: There is number of studies about neuroprotective effects of progesterone against global cerebral ischemia/reperfusion (I/R) injury.
Objective: The aim of the present study was to evaluate the protective effect of the progesterone (PG) against ovarian I/R injury by biochemical and histopathologic parameters.
Methods: 21 Female wistar albino rats were utilized for creating three groups. Group 1: Sham, Group 2: I/R, Group 3: IR+PG (8 mg/kg). Progesterone was administered intraperitoneally into the rats in group 3, 30 minutes before detorsion operation.
Main Outcome Measure(s): Ovarian ischemia-reperfusion injury evaluated in serum and tissue by using biochemical parameters including malondialdehyde (MDA), total antioxidant status (TAS), total oxidant status (TOS), oxidative stress index (OSI), Neutrophil Gelatinase-Associated Lipocalin (NGAL) and immunoflourescence staining by TUNEL method was also studied.
Results: Serum and tissue TOS levels were significantly lower in group 3 than group 2. Only tissue TAS levels were higher in group 3 than group 2 ($p < 0.001$). NGAL and MDA levels were similar between the groups. Histologic score including vascular congestion, hemorrhage, polymorphonuclear neutrophils, and interstitial edema was higher in group 2. Pre-treatment with progesterone decreased the score but this difference was not statistically significant. Apoptotic cell number was higher in group 2 than group 1 and 3. It was seen that the number of apoptotic cells was increased in the I/R group. TUNEL-positive cell number gradually decreased with progesterone in group 3.
Conclusion: Conservative treatment with progesterone is beneficial for I/R injury, as progesterone has an ovarian protective effects by antiapopitotic and antioxidative properties.

P171 Epithelial mesenchymal transition (EMT) and differentiation of SF1-mES cells into the steroidogenic cells

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Context: Steroidogenic factor 1 (SF-1) is essential for the development and function of steroidogenic tissues. Stable incorporation of SF-1 into embryonic stem cells (ESCs) has been reported to prime the cells for steroidogenesis.
Objective: To identify traits during differentiation of stably SF1-transfected mESC into the steroidogenic cell
Methods: We transfected mESCs with mouse SF1 gene (SF1-mESCs) by using the nucleofector and selected SF1-mESCs by G418 250 μg/ml. The selected cells were differentiated into granulosa-like cells through hanging-drops for 3 days, suspension culture for 1 day, then attachment onto 6-well plates. To test the phenotype for granulosa-like cell, transcripts of specific forkhead transcription factor (Foxl2) and follicle stimulating hormone receptor (Fshr) were measured by real-time PCR. Also, expression of EMT-related genes, such as E-Cadherin (Cdh1), N-Cadherin (Cdh2), Snai1, Snai2 (Slug), Twist, and Vimentin, was monitored.
Results: The steroidogenic enzymes such as 3β-hydroxysteroid dehydrogenase (Hsd3b1), cytochrome P450-containing enzyme (Cyp)-11a1, and Cyp19a1 were sequentially up-regulated. The mRNA levels of Foxl2 and Fshr representing granulosa-like cell were increased during differentiation of SF1-mESCs. Especially, the level of estradiol and Cdh2 was increased at specific differentiation time.
Conclusions: The SF1-mESCs were differentiated into granulosa-like cells and increased expression of mesenchymal markers with temporary generation of estrogen. These cells will be useful for further study and potential application of these cells in steroidogenesis.

P172 Vascular effects of dehydroepiandrostenedione and testosterone in vascular remodeling

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In recent years dehydroepiandrostenedione (DHEA) has placed as an alternative therapy for hypoandrogenic conditions, promoting local synthesis of active steroids from this precursor, process that has been called intracrinology. In this study we compared vascular effects of DHEA and testosterone (T) in processes involved in vascular remodeling, like cell migration and proliferation in human umbilical vein endothelial cells (HUVEC) and endothelial production of PAI-1 and uPA, factors that regulate vascular remodeling. We demonstrated that

PAI-1 expression was not affected by DHEA (2nM, 20nM and 200nM) while T induced a significant increase at all concentrations (0.1nM, 1nM and 10nM) at different treatment times, with a stimulation of 60–80% above control ($p < 0.05$). This T effect showed to be dependent of androgen receptor and independent of aromatization to estradiol. Regarding to uPA expression, 24h treatment with DHEA increased its expression (30% above control $p < 0.05$) while with T treatment no effect was observed in HUVEC cells. The effect of androgens on HUVEC proliferation (MTT assay) and cell migration (wound healing assay) were also studied. Time-response assays (12, 24, 36 and 48h) showed that both, T and DHEA, can stimulate cell growth (32% and 12% above control, 1nM T and 20nM DHEA $p < 0.05$). Both androgens promoted cell motility (2 ± 2, 16 ± 4, 60 ± 11 control, 1nM T, 20nM DHEA migrating cells/field $p < 0.01$) with a higher effect of DHEA (3.7 times higher than T). The presented results suggest that DHEA exerts a more favorable effect in terms of vascular remodeling, decreasing PAI-1 expression and stimulating uPA, these effects correspond to a higher stimulating action of DHEA on cell migration.

P173 Gene expression of small leucine-rich proteoglycans (SLRPS) in lacrimal gland of female mice with hyperprolactinemia induced metoclopramide

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Context: The SLRPs, are bioactive components of the extracellular matrix associated to the fibrillogenesis, and cell growth and apoptosis and tissue remodeling, and may be indicative of alterations on the functioning of the lacrimal glands.
Objective: This report aims to assess gene expression and immunolocalization of small leucine-rich proteoglycans, SLRPs (class I: biglycan and decorin) and (class II: lumican and fibromodulin).
Methods: 10 Female/groups: control group (Ctr): 0.2 mL of saline (vehicle) and the experimental group (HPrl): 200 μg/day of metoclopramide, dissolved in vehicle.
Intervention(s): Induction of hyperprolactinemia.
Main outcome measure: After 50 consecutive days of treatment, the animals were euthanized and the blood samples were collected for hormone measurements. The lacrimal glands were removed and processed for gene expression by RT-qPCR. The results were subjected to statistical test ($p < 0.05$).
Results: Gene expression alteration of the small leucine-rich proteoglycans (SLRP). Serum prolactin levels were higher in all the animals with metoclopramide, while the levels of estradiol and progesterone were lower compared to control group.
Conclusion: Our data suggest that the state of hyperprolactinemia changed differently the gene expression of the small leucine-rich proteoglycans (SLRPs). Fact that could explain the changes in the amount of collagen in the lacrimal gland in female mice with HPrl reported in a previous study conducted in our laboratory. These data suggest impairment in functioning of the lacrimal gland by elevated serum prolactin levels and decreased estrogen and progesterone.

P174 The Mechanism of estrogen inhibits vascular endothelial cell endoplasmic reticulum stress apoptosis

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Objectives: To study the signal transduction mechanism in which ERS induced apoptosis is inhibited by estrogen and to discuss the how the estrogen prevents atherosclerosis and protects the cardiovascular system.
Method: The effect and mechanism of estrogen on ERS apoptosis and the signaling pathway of ERS was examined in human umbilical vein endothelial cell (HUVEC) and measured by Western blot or Hoechst stains.
Results: (1) Compared with the blank control group, the expression of GRP78 and CHOP showed evident increase in TM/DTT group, with evident increase of apoptotic cells , while such increase in TM/DTT+E2 group reverted apparently, with evident decrease of apoptotic cells. (2) The protein expression on all three signaling pathways of ERS showed evident increase, with the most evident increase coming from the P-PERK/PERK signaling pathway, and the increase reverted after applying E2 beforehand. (3) After appending E2 receptor antagonists and the inhibitors of PI3K-Akt, ERK1/2, JNK and p38-MAPK, E2 became less effective in inhibiting the increase of P-PERK/PERK.
Conclusions: Estrogen can prevent atherosclerosis and protect the cardiovascular system by inhibiting the PERK pathway caused ERS apoptosis and protecting the vessel endothelial cell, while the mechanism of inhibiting ERS is mainly done by activating the PI3K/Akt pathway for the activated estrogen receptor.

P175 Experimental study of effect of cream, CO-formuated with clindamycin and miconazole, on fertility and fetal phase in female rats with bacterial and fungal vaginitis

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Infectious diseases of the genital tract are an actual problem of modern gynecology. It is known, that late treatment of acute bacterial and fungal vaginitis is one of the causes of chronic diseases of female reproductive system, complications at pregnancy and delivery. Treatment of infectious and inflammatory diseases of urogenital system is an integral stage of preconception preparation of women, with an important role of modern antimicrobials, especially of topical action. The objective of this work is the study of effect of new vaginal cream, consisting of clindamycin and miconazole, on fertility and perinatal fetal development in female rats, having bacterial and fungal vaginitis before fertilization. Therapeutic and preventive introduction of the new vaginal cream to female rats increases the fertilization rate by 33%, and improves the gestation course. Severe gestational pathology develops in untreated females after vaginitis, resulting in increased postimplantation losses, and actual reduction of weight and craniocaudal fetus size. Placenta weight reduces, showing the development of secondary placental dysfunction. Postimplantational embryo death rate has actually reduced by 61% in animals, administered with cream, containing clindamycin and miconazole, at treatment and preventive course. Fetus and placenta physical parameters have significantly improved: fetus weight and size has increased by 25% and 16.7% correspondingly, placenta weight – by 14.3% compared to the same indices of untreated animals. Considering the improving resistance of pathogens to existing antimicrobial drugs, the development and introduction of the new effective cream will reduce the complications of infectious and inflammatory processes in the clinical practice.

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Fertility/IVF/Sperm/ Egg donation

P176 Stres levels in Turkish infertile women

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Context: Infertility is a crisis situation, which causes stres. Couples define their infertility experience as the most stressful experience of their lives.
Objective: This study aims to determine the stress level during infertility treatment by Assisted Reproduction Technology (ART) methods.
Materials and Methods: The study included 108 women with primary infertility women who applied for ART to the Istanbul University Istanbul Medical Faculty between1st September and 31st November, 2015. Descriptive cross sectional model was used in this study. Infertility stress was measured by The COMPI Fertility Problem Stress Scale and for obtaining the infertility data, a questionnaire designed by the researchers was given to the subjects. Data were statistically analyzed using SPSS analytical software program.
Results: The mean age of the women was 30.8±5.2, years of marriage was 7.2±5.1, years of infertility treatment was 3.3±3.2, and number of treatment trial was 3.01±1.1. 67% women were housewife. According to the findings, infertility in 46% of subjects was due to female infertility, 19% to female, 10% to male & female and 33% was unexplained. Study results showed that in all sub-scales of The COMPI Fertility Problem Stress Scales had higher stress scores, and personal sub-scale had higher stres scores than marital and social sub-scale scores (Personel sub-scale was 14. ±4.4, marital sub-scale was 8.7±3.5, and social sub-scale was 4.9±3.2). The COMPI Fertility Problem Stress Scale score was related to women age using linear correlation ($p = 0.04$, $r = 0.12$), years of marriage ($p = 0.01$, $r = 0.23$), and was not related to number of treatment trial ($p = 0.45$, $r = 0.12$).
Conclusions: This study showed that stress is common in infertile women applied for ART. Thus special attention to this infertile women is necessary in order to control and decrease their stress levels.

P177 Menstrual cycle length is capable of improving the accuracy of biochemical/ sonographical ovarian reserve test in estimating the reproductive chances of women referred to ART

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Context: Padua University-Assisted Reproduction Unit.
Objective: To investigate whether menstrual cycle length(MCL) could be a marker of reproductive chance, improving the accuracy of biochemical/sonographical ovarian-reserve-test in women referred to ART.
Methods: Retrospective observational study evaluating the impact of MCL on IVF outcome according to patients' age and AMH serum values.
Patient(s): 455 Normo-ovulatory infertile women undergoing their first fresh non-donor IVF cycle.
Intervention(s): Patients were stratified in different classes according to age(Age_class_1 to 5 respectively for age >40 years, 35–40 years, 26–34 years and <26 years), AMH (AMH_class_1 to 3 respectively for AMH of 0.1–0.4 ng/ml, 0.5–1.1 ng/ml and >1.1 ng/ml) and MCL (MCL_class_1 to 5 respectively for MCL of >31 days, 30–31, 28–29, 26–27, <26).
Main Outcome Measure(s): MII oocytes, oocytes fertilization ratio, pregnancy rate and ovarian sensitivity index(OSI).
Result(s): In patients belonging to Age_class_1, MCL was positively related with the number of MII oocytes at pick-up ($p < 0.001$) and oocyte fertilization ratio ($p < 0.01$). Age_class_2 showed a poor oocyte fertilization ratio only if MCL was <26 days ($p < 0.01$). In patients <35 years, OSI resulted higher only if MCL was>31 days ($p < 0.001$). About Age_class_1 and 2, OSI decreased from MCL_class_2 to MCL_class_5 ($p < 0.05$). Patients with AMH <1.1 ng/ml showed a positive correlation between MCL and number of MII oocytes retrieved ($p < 0.01$), while no difference was found in case of AMH_class_1. Pregnancy rate was inversely correlated with patients' age, independently on MCL ($p < 0.05$).
Conclusions: MCL represent a valid tool to predict IVF outcome; it appears more predictive than AMH in discriminating expected from real poor responders, but female age remains the better parameter in predicting clinical pregnancy.

P178 Female infertility in Tanzania 2015 hormonal causes on the lead

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Context: Infertility is a common gynaecological condition worldwide. For a number of years, pelvic infection and its sequelae were the leading cause of infertility in many African communities. Of recent we observed a different, non-documented trend at our clinic in Dar Es Salaam. We thus decided to map the current pattern of infertility in the country.
Methods: We investigated all patients who attended our clinic from 1st February to August 31st 2015. Following a complete history and physical examination, investigations were requested. These included blood count, VDRL, urinalysis and vaginal swabs for microscopy, gram staining and culture. We requested hysterosalpingogram (HSG) to assess the tubal patency. Hormones assessed included lutenising hormone (lh), follicle stimulating hormone (fsh), prolactin, testesterone, progesterone (mid luteal phase value) and thyroid stimulating hormone (TSH).
Results: During the study period, 3312 patients were seen at the centre 54% of which had infertility. Among patients with infertility, 33.0% had hormonal disturbance as the sole cause while 24.5% had hormonal problems plus another cause. Tubal pathology as an isolated cause appeared in 11.1%. Uterine fibroids with tubal blockage were seen in 10.2% of cases and active infection was noted 2.5% clients. We could not identify a cause in 10.4% clients.
Conclusion: The study shows hormonal related problems to be leading as major causes of sub fertility in Tanzania. Infection and its related complications accounted for only one quarter of all cases of sub fertility. This could be the picture in other developing world. Further studies are required to establish why such changes are occurring.

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P179 Adenomyosis and infertility: possible association and treatment approaches.

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Objective: To estimate the infertility factors in patients with adenomyosis.
Methods: We estimated factors of infertility associated to adenomyosis and treatment outcomes after surgery, dydrogesterone and analogue of gonadotropin releasing-hormone (aGnRH) therapy.
Results: A few possible mechanisms are involved in infertility associated with adenomyosis. Enlarge of thickness uterine junctional zone may cause implantation failure result from inflammatory cascade produced ectopic endometrial gland. Disruption of the balance between hydroxyl radicals and antioxidant enzymes leads to embryo damage. Overexpression of endometrial aromatase and defect in progesterone receptors altered balance between estrogen and progesterone results in the overexpression of estrogen receptors thereby altering uterine receptivity. Conservative surgical technique can be used to restore fertility in women with adenomyosis. The results are elevated by administration of aGnRH (a spontaneous pregnancy rate – 25%, and IVF-pregnancy rate – 50%). Therapy with aGnRH decreases expression of aromatase cytochrome P450 in the eutopic endometrium and reduces inflammatory reactions. Routine use of dydrogesterone is offered in the periconception period, but whether it results to improve the incidence of clinical pregnancy unclear. However reproductive disorders are associated with the risk of obstetric complications and have a negative impact on pregnancy outcome, so dydrogesterone administration may be useful in the context of prophylaxis of pregnancy loss.
Conclusion: Several endometrial abnormalities related to infertility in women with adenomyosis. A better understanding of pathogenesis of infertility in such women may be useful in developing methods to improve pregnancy rate. Currently, only surgery and aGnRH can be considered a proven treatment for infertility associated with adenomyosis.

P180 The evaluation of gene-gene and gene-factor interactions in predicting the risk of primary infertility

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Context: The influence of different genetic and environmental factors are shown in the increased risk of primary infertility in women.
Objective: Identify adverse interactions between gene and factors among women with primary infertility to optimize prevention
Methods and Patients: We performed genetic analysis of FV (G1691A), FII (G20210A), PAI-I (675 5G/4G), MTHFR (C677T, A1298C), MTRR (A66G), MTR1(A2756G), ESR1(A-351G, T-397C) gene polymorphisms. The women filled out questionnaires (life style and family history). The study included 97 women with primary infertility and 78 with secondary infertility.
Main Outcome Measures: Patients with primary infertility had significantly often the following combination of genotypes: MTHFR(677CT)/MTR1 (66AG)/ESR1(-397TC) and FV(1691GA)/PAI-I(675 5G/4G)/ESR1(-351AG). We have found two predictive model of primary infertility risk based on genes interaction. Relatives of patients with primary infertility had significantly more likely cases of heart attacks and strokes (aged 50–75 years) compared with patients with secondary infertility (51.55% and 12.85%, respectively). Patients with primary infertility significantly often smoked aged 18–26 years and used low-calorie diet . The interactions study revealed two significant three-locus model: MTHFR(C677T)/MTR1 (A66G)/smoking and PAI-I(675 5G/4G)/ESR1(-351AG)/low-calorie diet.
Results: The risk of primary infertility was significantly associated with genotypes combinations. Among the relatives of primary infertility patients are dominated cases of heart attacks and strokes. Additional factors were smoking and low-calorie diet. We received predictive models of interactions in primary infertility risk.
Conclusions: The risk of primary infertility is associated with combinations of factors. It is necessary to define the infertility risk in adolescence and to reduce the harmful effects.

P181 Diagnostic accuracy of antenatal ultrasound for multicystic dysplastic kidneys

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Context: In current practice ultrasound is the gold standard method for fetal anomaly screening. When an anomaly is detected antenatally, it allows for a thorough examination with subsequent counseling for the parents. Antenatally, MCDK is one of the commonest renal anomalies detected on prenatal ultrasound. Although the ultrasound appearance of MCDK is characteristic, it may be confused with other renal anomalies, in particular hydronephrosis.
Objectives: The purpose of this study was to review the diagnostic accuracy of obstetric ultrasound at a tertiary Fetal Medicine Unit for the prenatal detection of unilateral and bilateral MCDK.
Methods: This is a retrospective database study in our tertiary fetal medicine unit between 1997 and 2015. The postnatal diagnosis was confirmed by findings documented on postnatal ultrasound reports.
Patients: We included all cases with an antenatal diagnosis of MCDK.
Intervention: We calculated the accuracy for the antenatal ultrasound diagnosis of MCDK by ultrasound.
Main outcomes: The overall number of postnatal confirmed MCDK was 93: of these 91 were diagnosed prenatally, while 2 were thought to be hydronephrosis prenatally and the diagnosis of MCDK was made after birth. In 3 out of 117 patients (2.5%) with an initial ultrasound diagnosis of MCDK the diagnosis was revised to moderate hydronephrosis. 13.9% of MCDK cases had associated abnormalities. Overall, the diagnostic accuracy for the use of antenatal ultrasound to detect postnatal MCDK was 92.3%.
Conclusions: Our data show that antenatal diagnosis of MCDK is accurate when compared against postnatal imaging and can therefore be used to guide antenatal counselling. Only 3.5% of cases the diagnosis was revised prenatally or postnatally; therefore parents can be counselled about a small risk of postnatal revision but that we can confidently predict postnatal outcome.

P182 Treating infertility – examination of 60 cases of pregnancy after infertility in Kosovo

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Recurrent abortion and conception after recurrent abortion requires special treatment. This work explores the auto-immune factor as one

of the causes of early abortion and surmises on the treatment with heparin during successful conception. From 2012–2014, 60 cases of conception have been analysed, which were treated in the Sterility Ward of Obstetrics and Gynaecology Centre in Prishtina. Patients were analysed, diagnosed and treated with methods we posses, namely endometrial biopsy, HSG, surgical intervention, laparatomy or laparascopy and treatment with medicine such as heparin. 38 of the 60 cases, namely 63% of the cases had experienced one abortion. 22 of the 60 cases, namely 37% of the overall examined cases, had experienced two abortions. While, 7 out of the 60 cases, namely 32%, were cases of habitual abortion. In the examined cases, pregnancies developed well with no malformations. However, out of 60 cases, (i) three births were premature: 1 child was born alive (weight 1600 grams) and 2 intra uterus dead fetuses (1000 grams); (ii) five other cases were missed abortion (from week 7 – 16); (iii) thirty-five of them were born spontaneously; and (iv) seventeen were delivered with caesarean section. The cohort of 60 cases were all treated with heparin and resulted in favourable outcomes in the treated patients. It seems reasonable to believe that the treatment assisted in lowering the possibility of spontaneous abortion, stillbirths, neonatal deaths, as well as congenital abnormalities (with little exceptions). It seems practicable, examining the specified cohort, to conclude on the success of treatment with heparin and the importance of timely treatment of conception after abortion. It would be of interest to discover difference between two groups, one cohort using heparin and the other not. This would give way to understand better the possibilities and risks.

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P183 Ovarian Reserve Test: an impartial means to resolve the mismatch between chronological and biological age in the assessment of female reproductive chances

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Context: Padua University-Assisted Reproduction Unit.
Objective:To detect the best predictive markers of ovarian reserve(OR), ovarian response, chances to obtain embryos and pregnancy after IVF cycles in elderly women.
Methods:Retrospective observational study on a cohort of infertile women undergoing IVF. We studied the accuracy of some hormonal and ultrasound markers before and during controlled ovarian stimulation in order to predict IVF outcome.
Patient(s): 105 Elderly(aged between 40–50 years) women scheduled for their first fresh non-donor IVF/ICSI cycles.
Intervention(s): Ultrasound measurement of AFC and endometrial thickness. Serum sampling of AMH, FSH, LH, E2.
Main Outcome Measure(s): Embryos number, pregnancy rate, ongoing pregnancy rate.
Result(s): Age, b(basal)FSH, bLH and bE2 resulted the best predictors of total dose of gonadotrophins to administer. AMH, AFC and maximum level of E2 before the pick-up were the best markers to predict number of oocytes retrieved (and maturation grade), number of embryo obtained and pregnancy occurrence. Ongoing pregnancy was found only with minimum value of endometrial thickness at pickup of 10 mm, of E2 before the pick-up $\geq$5.5 nmol/L, bAMH $\geq$0.6 mg/L, and AFC $\geq$4, bFSH values $<$9.9 IU/L, and age $\leq$46 years.
Conclusions: The combination of specific laboratory tests and ultrasound evaluation represent a valid approach to estimate the concordance between female chronological and biological age.

P184 The experiences of Iranian infertile couples

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Context: Research on infertility has indicated the significance of socio-cultural context in the formation of infertility experience.
Objective: This study aimed to explain how Iranian infertile couples confronting infertility.
Methods and Patient(s): This study adopted the grounded theory approach (Straus & Corbin 1998) to explore the experiences of infertile individuals presenting at Royan Institute, in Iran, from October 2013 to September 2014. Couples with infertility experience of at least two years were recruited using purposive sampling followed by theoretical sampling. A total of 41 interviews were conducted with 36 people. Data were collected through in-depth unstructured interviews and field notes.
Intervention: None.
Result(s): A sense of ''insecurity in personal and family identity'' shaped in the context of ''facing the cultural-economic dilemma'' was identified as the main concern of infertile couples. The couples deal with this concern through a series of strategies including gradual acceptance of infertility, seeking information and consultation, pursuing treatment, focus on saving the marriage, self-control and resilience, and fighting the inner turmoil. All these approaches suggested the concept of ''protecting personal and family identity'' as the core concept. These strategies could thus provide the couples with relative peace of mind. However, inhibiting factors such as lack of support and hard and stressful treatment caused constant threat to identity and sometimes forced the couples to abandon treatment.
Conclusions: In the economic and cultural context of Iran, where fertility is a gender indicator with family and social roles, facing the diagnosis of infertility and the process ahead leads to multifaceted insecurity. These findings clarify the strategic issues requiring interventions to improve infertility care services.

P185 L-Arginine aspartate improves endometrial thickness PCOS patients during cycle of clomiphene citrate treatment

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Aim: The primary objective of the investigation will L-arginine influence the endometrial thickness of PCOS patients in the clomiphene-stimulated cycle? The research study group was comprised of 36 anovulatory PCOS patients, who had at least three failures, from the previous clomiphene alone treated cycles. All the patients had insufficient endometrial thickness of less than 7 mm and responded well to the clomiphene. Clomiphene 100 mg was prescribed from 5 to 9 menstrual cycle days. Every patient had taken transdermal estradiol 2 mg/day from 10 to 15 days of stimulated cycle and dydrogesteronum 20mg/day (Duphaston 10 mg twice a day), trigger of ovulation was ChGH 5000IU . Twenty patients were taking L-arginine syrup per os 5g a day (Tivortin-aspartate 5ml fifth times) from 5 to 25 cycles' day as a NO-donator in addition to hormonal therapy.
Methods: Ultrasound monitoring follicles growing up and endometrial thickness was done from 10 till 19 cycle day. Endpoints were ovulation, endometrial thickness at the day of ChGH injection and in the middle of luteal phase, pregnancy rate in the treated cycles.

Results: The quantity and size preovulatory follicles were equal in both groups. Transdermal estradiol and dydrogesteronum had improved endometrial thickness in 11 from 16 patients (68.7%) hormonal therapy only group. Average thickness of endometrium in this group was 8.2±1.3mm in the ChGH injection day and 8.7±1.1mm in the +5 day. Endometrial thickness was improved in 18 from 20 patients (90.0%) in L-arginine treatments' group. Average thickness of endometrium was 9.9±1.2mm and 12.3±1.3mm respectively. 8 women from hormone therapy alone group capable conceive to and 15 from L-arginine group.
Conclusion: L-Arginine addition to clomiphene and hormonal treatment the PCOS patients improved endometrial thickness and strong likelihood would increase pregnancy rate.

P186 Hypoasthenozoospermia correlates with increased DNA sperm fragmentation

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UNAM

Objective: To evaluate the seminal parameters of infertile men evaluated at a fertility clinic in relation with sperm DNA integrity.
Design: A prospective cohort fashion, at Hospital Angeles del Pedregal reproduction center
Materials and methods: A prospective longitudinal survey comprised 250 semen samples of patients at ART reproduction infertility programs during 2011–2014. Conventional semen parameters, (WHO 2010 strict criteria) (Katie S. Murray, 2012), were measured. The DNA sperm integrity was evaluated with the sperm chromatin dispersion test (SCD) using the cutoff points of 30%. Spearman tests were used to detect significant differences.
Results: We found that in 250 samples the mean age was 38 (±6 years), the average; SCD value 29.1 (±13.6%), volume 2.6 (±1.5ml), pH 7.9 (±0.5), motility 45 (±17.2%), viability 74.1(±69.1%), liquefaction was 42 (±21.3 min), morphology 16.2 (±10.2%), concentration 102.8 (±77.6 mlls/ml). In neat semen, a positive correlation was found between the DNA sperm integrity and motility (Spearman $r = -0.3$ $p = 0.001$, 95% CI), age (Spearman $r = 0.219$ $p = 0.001$, 95% CI). Interestingly semen volume correlated with motility (Spearman $r = 0.2$ $p = 0.001$, 95% CI).
Conclusions: The DNA sperm integrity value with SCD correlates with sperm motility because it supports a functional sperm, but still stands out the correlation between volume and motility; it could be due to the testis micro-environment expressed in the seminal plasma. The age is also a factor that affects our population DNA sperm integrity could be related to aging testosterone decrease and dysfunctional tubular sperm formation.

P187 The acrosome expression of metalloproteinase 14, after sperm preparation increase potential penetration

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Background: Acrosome expression of MMP-14 (Metalloproteinase 14) increase after sperm preparation.
Objectives: Demonstrate the increase of acrosome expression MMP-14 after sperm preparation.
Methods: We study five patients with infertility and determine FSH, LH and testosterone serum concentrations. Semen sample was obtained by masturbation, at day 13 after the couple oocyte retrieval, the same sample use for fertilization. MMP-14 evaluated by immunohistochemistry and cytometer.
Patient(s): We study five semen samples, with no preparation and with sperm preparation, of infertility men.
Intervention(s): Comparative Observational; prospective study
Main Outcome Measure(s): Staining intensity of each antibody in sperm cells. Small sample because was a pilot cohort study.
Result(s): Percentage of MMP-14 at sperm acrosome expressing was positive in two patients 40%. Improving 10% after sperm preparation, confirm by cytometry. We confirm a sperm penetration in samples with positive MMP-14 acrosome expression.
Conclusions: The increase expression of MMP14 at sperm acrosome after sperm preparation, might be improve the penetration of the sperm to oocyte because the MMP-14 give the sperm a superior capacity to degrade apolipoproteins for an accurate oocyte penetration.

P188 Sperm DNA fragmentation and mitochondrial membrane potential combined are better for predicting natural conception than standard sperm parameters

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Objective: To evaluate whether DNA fragmentation and/or mitochondrial membrane potential (MMP) predict natural conception better than standard sperm parameters.
Method(s): Prospective cross-sectional study. University medical center.
Patient(s): Eighty-five infertile and fifty-one fertile men.
Intervention(s): Sperm DNA fragmentation, MMP and standard semen parameters; 6–12 month observation period.
Main Outcome Measure(s): Comparison between the results of DNA fragmentation, MMP and standard sperm parameters alone or combined, and achievement of natural conception.
Result(s): Twenty-six of the 85 (31%) men from infertile couples conceived naturally. The median values of DNA fragmentation and MMP in the men who conceived within the observation period were similar to those in the fertile controls. Optimal threshold values of DNA fragmentation and MMP were 25% as determined by ROC analysis (AUC 0.70 [95% CI: 0.58–0.82]) and 62.5% (AUC 0.68 [95% CI: 0.56–0.80]), respectively. The men in the infertile group with values of DNA fragmentation $\leq$25% and with MMP values >62.5% had significantly higher odds for conception (OR 5.22 [95% CI: 1.82–14.93] and OR 4.67 [95% CI: 1.74–12.5], respectively). Normal semen analysis alone had no predictive value for natural conception (OR 1.84 [95% CI: 0.67–5.07]). Both sperm function tests combined had significant odds for natural conception (OR 8.24 [95% CI: 2.91–23.33]) with probability of 0.607 (60.7%) for both normal values, and 0.158 (15.8%) for abnormal values.
Conclusion(s): Sperm DNA fragmentation and MMP combined may be superior to standard semen parameters in the prediction of natural conception.

P189 Human sperm express claudin-1 as a biomarker

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Objectives: Demonstrate the presence of claudin-1 at human spermatozoa.

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Methods: We studied five patients with infertility and determine FSH, LH and testosterone serum concentrations; semen sample was obtained by masturbation, at day 13 after the couple oocyte retrieval, the sample was used for fertilization. Claudin-1 expression was evaluated by immunohistochemistry.
Patient(s): We study five semen samples of men with infertility.
Intervention(s): Observational; prospective study
Main Outcome Measure(s): Staining intensity of each antibody in sperm cells. Small sample because was a pilot cohort study.
Result(s): Percentage of claudin-1 at human spermatozoa cell expressing was positive in two patients 40%. The expression of the claudin-1 was located at 80% of the sample in the middle piece, 10% was fully expression at sperm cell and 10% has not expression.
Conclusions: We demonstrated the expression of claudin-1 in human sperm confirmed by immunohistochemistry; predominantly located at middle piece of spermatozoa, this could demonstrate that the tight junction might participate at the spermatogenesis as described at Sertoli Cells. This may be a marker for functional interaction between sperm membrane and Sertoli Cell involving biochemical mechanism, possibly regulated through ERK pathways. Claudin-1 expression may be the key event for cell-cell interaction afterwards for functional sperm.

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P190 A comparative study of dydrogesterone and micronized progesterone for luteal phase support during in vitro fertilization (IVF) cycles

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Objective: The aim of the present study was to compare the efficacy, tolerability and patients' satisfaction after the use of oral dydrogesterone with vaginal micronized progesterone for luteal phase support among infertile women undergoing *in vitro* fertilization.
Methods: Randomized clinical trial.
Patient(s): A total of 210 women (aged 20–40 years old) with a history of infertility, who underwent controlled ovarian stimulation (COS) for fresh intra cytoplasmic sperm injection- embryo transfer (ICSI-ET) cycles, were included in the study. *Intervention(s)*: Consequently, they were randomized to receive luteal phase support with dydrogesterone 20mg twice daily ($n = 96$) or micronized progesterone 400mg twice daily at the day of oocyte retrieval ($n = 114$).
Main Outcome Measure(s): Clinical pregnancy rate.
Result(s): The clinical success rate (31% vs. 33%; $p = 0.888$), miscarriage rate (5.0% vs. 3.0%; $P = 0.721$), ongoing pregnancy rate (30.0% vs. 30.0%; $p = 1.000$), implantation (22.0% vs. 24.0%; $P = 0.254$) and multiple pregnancy rate (5.30% vs. 7.20%; $p = 0.394$) were comparable among the two groups. Serum progesterone levels were significantly lower among the patients receiving dydrogesterone than the control group (13.62 ± 13.83 ng/mL vs. 20.66 ± 18.09 ng/mL; $p = 0.001$). However, there was no statistically significant difference regarding the patients' satisfaction ($p = 0.825$) and tolerability (0.790) between the two groups.
Conclusions: Our results showed that oral dydrogesterone (40mg per day) is as effective as vaginal micronized progesterone considering its clinical outcomes and patients' satisfaction and tolerability, for luteal phase support among women undergoing *in vitro* fertilization.

P191 Recurrent IVF/ICSI-ET failure and its relationship with thrombophilia

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Context: The role of the hereditary thrombophilia in recurrent implantation failure is not clear. There is a conflicting data in the literature.
Objectives: This study investigates the relationship between hereditary thrombophilia and recurrent *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI)-embryo transfer (ET) implantation failure.
Patient(s): The study group included 100 consecutive women with at least three previously failed IVF/ICSI-ET cycles (Group A). Group B included 50 women with a live birth in her first IVF/ICSI-ET cycle. Group C consisted of 50 women who conceived spontaneously with at least one uneventful pregnancy and delivery.
Intervention(s): Peripheral blood was collected in Na2 EDTA vacuum tubes from the patients. The genotype of the three mutations – FVL mutation, prothrombin mutation, and MTHFR C677T and A1298C mutations – was detected by genomic DNA isolation using the spin colon DNA isolation method.
Main outcome(s): All women were tested for the presence of factor V Leiden (FVL), prothrombin gene, and methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C mutations.
Results: A similar prevalence of FVL, prothrombin, and MTHFR mutations was found in all groups. At least one inherited thrombophilic factor was detected in 95% of women with repeated IVF/ICSI failure (group A) and in 84% and 94% of women in groups B and C, respectively. Combined thrombophilia (two or more thrombophilic factors) was 40%, 26%, and 30% for groups A, B, and C, respectively. No statistical association was found between repeated IVF/ICSI failure and these thrombophilic factors.
Conclusions: Our results suggest that FVL, MTHFR, and prothrombin gene mutation do not have a significant role in IVF/ICSI-ET implantation failure.

P192 For the infertile couple: ethical practice in donor conception and 5 things you need to know

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Donor Sibling Registry

The Donor Sibling Registry (DSR) is a US based, global registry where those connected via gamete donation can make mutual consent contact. It allows donors, recipients and offspring to connect, and to pass on important medical information. Since it's inception in 2000, the DSR has helped to connect more than 12 250 of its 46 000 members with their first-degree genetic relatives.
1. Donors and recipients are not properly educated, counseled, or informed beforehand.
2. There is no comprehensive medical and genetic testing conducted by clinics and sperm banks. In the US the FDA only mandates for STD testing and for a handful of other diseases. Testing for STD's does nothing to prevent transmission of genetic illness. Proper genetic testing of all donors is critical.
3. There is little to no regulation or oversight of the US reproductive medicine industry, which ships sperm to over 40 countries around the world. This industry is not required to maintain records regarding genetic disease transmitted to donor offspring. Information about inherited physiological and psychological predispositions are a significant element in obtaining appropriate medical care, particularly in preventative health care including screenings, diet, and other

lifestyle choices. Examples: genetic predisposition of heart disease, alcoholism and bowel cancer.
4. No accurate record keeping exists about how many offspring are conceived for any one donor. Records, if any are kept, are most often incomplete regarding the number of offspring from each donor. Therefore, there are many many large cohorts of half-siblings, some as large as 200.
5. Almost 3/4 of surveyed donor offspring advise that prospective parents do not use anonymous donors. Many countries have banned anonymous donation and we all need to ask the question ''what is in the best interests of the child to be born?''

P193 Liver and kidney function of patients undergoing to a controlled ovarian hyperstimulation (COH) during an in vitro fertilization (IVF) cycle

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Context: The main issue of *in vitro* fertilization (IVF) cycles is represented by ovarian hyperstimulation syndrome (OHSS) characterized by ovarian enlargement and acute fluid passage into the extravascular space. The reduction of intravascular volume takes to renal and liver injury, which could hesitate to organ failure and, eventually, to death of the patient.
Objective: To evaluate liver and kidney function tests in normal patients without OHSS.
Methods: All patients received a long stimulation protocol with GnRH analogues by daily administration since the twenty-first day of the previous ovarian cycle, followed by controlled ovarian hyperstimulation (COH) with recombinant FSH. The daily dose of exogenous gonadotropins for every single patient was modified related to her follicular growth. The oocytes were retrieved during the oocyte pick up and were fertilized by standard procedures of ICSI.
Patient(s): The study sample was represented by 422 women aged between 19 and 44 years (mean age: 32.88), with a mean BMI of 24.68 Kg/m2.
Intervention(s): The blood samples to evaluate liver and kidney function test were taken at the 7th day of ovarian stimulation.
Main Outcome Measure(s): Liver and kidney function tests
Result(s): The oocytes retrieved were 9± 5.36. The mean values of Blood Urea Nitrogen were 29 ± 6.78 mg/dl; Creatinine 1± 0.45 mg/dl; Uric Acid 4 ± 1.95 mg/dl; Total Protein 7 ± 3.93 mg/dl; Aspartate Aminotrasferase 18 ± 6.29 mU/ml; Alanine Aminotrasferase 19 ± 10.41 mU/ml; Phosphatase Alkaline 81 ± 45.25 mU/ml; Total Bilirubin 1 ± 0.35 mg/dL. All the results were considered as in a normal range following the Medical Council of Canada.
Conclusion(s): The preliminary data suggest that, unlike patients with OHSS, the controlled ovarian hyperstimulation does not determine alterations in kidney and liver function.

P194 A randomised study comparing two regimen of ovarian stimulation using pergoveris and cetrorelix

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Context: The GnRH antagonist, Cetrorelix, is used for controlled ovarian stimulation for IVF/ICSI and the optimum regimen is not known.
Objective: To investigate treatment using Pergoveris (150IU rFSH/75IU rLH) with Cetrorelix (CT) administration from day 2 versus day 7 of menses results in more top quality embryos (TQE).
Methods: Randomised controlled pilot study.
Patients: 80 Women undergoing IVF/ICSI <38 years; BMI 18–28 kg/m2; <3 previous treatment cycles and AMH >6pmol/l.
Interventions: Patients were randomised to receive CT 0.25mg on day 2 (early administration, EA) or day 7 of menses (late administration, LA). Pergoveris 150IU was started on cycle day 2. Ovulation was triggered with Ovitrelle when 3 follicles were >17mm.
Main Outcome Measures: No. of TQE.
Results: Both groups had similar baseline characteristics. The mean (SD) of AMH was significantly higher in the EA vs. LA group (27.1[11.5] vs. 21.5 [9.7]pmol/l; $p = 0.02$). The mean (SD) of TQE was 4.2 (2.3) in the EA vs. 3.5 (2.1) in the LA group [$p = 0.2$]. There was no significant difference in the LH, E2 or P4 on the day of Ovitrelle administration between both groups. In the EA group on cycle day 7, 21/40 women had LH <1U/L. Nine women (23%) had premature LH surge (LH>10U/l) in the LA with none in the EA group ($p = 0.002$). The on-going pregnancy rate/cycle was 45% (18/33; 55% per ET) in the EA and 42.5% (17/39; 43.5% per ET) in the LA group respectively. Seven women in EA group (1 with E2 >18000pmol/l, 2 failed fertilisations, 4 elective embryo freezing for OHSS) and 1 in LA group did not have ET.
Conclusions: Pergoveris in combination with both regimens of CT administration is safe, convenient with a high pregnancy rate. No significant difference in TQE or ongoing pregnancy rates were found in both groups. Further studies are required to confirm these findings.
This study was supported by Merck.

P195 Manufacturing of recombinant human follicle-stimulating hormone Ovaleap® (XM17): comparability to Gonal-f®, formulation, and stability

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Context: Ovaleap® (XM17), a recombinant human follicle-stimulating hormone for assisted reproductive technology procedures, was approved in 2013 by the European Medicines Agency as a biosimilar to follitropin alfa (Gonal-f®). Information on the rigorous manufacturing procedures for biosimilars is often inaccessible/unavailable.
Objectives: To report on validation procedures for the Ovaleap® manufacturing process, compare the characteristics of Ovaleap® versus Gonal-f®, and describe the stability of Ovaleap®.
Methods: Formal validation of the manufacturing process, consisting of several consecutive fermentation and purification runs, was performed at full commercial scale. Characterization and comparison to Gonal-f® involved numerous orthogonal techniques, such as mass spectroscopy, UV spectroscopy, and liquid chromatography. Long-term and thermal stability of the drug was assessed.
Results: In the fermentation process, product intermediate of comparable quality and within all specifications was produced from run to run as shown by protein content and analyses of glycosylation patterns. In the purification process, step recoveries and yields showed consistent and reproducible manufacturing of bulk product. No substantive differences were found between Ovaleap® and Gonal-f® with respect to molecular mass, primary/secondary structure, isoform distribution, potency, and product-related impurities. The Ovaleap® formulation demonstrated stability at a storage temperature of 5°C ± 3°C for up to 24 months, plus 1 to 3 month temperature excursions of 25°C.
Conclusions: The manufacturing process for Ovaleap® is robust, yielding a product of consistently high quality and stability. Results from this analysis and previous trials demonstrating the biologic and

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therapeutic equivalence of Ovaleap® and Gonal-f® support Ovaleap® as a useful therapeutic option.

P196 Immunogenicity assessment of Ovaleap® (XM17) recombinant human follicle-stimulating hormone in infertile women undergoing assisted reproductive technology (ART)

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Context: Ovaleap® (XM17) is a recombinant human follicle-stimulating hormone (FSH) approved in 2013 by the European Medicines Agency as a biosimilar to follitropin alfa (Gonal-f®) for use in controlled ovarian stimulation. Biological drugs can potentially elicit an anti-drug antibody (ADA) response, which may lead to reduced efficacy and/or adverse reactions.
Objective: To examine ADA response of Ovaleap and assess its impact on efficacy and safety in women using ART.
Methods: Serum samples were collected from patients enrolled in the main study phase of a phase 3 clinical study comparing Ovaleap to Gonal-f and in the follow-up study phase for safety and immunogenicity measurement of extended Ovaleap administration. Validated assays for antibody screening, confirmation, titer, and neutralizing antibody characterization were implemented for the immunogenicity assessment.
Patients: Infertile, ovulatory women aged 18–37 using ART.
Interventions: Main study phase: 150 IU/day of Ovaleap or Gonal-f on Days 1–5, followed by dose adaptation phase; follow-up study phase: Ovaleap dose at investigator's discretion (max 450 IU/day).
Results: Over the main and follow-up study phases, 22 (7.4%) of 297 Ovaleap- and/or Gonal-f-treated patients evaluated for immunogenicity showed antibody development mainly against Neu5Gc, a common finding in the general population. No samples demonstrated neutralizing activity. Numbers of oocytes retrieved (primary study endpoint) and incidence rates of biochemical and clinical pregnancy were similar in patients with and without antibody development, irrespective of treatment. No patient had a hypersensitivity reaction.
Conclusion: In this study of infertile women using ART, the risk of immune response with Ovaleap was negligible. The immunogenicity of Ovaleap and Gonal-f can be considered similar.

P197 Medical experiences of women fertilized with egg donation

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Context: There has been a dramatic increase over the past few decades in the use of modern fertility technologies and the demand by infertile couples for using these techniques have increased as well. No studies have yet been conducted to understand the medical experiences of women fertilized with egg donation technique.
Objective: To explore and explain the medical experiences of women fertilized with egg donation.
Materials/Patients and Methods: Data were analyzed simultaneously as they were being collected and according to the conventional content analysis method. The study began in July 2013 and continued until September 2014. Fourteen unstructured, in-depth interviews were conducted with 12 infertile women who had been fertilized or had given birth to children through egg donation. Royan institute (One of Tehran's referral centers for infertility), was used as the study setting. All participants submitted their written consent prior to beginning the study.
Intervention: None.
Result(s): Analysis of the findings revealed ''difficult and stressful treatment'' as the final category with 5 subcategories, including: 1. religious barriers, 2. treatment derivatives, 3. treatment failure (including the following subcategories: physical complications, fatigue and despair, and the experience of frequent failures), 4. dissatisfaction with the services provided, 5. confusions in treatment.
Conclusions: Exposure to various assisted reproductive technologies, including egg donation, is a stressful process, and providing emotional support to patients is one of the most essential care services they require from treatment centers. The results of the present study can assist in planning future strategies for meeting the specific needs of these distinguished patients.

Keywords

Assisted reproductive techniques, infertility, nursing care, oocyte donation

P198 Demographic and clinical silhouette of the poor responder: is the Bologna criteria relevant to the Indian scenario?

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Context: The ESHRE brought forth the Bologna Criteria in 2011, in an endeavor to provide a standard definition for the poor responder.
Objective: To study the demographic & clinical profile of the Indian poor responder. To determine if the recent Bologna criteria is relevant to Indian scenario.
Methods: Retrospective study, from September 2011 to September 2015, conducted at department of Obstetrics and Gynecology, AIIMS New Delhi. Poor response was defined as retrieval of $\leq$ 3 oocytes. We considered this parameter as best defining the ovarian response and calculated our regional cut off values of age, AFC and AMH in sync with it, in an attempt to validate the Bologna criteria.
Patients: A total of 1389 women underwent IVF over 4 years. 121 women had a poor response and were included in Group A. 150 women who had retrieval of $>$ 3 oocytes were included in Group B. Demographic and clinical details of the ART cycles were compared between the two groups.
Interventions: The 1389 women underwent an ART cycle each
Main Outcome Measures: To calculate regional Indian cut off values of Age, AMH and AFC that would predict a poor response (retrieval of $\leq$3 oocytes)
Results: Incidence of poor response at our center was 8.7%. Mean age, FSH levels, starting dose and total dose of gonadotrophins were significantly higher in Group A. AFC, AMH levels, E2 levels on the day of HCG trigger and pregnancy rates were significantly lesser in Group A. Our study determined cut off values, much disparate from those mentioned in the Bologna criteria [Age – 33 years (sensitivity 65.3%, specificity 61.3%, AUC 0.64), AFC – 10 (sensitivity 64%, specificity 64.3%, AUC 0.77) and AMH 2.8 ng/ml (sensitivity 64%, specificity 64.4%, AUC 0.70)] to predict poor response in the Indian women undergoing ART.
Conclusion: The Bologna criteria does not seem fully relevant to the Indian scenario.

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P199 Intrauterine insemination: which protocol and which combination of gonadotropin should be considered as better for each infertility condition? A single center large retrospective analysis

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Context: Padua University-Assisted Reproduction Unit.
Objective: To determine the best stimulation protocol for intrauterine insemination(IUI) according to different causes of infertility.
Methods: We performed a retrospective analysis of 419 IUI cycles with two different protocols of stimulation: recombinant-FSH(r-FSH) versus urinary-FSH(u-FSH). We also compared cycles preceded or not by pre-treatment with combined oral contraceptive(COC).
Patient(s): 419 IUI cycle grouped according to the diagnosis of infertility: GroupA(104 cycles: anovulation), GroupB (83 cycles: mild male factor), GroupC (29 cycles: stage I-II endometriosis), GroupD (203 cycles: unexplained infertility).
Intervention(s): We divided cycles according to stimulation protocol: ProtA (fixed scheme with u-FSH 150 IU/day) and ProtB (fixed scheme with r-FSH IU/day). Additionally, we distinguished cycles in two periods according to pre-treatment with COC: Period1(225 cycles, no pre-treatment with COC) and Period2 (194 cycles preceded by 21 days of COC).
Main Outcome Measure(s): Clinical pregnancy rate (CPR)
Result(s): In GroupA we found a 10% of CPR after ProtA versus 20.4% after ProtB [$p < 0.01$]; in GroupB we found a 4.3% of CPR after ProtA versus 10.8% after ProtB[$p < 0.01$]; in GroupC we found a 6.7% of CPR after ProtA versus 14.3% after ProtB[$p < 0.01$]; in GroupD we found a 7.8% of CPR after ProtA versus 14% after ProtB[$p < 0.01$]. Regarding the pre-treatment period: in GroupA we found a 13% of CPR in Period1 versus 20.6% in Period2[$p < 0.01$]; in GroupC we found a CPR of 7.1% in Period1 versus 13.3% in Period2[$p < 0.01$]. On the contrary, no differences were found in GroupB and in GroupD.
Conclusions: Stimulation with r-FSH in IUI cycles seems to increase CPR in all case of infertility, while pre-treatment with COC may be useful in patient with anovulation and endometriosis.

P200 Melatonin action on luteal – granulosa cells in women with marital infertility undergoing in vitro fertilization

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Objective: This study aims to evaluate melatonin action pathways in granulosa cells in the ovaries of women with infertility. To achieve our aim, we will use molecular biology, involving diverse signaling pathways, such as angiogenesis.
Methods: We included 60 patients, aged between 20 and 35 years, treated at Human Reproduction Division of the Federal University of São Paulo, undergoing *in vitro* fertilization treatment. After performing all preparatory procedures, the granulosa-luteal cells were removed and prepared to the cell culture. The cells were divided into four groups: a) vehicle; b) 0.1 uM Melatonin; c) 1 uM Melatonin; d) 10 uM melatonin. After a period of 10 days, the cells were trypsinized for the extraction of total RNA and subsequent gene expression analysis by qRT-PCR of angiogenesis signaling pathway.
Results: Our data assessed 96 genes, which are related to angiogenesis pathway. The results showed transcriptional expression of important genes involved in this pathway are overexpression after treatment with melatonin. The main overexpression genes were gene fibroblast growth factor 1 (FGF1); interleukin 1 beta (IL1B); receptor tyrosine kinase (VEGFR-2); regulatory genes of folliculogenesis (TGFB1). They act in the dynamics of follicular growth. Since the genes factor hypoxia inductor 1-alpha (HIF-1a), fibroblast growth factor 2 (FGF2), insulinóide growth factor 1 (IGF-1) and vascular endothelial growth factor (VEGFA), treatment with doses higher melatonin decreased the expression.
Conclusion: Our data suggest that melatonin may negatively modulate the ovarian angiogenesis in granulosa cells in patients with infertility.

P201 Intrauterine saline infusion as endometrial injury during IVF cycles improves pregnancy outcome in patients with recurrent implantation failure (RIF)?

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Objective: The study aimed to investigate the effects of intrauterine saline infusion as endometrial injury (EI) performing at days 3–5 of ovarian stimulation during fresh *in vitro* fertilization-embryo transfer (IVF-ET) cycle on reproductive outcomes among patients with recurrent implantation failure (RIF).
Methods: Randomized clinical trial.
Patient(s): Patients undergoing Assisted Reproductive Technology (ART) were randomly divided to undergo either local endometrial injury by intrauterine saline infusion during day 3–5 of the ongoing controlled ovarian stimulation (COS) cycle or IVF protocol continued without intervention.
Main Outcome Measure(s): Clinical pregnancy rate.
Result(s): Patients who received intra uterine saline infusion had significantly lower clinical pregnancy (5.3% vs. 39.1% $p < 0.05$) and implantation (4.7% vs. 41.6% $p < 0.05$) and multiple pregnancy rates (3.1% vs. 13% $p < 0.05$) compared to controls. However, there was no significant difference in miscarriage rates between the two groups (9.4% vs. 8.7% $p = 0.4$).
Conclusions: When intrauterine saline infusion as endometrial injury is performed during the ongoing *in vitro* fertilization (IVF) cycles, instead of injuries during the preceding IVF cycles, this will have negative effects on clinical outcomes in patients with recurrent implantation failure.

P202 Use of complementary and alternative medical therapies by women who assisted reproductive technology

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Objective: This research was carried out to determine the use of complementary and alternative medicine therapies of women undergoing assisted reproductive treatments.

Materials and Methods: This descriptive and cross-sectional study was carried out with 127 women, who applied to Reproductive Endocrinology and Infertility Department in İstanbul for assisted reproductive treatment between June and December 2015. Research data were collected using the Personal Description Form and Complementary and Alternative Medicine Scale.
Results: The mean age of participants was 30.57±5.08, most of them (74%) have primary education, more than half of them (66.1%) are housewife, and 3.44 ± 3.50 years are undergoing treatment for infertility. Complementary and alternative medicine (CAM) was used by 78% of the women. Accordingly, the most preferred approaches were praying (100%), laughing (98%), visiting a neighbour (91.9%), and perform namaz (79.8%). Reasons of using CAM are thinking harmless and natural way (89.9%), feeling stronger (71.7%), trying all options (47.5%). They also stated that onion, parsley, fig, lady's mantle, and carrot mosly preferred. They learned CAM from television (72.7%), neighbour (68.7%), relatives (58.6%), internet (41.4%), friends (36.4%), and health professionals (13.1%).
Conclusions: CAM are often preferred by women undergoing assisted reproductive treatments. Health professionals must question the use of CAM when getting stories from individuals and provide information on proven practices. It is important for treatment success.

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P203 Leukocyte immunotherapy as effective method of treatment and prevention of reproductive failure

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Objective: Introduction of method of leukocyte immunotherapy (LIT) with allogenic lymphocytes as prevention of recurrent miscarriage (RM) began with works of A.Beer. From the moment of the first use of this method discussion concerning efficiency of its management doesn't stop. A large number of works are carried out to answer a question ''can LIT increase the frequency of pregnancy approach and childbirth in women with RM?''.
Methods: This is retrospective study of 640 cases with reproductive failure for the period of 4 years (2011–2014).
Intervention: In this couples integrated investigation (consultation of the immunologist, HLA-genotyping) and LIT was done.
Patients: In 42% of cases it was the history of primary infertility; in 15% of cases – secondary infertility; 29% of couples had 1 case of RM; 14% of couples had 2 or more cases of RM. In all groups the vast majority of patients completed a course of immunization with lymphocytes of the husband (89.2%, 92%, 75%, in 91%). Allergic reactions to proteinaceous drugs, the antifosfolipid syndrome, autoimmune diseases in the anamnesis was considered as contraindications to LIT.
Results: Frequency of pregnancy approach was the highest in group 4 – 83.6%, in group 3 – 75%, in group 1 – 54.1% and in group 2 – 52%. In the analysis of frequency of pregnancy approach and an assessment of the phenomena of threat of interruption of pregnancy at women in various groups accurate communication with number of the carried-out LIT procedures was revealed. After 1 LIT procedure pregnancy came in 18.1% of cases; after 2 – in 47.7% of cases; 3 procedures – 86%, 4 and 5 procedures – 85% respectively.
Conclusion: LIT is an effective method of treatment and prevention of RM,in women with one abortion, infertility primary and secondary.

P204 L'amh come predittore di riserva ovarica ed il ruolo dell'autoimmunita' tiroidea nei protocolli di procreazione medicalmente assistita

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Introduzione: La predizione dell'outcome della stimolazione ovarica controllata (controlled ovarian hyper-stimulation, COH) richiede l'individuazione di marcatori di riserva ovarica, tra cui l'ormone anti-mulleriano (AMH) è oggi riconosciuto come il più affidabile. E' altresì riconosciuto che l'autoimmunità tiroidea (autoimmune thyroid disease, ATD) si può associare ad una riduzione della fertilità, e ad un minor tasso di successo della COH. Scopo Valutare la relazione tra ATD ed AMH e la loro rispettiva influenza sulla riuscita della COH.
Materiali e metodi: 288 Donne subfertili di età < 40 anni, afferenti ad un unico centro per la di Medicina della Riproduzione, di cui 55 affette da ATD (ATD +) e 233 non-affette (ATD -). Sono stati misurati i livelli sierici basali di AMH, FSH, LH, estradiolo (E2), e TSH, e successivamente il valore di E2 il giorno del pick-up ovocitario, calcolando il rapporto tra questo e la dose totale di FSH-ricombinante (r-FSH) somministrata (rapporto E2/r-FSH).
Risultati: I livelli di AMH erano significativamente inferiori nelle donne ATD+ rispetto a quelle ATD-, correlati inversamente alla dose totale di r-FSH somministrata, e direttamente al rapporto E2/r-FSH ed al numero di ovociti MII recuperati, sia nella donne ATD- che ATD+. Nella fascia bassa di AMH (valori inferiori alla mediana), il successo della procedura era poco probabile, indipendentemente dalla coesistenza di ATD. Nella fascia alta di AMH, le donne ATD+ presentavano invece un rapporto E2/r-FSH meno favorevole, una dose totale di r-FSH più elevata, e un minor numero di ovociti MII recuperati rispetto alle donne ATD-.
Conclusioni: Indipendentemente dalla presenza di ATD, donne con bassi livelli di AMH hanno minor probabilità di successo della COH. In caso di buona riserva ovarica (alti livelli di AMH), la coesistenza di ATD può ridurre probabilità di successo della COH.

P205 Iperstimolazione ovarica e rischio di cancro tubo-ovarico

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Introduzione: La maggioranza dei cancri ovarici (OC) deriva dalla diffusione sulla superficie ovarica di un carcinoma sieroso intraepiteliale di alto grado, originato dalle tube di Falloppio (FT). L'iperstimolazione ovarica può aumentare il rischio di OC, in particolare tumori ovarici borderline (BTOs). Dati epidemiologici hanno evidenziato un rischio aumentato di BTOs nelle donne infertili trattate con IVF e circa due terzi dei BTOs risultano caratterizzati da mutazioni kras che determinano un aumento significativo della ciclina D1. Lo studio è stato condotto al fine di comprendere se ripetuti cicli di stimolazione ovarica con gonadotropine possano modulare la localizzazione ed il contenuto delle proteine di controllo del ciclo

cellulare nelle ovaie e nelle FT di topi spontaneamente ovulanti e di topi sottoposti a cicli di iperstimolazione ovarica.
Materiali e Metodi: Ovaie e FT di topi spontaneamente ovulanti e di 48 topi sottoposti a 2–3-4 cicli di stimolazione con gonadotropine, distanziati di 7 giorni secondo il protocollo di Van Blerkom, sono stati analizzati con tecniche di immunoistochimica, immunofluorescenza e Western blot per rilevare la localizzazione e l'espressione dei livelli di Oct-3/4, Sox-2, p53, β-catenina, pAKT e ciclina D1. Gli ovociti ovulati sono stati analizzati per valutare i fusi meiotici e l'allineamento dei cromosomi.
Risultati: Dopo il quarto ciclo di stimolazione ovarica, ovaie e FT dei gruppi ctr e post-trattamento non-hanno mostrato differenze nella localizzazione e nel contenuto di Oct-3/4, Sox-2, β-catenina, p53 e pAKT. Al contrario, il livello di ciclina D1 è aumentato in modo significativo nelle FT dei topi trattati. Il numero e la qualità degli ovociti è diminuito e la frequenza di fusi meiotici anomali è aumentata con i trattamenti.
Conclusione: Ripetute stimolazioni con gonadotropine non-hanno indotto cambiamenti in un insieme di proteine coinvolte nel ciclo cellulare ed alterate negli OC. Il significativo aumento della ciclina D1 rilevato nelle FT sembrerebbe dimostrare l'aumentata incidenza di BTOs nelle pazienti sottoposte a cicli di iperstimolazione ovarica. La ridotta qualità ovocitaria è conseguenza dell'iperstimolazione ovarica stessa.

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P206 Testosterone patches and antagonist protocol after 5 or 7 days interval following contraceptive pill pre-treatment in poor ovarian response

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Aims: To compare the testosterone transdermal patches co-adjuvant therapy in Poor Ovarian Response (POR) IVF patients, following 5 or 7 days interval free of contraceptive pill (FOP) pre-treatment.
Main outcome: Pregnancy rate/patient
Secondary outcomes: Duration and total dose of stimulation
Material and methods: Retrospective analysis of POR patients (low ovarian reserve or Bolognia criteria) treated between January 2014 and October 2015.
Statistics: Mean values and standard deviation, Chi-squared, Pearson or Fisher exact *t* tests and 95% confidence interval.
Treatment: contraceptive pill for 14–20 days, followed by 5 (5D-Group, patients treated during 2014) or 7 (7D-Group, patients treated during 2015) days FOP and daily testosterone patches. Stimulation with hp-HMG+rFSH and ganirelix protocol.
Results: A total of 185 patients were analyzed: 5D-Group $p = 127$; 7D-Group =58. There were no differences in the basal characteristics of the patients in both groups: age=37.67±3.47 years, BMI= 22.71±3.28, AFC=6.80±3.4 and AMH=0.52±0.48 ng/ml. In total, 137 patients had embryo transfer and 35 achieved pregnancy, giving a 23.0% pregnancy rate per patient, and 25.5% per embryo transfer. Patients in 5D-Group needed more days of stimulation (10.33±2.23days) and total dose of gonadotropins (3381.8±1429 IU) than patients in 7D-Group (8.72±1.95days and 2779.2±897.57 IU, respectively), although not statistically significant. There were significantly more cancelled cycles in 7D-Group (8.6%) compared to 5D-Group(1.6%), $p < 0.05$.
Conclusion: Delaying the initiation of gonadotropin treatment for the ovarian stimulation in poor reserve/POR patients, after pre-treatment with contraceptive pill and testosterone patches, provides shorter duration of stimulation and lower total gonadotropin consum, but does not seem to influence pregnancy rates.

P207 The impact of dual trigger in gonadotropin releasing hormone antagonist cycles for final oocyte maturation on IVF outcomes in comparison with standard human chorionic gonadotropin trigger

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Context: *In vitro* fertilization.
Objective: To compare IVF outcomes in cycles with GnRH antagonists after dual trigger with combination of gonadotropin releasing hormone agonist and human chorionic gonadotropin(hCG) versus hCG alone.
Methods: A total of 995 cycles (471 hCG trigger: 471; 524 dual trigger) that underwent IVF treatment with GnRH antagonist protocol were evaluated retrospectivelty. IVF outcomes of each group was also compared in cycles with poor (retrieved oocyte number $\leq$3) and hyperresponse (retrieved oocye number $\geq$20).
Interventions: Standard hCG trigger (6500 IU recombinant hCG) versus dual trigger (0.2 mg triptorelin plus 6500 IU recombinant hCG).
Main Outcome Measures: Clinical pregnancy, fertilization, implantation and retrieved mature oocyte rates.
Results: A total of 995 cycles with 860 completed cycles with embryo transfer were enrolled (standard hCG trigger group n:471, dual trigger group n:524). Antral follicle count is signifanctly higher in dual trigger group (11.6±5.8 vs. 10.8±6.6) other demographic properties of each group was identical. Retrieved mature oocyte rate (%71.8 vs. %70.2), fertilization rate (%73.9 vs. %71.3) and clinical pregnancy rate per cycle (%41.4 vs. %34.4) were significantly higher in dual trigger group. There were no significant difference between standard hCG trigger and dual trigger group in terms of implantation and pregnancy rate per embriyo transfer (%20 vs. %21.8 and %40.9 vs. %46.8, respectively). In poor responders clinical pregnancy rate per cycle and per embryo transfer was significantly higher in dual trigger group (%7.3 vs. %22.4 and %13.6 vs.%33.3). In hyperresponders there were no significant difference between groups in terms of pregnancy rates.
Conclusion: Addition of GnRH agonists to hCG in IVF cycles wih GnRH antagonists increases retrieved mature oocyte and pregnancy rates.

P208 The impact of chronic endometritis on IVF outcomes in patients with previous IVF failure history

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Context: *In vitro* fertilization.
Objective: To investigate the impact of chronic endometritis (CE) in patients underwent antibiotic therapy on IVF outcomes with previous IVF failure history.
Methods: This is a retrospective study performed between January 2014 and January 2015. Fifty seven patients with previous IVF failure despite high-quality embryo transfer and who underwent endometrial biopsy after IVF failure were evaluated based on the presence or absence of chronic endometritis.

Interventions: Patients with previous IVF faiulure underwent endometrial biopsy with pipelle. The patients with CE underwent antibiotic treatment with ciprofloxacin and metranidazol. Further IVF treatment was initiated within 6 months after previous attempt in both groups.
Main Outcome Measures: The implantation rates, clinical pregnacy rates were compared.
Results: Chronic endometritis was identified in 54.3% of patients with previous IVF failure. 3 patients in the CE group concieve spontaneously after the treatment of chronic endometritis. 54 patients underwent further IVF treatment. There were no significant difference between CE and non-CE group in terms of implantation and ongoing pregnancy rates (40% vs. 21.4% and 28% vs19.4%, respectively).
Conclusion: Chronic endometritis treated with antibiotics are similar with the normal endometrial biopsy group in terms of IVF outcomes. Antibiotherapy might be a treatment option for the patients with chronic endometritis before the beginning of a new IVF cycle.

P209 Day 1 versus Day 3 embryo transfer in ICSI Patients: a retrospective study

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Context: Clinical research has focused attention on determining the ideal time for embryo transfer (ET) in IVF cycles for improving implantation and pregnancy rates.
Objective: To demonstrate comparable outcomes of Day 1 versus Day 3 ET.
Methods: Retrospective Study: 461 ICSI Cycles performed at our IVF Unit from May 2010 to July 2013 where ET was performed on day 1 or on day 3.
Embryo transfer on Day 1: 183 ICSI Cycles, 398 pronuclear stage embryos.
Embryo transfer on Day 3 (control group): 278 ICSI Cycles, 634 cleavage stage embryos.
Statistical analysis: chi square test, difference not significant (ns): $p < 0.05$ (SPSS software).
Patients: 428 women undergoing ICSI cycles, aged 26–42 yrs (mean 35.9 yrs), male partner aged 30–51 yrs (mean 39.7 yrs) . All patients were nulliparous with previous failed IVF cycles ranging from 1 to 4. Basal FSH <10 mIU/ml or E2 <50 pg/ml on cycle day 3.
Interventions: COH long protocol, daily monitoring of follicles size (by US) and plasma levels of E2 and progesterone. Ovulation triggering with 10 000 IU hCG i.m. when plasma E2 was 1000–3000 pg/ml and with at least 4 follicles >18 mm mean diameter. Oocyte retrieval 36 h after the injection of hCG. Semen samples were prepared according WHO protocol. ICSI procedure was performed as reported by Palermo. Oocyte fertilization was assessed and scored 16–18 hours after ICSI according to Giannaroli; for Group B, embryos were scored according to Veeck, at 40–42 and 72 hrs after ICSI. Embryo transfer was performed at Day 1 (Group A) or Day 3 (Group B) after oocyte retrieval.
Main Outcome Measures: Implantation Rate (IR); Abortion Rate (AR); Pregnacy Rate (PR).
Results: IR: Group A 19.8%, Group B: 20.3% (ns). AR: Group A 18%, Group B 18% (ns). PR: Group A 32.7%, Group B: 33.9% (ns)
Conclusions: Day 1 ET appears a viable option for IVF, resulting in pregnancy rates comparable to those reported for Day 3 ET.

P210 The positive effect of homotoxicological treatment of infertility in woman with endometrial pathology: clinical case

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Background: Structural and functional readiness of the endometrium is one of the key factors in ensuring the effectiveness of ''implantation window''. Approximately 2/3 of implantation failures are due to defects in endometrial receptivity.
Objective: The choice of therapy with the potential to restore the receptivity and the readiness of the endometrium as an important goal of infertility treatment.
Methods: Presentation of clinical case.
Patients: Women 34-year-old with complaints of scanty menstruations, absence of pregnancy within 3 years of regular sexual life. Medical history: two miscarriages and two appropriate diagnostic curettages in 2011 and 2012; two hysteroscopies in February and July 2014 when gross adhesions of the uterine cavity were revealed and dissected.
Result(s): In February 2015, the homotoxicological treatment was administered: microclysters – Metro-Adnex-Injeel, Mucosa compositum, Traumeel S – 2 times a week, N20; Ginekohel 10 drops 2 times a day – 2 cycles (except spotting days), Lymphomyosot 10 drops 2 times a day from 5th to 14th day of the cycle – 2 cycles. The endometrial thickness according to prior dynamic ultrasound did not exceed 3.8mm, in March 2015 (after homotoxicological treatment) it was 6.7 mm, in May 2015 – 10.3 mm. In May, 2015 our patient became pregnant and gave birth in December 30.2015.
Conclusions: Our patient is a typical carrier of endometrial pathology after post-operative injury of the basal layer of the endometrium. The previous conventional medical treatment was not effective. On the basis of the positive effect of the homotoxicological treatment in our case, we believe that it is possible to conduct additional studies to assess the applicability of this non-specific treatment for the recovery of the endometrium as an supporting effective approach.

P211 A pilot experience with fertility preservation by oocyte vitrification for female-to-male transsexuals in Sweden

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Context: In 2013 a previous requirement of sterilization for legalization of gender change was ruled unconstitutional in the Swedish court. Hence, transsexuals may now be included in clinical programs of fertility preservation (FP) before sex-reassignment surgery.
Objective: To report a pilot experience with counseling and performance of FP in transsexual men.
Methods: Prospective study.
Patients: Nine transsexual men referred for FP.
Intervention: Counseling and performance of FP by oocyte virification. A protocol using GnRH antagonist and letrozole alongside gonadotropins was used to maintain low systemic estradiol levels and improve patients' compliance.
Main Outcome Measures: FP treatments' s outcomes and acceptance to the FP treatment.

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Results: Patients received reproductive counseling (mean age 27.4 ± 6.0 y, range 19–35; mean time after diagnosis 4.0 ± 2.8 y, range 1–7). Three individuals were on daily transdermal testosterone and two on intra-muscular injections; two had previously undergone surgery of reproductive organs and four were mastectomized. Serum gonadotropins, AMH and Inhibin-B concentrations were all within normal ranges of reproductive age females. Upon transvaginal egg retrieval, a mean of 13 oocytes with a maturity rate of 88% was obtained. All oocytes were vitrified. Standard visual aids used to explain the process of ovarian stimulation and egg retrieval were critizized by the men, who considered the pictures offensive, by reminding them of the female body. The men preferred illustrations allowing the perception of presence of ovaries in a male body.
Conclusion: This is the report of a preliminary experience of FP among transsexual men. Psychological aspects of FP could be evaluated during FP counseling and treatment. High patient acceptance was observed by using the protocol with aromatase inhibitor alongside gonadotropins.

P212 Fertility recovery in patients with nonclassical congenital adrenal hyperplasia

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Context: Very little research has been devoted to the studying fertility problem in nonclassical congenital adrenal hyperplasia (NCAH). Spontaneous abortions occurred more frequently prior to glucocorticoid treatment. It is difficult to draw definitive conclusions regarding the need for glucocorticoid therapy in NCAH women based on limited data. Therefore, evaluating fertility in patients with NCAH and exploring the possibility of correcting its disturbances seemed to us to be a matter of importance.
Objective: To evaluate the reproductive function of patients with NCAH and explore potential treatments for this disorder.
Methods: ACTH–stimulation test, direct analysis of the CYP21A2 gene.
Patients: 60 Women with NCAH.
Intervention: Glucocorticoid therapy.
Main Outcome Measures: Physical examination including an assessment of menstrual function; hirsutism scoring; hormone measurements; ultrasonography.
Results: Overall, the patients complained of menstrual cycle disorders (60%), infertility (28%), miscarriage (50%), hirsutism (63%). Once the diagnosis of NCAH was made, 58 women started receiving glucocorticoid therapy, 39 of whom became pregnant (67%). The miscarriage rate was significantly lower in patients receiving glucocorticoid treatment compared with women who did not receive treatment (50% versus 10.3%). There was no difference in the miscarriage rate between patients who received or quit glucocorticoid therapy during pregnancy.
Conclusions: Glucocorticoid therapy is a highly efficacious method of fertility restoration in NCAH patients. Use of glucocorticoids during pregnancy planning significantly reduced the miscarriage rate. No difference in pregnancy outcome between the patients who received glucocorticoid therapy during pregnancy as opposed to those who did not indicates the advisability of treatment discontinuation once pregnancy is determined.

P213 Aspirazione eco-guidata di sangue in cavità endometriale in pazienti con istmocele prima del trasferimento di embrioni: uno studio pilota

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Introduzione: L'istmocele può associarsi non-solo alla presenza di sangue mestruale nel recesso anomalo della parete uterina anteriore, ma anche alla presenza di sangue nella cavità endometriale (SCE). Nelle pazienti con istmocele, il SCE può interferire con il trasferimento di embrioni e il loro impianto. Questo studio ha lo scopo di valutare se l'aspirazione eco-guidata di SCE è efficace prima di eseguire il trasferimento di embrioni.
Materiali e Metodi: Criteri d'inclusione: diagnosi ecografica di istmocele e conferma tramite isteroscopia, utilizzo per il trasferimento di embrioni congelati o embrioni derivanti da ovociti donati, spessore di SCE ≥3.5 mm, almeno un trasferimento di embrioni fallito dopo diagnosi di istmocele. Per l'aspirazione è stato utilizzato un catetere endometriale a palloncino, introdotto sotto guida ecografica. L'aspirazione è stata eseguita quando lo spessore di SCE era ≥3.5 mm, con l'obiettivo di rimuovere ogni raccolta fluida. L'ecografista ha giudicato l'aspirazione attraverso una scala di Likert a 3 punti. Dopo l'aspirazione, un altro ecografista ha valutato la presenza di SCE ogni due giorni fino al trasferimento degli embrioni.
Risultati: 13 pazienti inclusi nello studio. Al momento dell'aspirazione lo spessore medio (± DS) di SCE era di 4.2 (± 0.6) mm. L'aspirazione è stata giudicata soddisfacente in 9 pazienti (69.2%). Due giorni dopo l'aspirazione, lo spessore di SCE era di 0 mm in 4 pazienti, tra 0 e 3.5 mm in 4 pazienti, e ≥3.5 mm in 5 pazienti. Il trasferimento di embrioni è stato eseguito in 6 pazienti, con spessore medio (± DS) di SCE di 1.4 (±1.0) mm. Due pazienti hanno concepito.
Conclusioni: L'aspirazione eco-guidata di SCE può essere considerata in pazienti con SCE causato da istmocele, evitando la chirurgia. Il tasso di gravidanza è basso, probabilmente per la persistenza di SCE e il suo effetto dannoso sull'impianto.

P214 The link between adenomyosis and infertility – from theory to practical issues

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Context: Adenomyosis is the benign invasion of endometrium within the myometrium. It is characterised by islands of endometrial glands and stroma, surrounded by myometrial hyperplasia and hypertrophy. The mechanisms by which adenomyosis can affect fertility (disturbed miometrial architecture and hence miometrial contractility, change in endometrial receptivity, changes in intraendometrial metabolism, lack of secretion of immunologic implantation markers) are not yet well defined.
Objective: To evaluate the extension of adenomyosis in infertile patients.
Methods: A group of 10 patients with infertility of unknown etiology were evaluated by the new imagistic criteria for diagnosis of adenomyosis: MRI and transvaginal ultrasound detects areas at the endometrium–myometrium junction that normaly does not exceed 5mm. The stages of adenomyosis are: simple hyperplasia of the junctional area (over 8 but not exceeding 12 mm in patients under 35 years), partial or diffuse adenomyosis (thickness 12 mm, with well defined myometrial outbreaks, with intense signal, affecting myometrium in one, two or all thirds) and adenomyomas.

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Patients: A group of 10 patients were followed for one year in the Department of Obstetrics and Gynecology of The Emergency Universitary Hospital Bucharest.
Interventions: One patient had an excision of adenomyoma by histeroscopy, 9 patients received treatment with GnRH for a period of 6 month being monitorised by ultrasound.
Main outcome: Achievement of pregnancy.
Measures: Serial imagistic evaluation was performed (MRI and ultrasound).
Results: Reduction of adenomyosis dimensions and reduced simptomatology.
Conclusion: A thorough imagistic diagnosis is necessary to improve prognosis in subfertile or infertile patients, when adenomyosis is suspected.

P215 Choice of oocyte maturation triggers for OHSS prevention in women with PCOS during controlled ovarian stimulation in assisted reproductive technologies

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Context: PCOS patients are at a high risk of OHSS. Rational choice of oocyte maturation triggers reduces OHSS risks and improves IVF outcomes.
Objective: To compare GnRH agonists and HCG for oocyte maturation in terms of OHSS risk, blastocyst growth, pregnancy rate.
Methods: 339 Women with PCOS formed 3 groups according to the maturation triggers.
Patients: Average age 27±2.9 years; Rotterdam PCOS criteria, no previous IVF attempts. Maturation triggers: Group A ($n=109$) – Ovitrelle 5000 IU; Group B ($n=112$) – Decapeptyl 0.1mg+HCG 1500 IU on day 3 after follicle aspiration, on ET day, and on day 5 after ET; Group C ($n=118$) – Decapeptyl 0.1 mg as trigger + HCG 1500 IU on the follicle aspiration day.
Interventions: Short protocol with Gonal was used; GnRH-antagonist added from stimulation day 7 till the trigger administration at follicle diameters >18 mm. Follicle aspiration was followed by ICSI; embryo transfer was on blastocyst stage.
Main Outcome Measures: Group A – embryos quantity 9.1±3.5; blastocysts 52.8%; fertilization rate 82.1%; pregnancy rate 40.8%. Cancelled ET 11.2%; mild and moderate early OHSS 10.9%; mild and moderate late OHSS 11.9%. Group B – embryos quantity 9.5±3.3; blastocysts 63.8%; fertilization rate 84.9%; pregnancy rate 40.1%. Cancelled ET 0; mild and moderate early OHSS 0; mild and moderate late OHSS 0.89%. Group C – embryos quantity 9.3±2.9; blastocysts 60.6%; fertilization rate 82.3%; pregnancy rate 40.6%. Cancelled ET 4.2%; mild and moderate early OHSS 5.9%; mild and moderate late OHSS 7.6%. Severe OHSS in all groups – 0 cases.
Results: Decapeptyl 0.1mg as trigger resulted in higher blastocyst percentage, significantly lower OHSS risks and fewer cancelled ET. Pregnancy rate in all groups was >40%.
Conclusions: GnRH agonists should be used as oocyte maturation triggers for patients with PCOS to minimize OHSS risk and improve IVF outcomes.

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Pregnancy

P216 Features of flow fibrocystic breast in women of childbearing age with hyperprolactinemia

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Out of 96 W (women) with HP (hyperprolactinemia) surveyed 31(32.3%) were diagnosed with FBD (Fibrocystic Breast Disease). Of these 31 W with FBD 10(32.2%) had HP due to pituitary micro-adenoma, 2 (6.4%) – symptom of empty sella, and 19(61.2%) of W – without organic changes in the pituitary. Of 31 W 8 (25.8%) were with palpation and u/s revealed no pathology of the thyroid gland; 7(22.5%) with various forms of goiter euthyroid state; 14(45.2%) revealed subclinical hypothyroidism & 2(6.4%) W with hypothyroidism. Among W we surveyed in 23(74%) thyroid disease was found, of which 16(51.6%) with impaired functional state. In 2(6.4%) W nodal mastopathy was identified. Furthermore, patients with FBD were divided by genotype of polymorphic C3420T gene DRD2: CC genotype in 12(38.7%) W; CT genotype in 16(51.6%) W; TT genotype in 3(9.6%) W. In this group of W the HZ(heterozygous) type of polymorphisms prevailed, comprising 51.6%. All carriers of the TT genotype decrease thyroid function. Among carriers of the CT genotype 3(18.7%) W were without thyroid disease, the remaining 13(81.3%) with a variety of diseases of the thyroid gland. Of the 12 W with the CC genotype in 5(41.6%) patients with FCD disorders of the thyroid gland were not diagnosed. Consequently, analysis of the results indicate polyetiology of FBD in W with HP.
Conclusions: FC changes in the breast are of polyetiology character. Of the 31 W with FCD in 8(25.8%) W on palpation and u/s revealed no pathology of the thyroid gland, in 7 (22.5%) W with different forms of goiter euthyroidism, 14 (45, 2%) of W diagnosed subclinical hypothyroidism and 2 (6.4%) W with hypothyroidism. In patients with FC breast changes are prevalent type of HZ polymorphism C3420T gene DRD2. Carriers mutant TT genotype in patients with FCD all W decrease thyroid function.

P217 Miscarriage and reproductive health

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Context: According to statistics in Uzbekistan every fourth pregnancy ends with miscarriage.Missed abortion (MA) negatively impacts on the reproductive function of 27.4% women, and as a result subsequently observes habitual miscarriage.
Objective: Evaluate the reproductive health and analysis of the course of pregnancy in women with MA in history.
Methods: Study included 60 women aged 20–40 years. Analyzed the medical history, pelvic examination, infection, screening for bacterial and viral infections and pelvic ultrasound. *Results*: Menstrual dysfunction was observed in 13.3%. It should be noted that almost every tenth woman was akin to marriage. Study of infection in 17% of women the infection is not detected, only HPV 2 revealed – at 15.6%; at the same time the association of CMV + HPV was observed in 31% of women. However mixed infection was observed in various combinations in majority of cases (40%). Miscarriage observed in 1st pregnancy at 40% and after parity in 33%. Missed abortion 2–3 times was observed in 13% of cases; 4 times occured in 6.7%, and repeated in 22% of cases when intergenetic range was up to 4 months.
Conclusions: Miscarriage plays an important role in the development of subsequent pregnancy complications. The development of miscarriage affect the presence of chronic somatic diseases, closely related

marriages and the presence of considerable importance is the association of bacterial and viral infections.

P218 Efficiency of introduction of modern technologies in perinatal center

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Context: Premature labor and birth of prematurely born child is an actually problem in obstetrics. Frequency of premature labor does not go down. A premature break of fetus shells is one of the frequent complications of pregnancy.
Objective: The aim of this research is determination of efficiency of introduction of modern perinatal technologies at premature delivery.
Methods: We are studied comparative data on the improvement of survival among prematurely born children before and after introduction of modern perinatal technologies. Research were conducted in the perinatal center of the Fergana region of Uzbekistan. The basic problem of the prematurely born children is respiratory distress syndrome and death of newborn babies in 2007 was rate to 1th place in the structure of perinatal mortality and reached to 50‰.
Results: After introduction of the program of prophylaxis of distress of fetus and reanimation of newborn babies death from an asphyxia went down and appeared on the last place among reasons of mortality. Now this index hesitates in limits from 21 to 23‰. Almost in 2 times decreased the index of perinatal morality in compared to 2006. Application of antibiotic prophylactics for pregnant with the predelivery break of fetus amniotic fluid shells and prophylactics of distress syndrome of fetus by steroids resulted in the improvement of survival and morbidity among newborns and considerably went down the percent of septic complications of mothers and newborns. In the most extraordinarily small gravimetric category from 500 to 1000g survival in 2015 rate on the area of 23.8, in category up to 1500g rate of 77.2, in categories up to 2000g – 97.1, and in category of more than 2500g – 99.8%.
Conclusion: Creation of perinatal centers and perfection of perinatal technologies assist upgrading of providing of services and survival of prematurely born children.

P219 Correlation between parturients` VDR Fok1 polymorphism (rs2228570) and duration of pregnancy in Polish population

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Context: Vitamin D receptor (VDR) influences expression of numerous genes responsible for mineral metabolism, cell growth and differentiation. Some studies indicate various effects of individual variants of the VDR on the immunological system. Presence of a shorter variant of VDR is associated with development of some autoimmune conditions. Occurrence of various variants of VDR may also cause various effect of vitamin D on pregnancy.
Objective: Aim of this project is determination of an correlation between the occurrence of a particular genetic variant of the VDR and duration of pregnancy.
Methods: Venous blood was used for comparison of nucleotide sequence in the coding region of the gene for VDR. Determination of polymorphism for VDR was assayed using the rt -PCR method with an appropriate set of starters and probes. Patient(s): 201 Caucasian women at childbirth. The study group was divided into two parts: 100 patients who gave a spontaneous premature birth and 101 patients who gave birth at full term.
Main Outcome Measure(s): Multivariable regression models tested the association Fok1 polymorphism with duration of pregnancy. Result: Three different genotypes were found in the analyzed population. No significant differences in the frequency of particular genotypes in compared groups were found. Significant association was present between the A-T haplotype, consisting of minor alleles, and preterm birth (OR = 0.37; 95%CI: 0.14–1.01; $p = 0.05$). ff presence reduces the risk of premature birth by 63%.
Conclusion: The results of the present study suggested that VDR gene variants seems to be one of genetic risk factors for preterm birth but extension studies are needed.

P220 Correlation between parturients` serum vitamin D level and duration of pregnancy in Polish population

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Context: Pregnant women belong to the group exposed to a higher risk of vitamin D deficiency. There are single reports regarding effect of vitamin D on duration of pregnancy. Vitamin D participates in immunological processes and response of the immunological system to bacterial invasion, which may partially explain its intermediate effect on duration of pregnancy. *Objective*: Aim of this project is determination of an correlation between the level of vitamin D in blood serum of and duration of pregnancy in Polish population.
Methods: 25(OH)D level was determined in venous blood, using immunological assay method (ELISA). Standardised history of each patient was recorded. The history included: general medical history, data regarding course of the pregnancy, and social and economic status of a patient; information about health-related behaviour that could influence vitamin D concentration. Patient(s): 201 Caucasian women at childbirth. The study group was divided into two parts: 100 patients who gave a spontaneous premature birth and 101 patients who gave birth at full term.
Main Outcome Measure(s): Multivariable regression models tested the association between 25(OH)D level and duration of pregnancy. Result Vitamin D deficiency was very common in both groups (69.6% patients in premature group and 72.0% in control group) . Patients who gave premature birth had severe vitamin D deficiency (less than 10 ng/ml) more often than in control group (14.2% vs. 34.0% $p < 0.05$). Severe vitamin D deficiency increased risk of premature delivery but the correlation was not statistically significant. (OR = 2.47; 95%CI: 0.86–7.15; $p = 0.094$).
Conclusion: Vitamin D suboptimal level is common among Polish pregnant women. Severe vitamin D deficiency may be a risk factor for preterm birth but multiple centres clinical trials with bigger number of patients are needed.

P221 Could blood type affect thyroid function in early pregnancy?

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Context: Untreated hypothyroidism can adversely affect gravidity outcome. It mostly arises from autoimmune basis. Its detection

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based on the known statistically significant risk factor is considered to be insufficient, 30–50% of women thus escape diagnosis.
Objective: To evaluate influence of known risk factors on thyroid stimulating hormone (TSH) level in early pregnancy within unselected population of Slovak women. To verify if TSH level differs according to AB0 blood type (BT).
Methods: The data from medical records was tested by Chi-Square tests and simple Logistic regression.
Patients: All pregnant women, who attend prenatal care this particular clinic in the period 2010–2015 ($n = 271$).
Intervention: Retrospective study.
Main Outcome Measures: TSH level measured in 10–13th week of gestation, analyzed at four levels: TSH $\geq 4 \geq 3.5 \geq 3 \geq 2.5$ mU/l.
Results: TSH ≥ 4.0 mU/l was found in 10.7% of pregnant, while BT were not represented equally. Women with BT B has almost double the chance of increasing levels of TSH ≥ 4.0 compared to women with BT "0". (OR = 1.768 but with 95% CI 0.634 to 4.929). For TSH ≥ 3.0, OR = 1.515 with 95% CI 1.515 to 3.520. Blood type AB has three times less chance of occurrence thyreopathy, compared to the reference type "0" (OR 0.332 but with 95% CI 0.039–2.816).
Conclusions: Increased BMI significantly affects a higher proportion of pregnant women with TSH ≥ 3.0 mU/l ($p = 0.007$) and TSH ≥ 2.5 ($p = 0.036$). Age and smoking had no significant effect. The chance of hypothyroidism in early pregnancy is increased according to blood type, in order AB < A < 0 < B. However, the differences found were not statistically significant. These preliminary results require further verification.

P222 The efficacy of insertion of the Arabin pessaries for correction of cervical incompetence and prevention of preterm birth

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Context: The rate of preterm birth (PB) in Russia is 14%, in St. Petersburg up to 18%. PB syndrome is a multifactorial pathology, which is caused by both uterine contractile activity and structural changes of the uterine cervix in 22–36 weeks of gestation. In up to 50% of cases CI is the major cause of preterm birth.
Objective: To evaluate the efficacy of Arabin Pessary (AP) insertion for CI correction and prevention of PB.
Methods and Interventions: All pregnant women included in the study were classified into 6 groups: I – 29 with CI in II trimester, II – 86 with CI in the III trimester, III – 46 with threatening preterm delivery, IV – 12 with CI and cervical suture, V – 4 with a history of preterm birth, VI -12 with a multiple pregnancy. The average term of AP insertion were as follows: I – 18.9±0.2; II – 25.4±0.6, III – 24.1±0.7, IV – 18.3±0.2, V – 25.6±0.1, VI – 22.1±0.1 weeks of gestation. All patients received conserving therapy, prevention of fetal RDS, physical and sexual rest. PB before 28 weeks of gestation were registered in Groups I, IV and VI (20.6%, 16.6%, 8.3%). PB in 29–34 weeks of gestation were in Groups I, II and VI (11.5%, 13.9%, 8.3%). PB in 35–37 weeks of gestation occurred in Group VI (50%), PB was not registered in V Group, and the PB rate did not differ in other groups. Most often term deliveries were registered in V -100% and III -91.3% groups, less in groups I, II, IV (57.7%, 69.8%, 66.6%); the lowest rate was in VI group (33.3%).
Patients: Overall, we analyzed the outcomes of pregnancy and childbirth in 189 patients treated with AP.
Results: The use of the AP in groups with threatening pregnancy termination as a prophylactic measure allows to prolong pregnancy to full-term in 95.6% cases, and in groups with CI in 65% of case.
Conclusions: We have noted a high efficacy of CI correction by use of the Arabin pessary in the complex PB preserving therapy.

P223 Peculiarities of somnological status and melatonin metabolism in pregnant women in the dynamics of physiological pregnancy and in case of metabolic syndrome

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Context: Deterioration in the quality of sleep and changes in melatonin metabolism are risk factors in developing of obstetrics complications. The objective of our study was to reveal the peculiarities of somnological status and melatonin metabolism in pregnant women and in case of metabolic syndrome.
Methods, patients, interventions and outcome measures: We conducted polysomnography and studied the level of 6-sulfatoximelatonin in morning urine in 291 patients: 147 women with physiological pregnancy and 144 women with metabolic syndrome. EEG analysis was carried out in an abandoned mode on epochs of 20 seconds.
Results: In the dynamics of physiological pregnancy we detected an increase in the duration of stage I of sleep, increased total waking time, the amount of movement during sleep and nocturnal awakenings and decreased sleep efficiency. In the sleep patterns we revealed an increase in the duration of the superficial stages of slow-waves' sleep and decrease of the duration of paradoxical sleep, as well as increasing segmentation of its phases. In metabolic syndrome, we found the predominance of slow-wave phase in all cycles of sleep. The segmentation of its phases increased significantly (by 45% compared to physiological pregnancy), the duration of superficial stages of slow-wave sleep increased. We detected the decrease of paradoxal sleep, until obstructive apnea. We also found the reduced total sleep efficiency.
Conclusion: These changes in the structure and quality of a night's sleep are revealed on the background of a gradual increase in the level of 6-sulfatoxymelatonin in the morning urine of women with increasing gestation of physiological pregnancy, and, conversely, the reduce of it – in the metabolic syndrome.

P224 The peculiarities of angiogenic factors' system and cytokines' system in women with physiological and complicated pregnancy in second and third trimesters in dependence on fetal sex

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Context: Significant violations of angiogenesis, which are accompanied by changes in expression of endothelial growth factors and interleukins, are observed in placental insufficiency. The objective of this study was to explore the peculiarities of angiogenic factors and cytokines system in women with physiological pregnancy and in case of placental insufficiency in dependence on fetal sex.
Methods, patients, interventions, main outcome measures: We studied 2 groups of women: 390 women with physiological pregnancies (203 women with male fetuses and 187 with female fetuses) and 345 women with placental insufficiency (176 women with male and 169 with female fetuses). The levels of VEGF-A, EGF, PlGF, ET-1, TNF-α, IL-1, IL-6, IL-10, IL-12 were determined in blood serum with the help of ELISA method in II and III trimesters of gestation.

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Results: We detected a higher expression of VEGF-A (1.5 times), ET-1 (2.5 times), EGF (1.6 times) in physiological pregnancy in women with female fetuses than in women with male fetuses. Higher levels of IL-1β (1.5 times), IL-6 (1.8 times) and IL-10 (5.7 times) were revealed in mothers of girls in pregnancies with placental insufficiency. Our study showed that changes in expression of angiogenic factors and cytokines contribute to the development of oligohydroamnios (11.4%), polyhydroamnios (9%), preeclamsia (6.8%) and unfavorable indices of fetal biophysical profile in pregnant women with male fetuses.
Conclusion: Identified differences in the expression of angiogenic factors and cytokines suggest the existence of a special ''request'' from the utero-placental-fetal complex defined by the sex of the fetus. High activity of angiogenic factors and cytokine system in women with female fetus both in physiological and complicated pregnancies indicates a higher adaptability of its ''mother-placenta-fetus'' system.

P225 Influence of fetus sex on blood coagulative system in physiological pregnancy

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Context: Sex of the fetus is a genetically determined factor in the formation of certain differences and in the functioning of various parts of the functional system ''mother-placenta-fetus''. Determining the level of D-dimer in venous blood of women is one of the most valid methods for diagnosis of pregnancy complications. Studying the features of the blood coagulation system of women at various stages of physiological pregnancy, depending on the sex of the fetus, is the objective of this research. Methods, patients, interventions and main outcome measures. Retrospective evaluation of blood coagulation in 259 women (116 with female fetuses – 1 group and 143 with male fetuses – 2 group) with physiological pregnancy in I, II and III trimester was conducted. Hemostasis parameters – hemoglobin, hematocrit, red blood cells, erythrocyte sedimentation rate, fibrinogen, platelets, aPPT, thrombin time, prothrombin index, INR, SCFM were determined using an automatic hematology analyzer.
Results: We found that with increasing gestational age the increased activity of coagulative hemostasis was noted in both clinical groups, but the rate of these changes was higher and reached a maximum in II trimester in women with a male fetus, whereas in women with female fetus pace of these changes was less pronounced. D-dimer levels were higher in women with male fetuses ($p = 0.0478$), especially in the II trimester (21%). In II trimester of pregnancy in women with a male fetus we revealed a tendency to a higher fibrinogen.
Conclusions: These results indicate the existence of differences in the ''functional behavior'' of individual components of the system of hemostasis in various stages of physiological pregnancy. In women with male fetuses we revealed higher coagulation readiness in physiological pregnancy, indicating the tension of coagulation system in this variant of sexual dimorphism.

P226 Pregnancy outcomes in women with hyperglycemia in the morning

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Background and aims: In 2013 it was changed criteria of diagnostic of gestational diabetes mellitus (GDM), which based on HAPO (Hiperglycemia and Adverse Pregnancy Outcomes) study results: Retrospective analysis of medical histories was performed for revealed hyperglycemia according HAPO-study and pregnancy outcome.
MaterialS and Methods: Retrospective analysis of medical cases of 95 pregnant women in Moscow region who delivered from January 2013 to December 2013. Age 28.1±6.1 ys, BMI 23.8±4.8 kg/m2.
Results: All pregnancies had fasting glucose level, nobody had 75 g OGTT. 18 women (19%) had an increased fasting glucose (5.4±0.3 mmol/l), 77 women (81%) had a normal glucose level (4.0±0.6mmol/l). No difference in age, BMI and time of delivery ($p > 0.05$). Premature delivery and caesarian section were similar in both groups (16.6% vs. 10.3%, 22% vs. 18%, $p > 0.05$). Adverse pregnancy outcomes (clavicle fracture, asphyxia, intrauterine hypoxia and stillbirth) were more frequent in group with fasting hyperglycemia (44% vs. 10.5%, $p < 0.0001$). Macrosomia was fixed only in women with normal glucose level (10.5%).
Conclusions: The pregnancy with hyperglycemia in the morning according HAPO study have adverse pregnancy outcomes in 44%. The prevalence of GDM may increase up to 19% using a new diagnostic criteria.

P227 Fibrinolysis in pregnant women with subchorionic hematoma in the I trimester

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Context: Detachment of the chorion with the formation of subchorionic hematoma (SCH) is an early and frequent complication of gestation, which, in fact, is a hemorrhagic complication, and congenital or acquired thrombophilia can play the leading role in its pathogenesis.
Objective: To evaluate the indicators of fibrinolysis in pregnant women with SCH in the I trimester.
Methods: The study was conducted in the Rostov-on-Don Perinatal Centre for the period from 01/01/2013 to the 01/01/2015 year and included analysis of hemostasiograms in the 1 trimester. *Patients*: The study group included 115 pregnant women with SCH in the period of 6–12 weeks (group I). The control group (II group) included 79 apparently healthy pregnant women. *Interventions*: Indicators of hemostasiograms of pregnant women in studied groups, made in I trimester of pregnancy, were analyzed.
Main Outcome Measures: Trombin time, INR, aPTT, fibrinoge, D-dimer and SFMC were evaluated.
Results: Thrombin time, INR, aPTT and fibrinogen were not significantly different in the patients of studied groups. In group I there was a statistically significant increase of D-dimer index compared with the II group – 533.0±226.6 (195.0–960.0) ng/ml, and 360.5±179.0 (92.0–753.0), respectively ($p = 0.000038$). The average level of SFMC in group I was 4.1 (3.0–11.0) mg%, which is greater than the permissible limit and exceeds similar values in group II 1.2 times – 3.3 (2.0–4.5) mg% ($p = 0.000003$). Using regression analysis, we found a link between elevated values of SFMC and D-dimer and formation of RCG ($p = 0.000084$ and $p = 0.003948$, respectively).
Conclusions: Elevated values of SFMC and D-dimer in pregnant women with RCG indicate the abnormal activation of the hemostatic system (in particular, phase of fibrinolysis) with an increased risk of intravascular tromboproduction, and can be predictors of RCG formation.

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P228 The use of plasmapheresis in the complex treatment of complications of pregnancy in patients with congenital thrombophilia and recurrent miscarriage

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Context: One of the main aims of modern obstetrics and perinatology is to reduce maternal and perinatal morbidity and mortality.The study of the role of gene polymorphisms that affect the functional activity of the hemostatic system in women with recurrent miscarriage (RM) is of great interest. The objective of our study was to examine the efficacy of plasma exchange in the treatment of complications of pregnancy and in improving perinatal outcomes in patients with a history of RM and congenital thrombophilia.
Methods, patients, interventions and outcome measures: The study included 37 pregnant women with a history of reproductive losses and genetically determined thrombophilia and 35 apparently healthy pregnant women without a history of reproductive losses. According to the results of molecular genetic studies we revealed the most common polymorphisms of genes in women with RM: MTHFR C677T, MTRR A66G, FGB G455A, ITGB3 T1565S. Women with RM were divided into 2 groups: 1 – 17 women treated during pregnancy with low molecular weight heparins, 2 group – 20 women, who in addition to the low molecular weight heparin were conducted 3 sessions of therapeutic plasmapheresis in the second half of pregnancy.
Results: Patients of the 1 group had significantly higher levels of activation markers of coagulation and fibrinolysis (Group 1: D-dimer 2890 ng/mL, SFMC 9.00 mg/100 ml, group 2: D-dimer 1286 ng/mL, SFMC 5.3mg/100ml $p = 0.02$ and $p < 0.0001$, respectively). In patients of the 1 group premature births occurred significantly more often: in 7 women (41.2%), while in group 2 – in 1 (5%) ($p = 0.014$). Also in group 1 there were significantly more children born with growth retardation (group 1 – 6 children (35.3%), Group 2 – 1 child (5%), $p = 0.033$).
Conclusions: The use of plasmapheresis in patients with RM and hereditary thrombophilia can improve pregnancy outcomes.

P229 Associazione tra malattie reumatiche autoimmuni e ipotiroidismo autoimmune subclinico diagnosticato al primo trimestre di gravidanza

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Premessa: Le patologie autoimmuni reumatiche e tiroidee sono spesso associate, con sintomi e patogenesi immunitaria simili. Entrambe aumentano il rischio di eventi avversi in gravidanza. Pochi soni i dati in letteratura sulla frequenza dell'associazione tra malattie reumatiche e tiroidee autoimmuni durante la gravidanza e sulla positività di anticorpi antinucleo (ANA) in pazienti affette da patologia tiroidea autoimmune. Questo studio indaga la prevalenza di malattia reumatica autoimmune in pazienti gravide affette da ipotiroidismo autoimmune con diagnosi al primo trimestre di gravidanza e l'impatto sulla riproduzione.
Metodi: Sono state arruolate 3450 donne al primo trimestre dal 2009 al 2013 e screenate per ipotiroidismo autoimmune e per la presenza di patologie reumatiche autoimmuni mediante un questionario e il dosaggio autoanticorpale.
Risultati: A 3% delle pazienti arruolate si è diagnosticata una patologia tiroidea autoimmune con ANA positivi nel 16.9% dei casi. Tra i casi il 26.4% avevano sintomi ascrivibili a una malattia reumatica; di questi al 17.8% si è diagnosticata una malattie reumatica autoimmune. Le patologie autoimmuni tiroidee erano associate significativamente a un maggior rischio di preeclampsia, restrizione di crescita intrauterina e di complicanze ostetriche in toto rispetto ai controlli e a un aumentato indice di pulsatilità delle arterie uterine, suggerendo il coinvolgimento di una placentazione anomala. La positività agli ANA si associava a complicanze ostetriche di grado moderato/severo nelle pazienti affette da patologia tiroidea autoimmune (OR 9.65).
Conclusioni: Le malattie autoimmuni del connettivo si associano spesso a patologie tiroidee autoimmuni con diagnosi nel primo trimestre di gravidanza. La presenza di autoimmunità tiroidea e l'ANA positività aumentano in modo indipendente il rischio di eventi avversi in gravidanza.

P230 The metabolic syndrome during the menopausal transition

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Background: The prevalence of metabolic syndrome (METS), and its components, increases after the menopause and as women age; however, most research focuses on the METS after the menopause.
Objective: To determine the prevalence of the METS (Modified ATP III criteria) and its components in mid-aged women and compare results in each menopausal stage.
Method: This is an ongoing cross-sectional study reporting preliminary data of 127 pre-, peri, and postmenopausal women aged 40–65, invited to participate in a METS screening program. Weight (kg), height (m), body mass index (BMI, kg/m2), waist circumference (cm) and blood pressure were registered. In addition fasting HDL-C, triglyceride and glucose levels were determined.
Results: For the whole sample, median [IQR] age was 50 [9.0] years, prevalence of the METS 15% and 3.9% used hormone therapy. A 26% were pre-, 16.5% peri-, and 57.5% postmenopausal. Abdominal obesity and hypertension were the two main components of the METS among all participants and only among those with the METS. Prevalence of the METS and four of its components did not differ when menopausal stages were compared; nevertheless, abdominal obesity showed a significant increasing trend through the different stages.
Conclusion: In this preliminary data, while the prevalence of the METS did not differ according to menopausal stage, obesity an important feature of the syndrome increased throughout the stages.

P231 Pregnancy outcome was similarly adverse in adolescent mothers with severe preeclampsia independent of their age

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Objetive: To describe pregnancy outcomes (maternal and neonatal) among singleton adolescent pregnancies complicated with severe

preeclampsia in a low income setting hospital and compare results according to age.
Methods: Maternal and neonatal outcome of 213 adolescent mothers complicated with severe preeclampsia delivering at the Enrique C. Sotomayor Obstetrics and Gynecology Hospital (Guayaquil, Ecuador) were analyzed and compared according to their age (16 or less years, $n = 82$ vs. 17–19 years, $n = 131$).
Results: Cesarean section rate was high in both studied groups; otherwise, obstetrical outcome did not differ and there were no maternal deaths or severe complications. Neonatal outcome was adverse in the two groups evidenced by high rates of preterm birth, small for gestational age and low birth weight infants, low first minute Apgar scores and admissions to neonatal intensive care; however, not significantly different between analyzed groups. There was a non-significant trend for more neonatal deaths in the 17 to 19 age group.
Conclusion: Pregnancy outcome in this adolescent population with severe preeclampsia was similarly adverse, independent of maternal age.

P232 Diabetes insipidus in pregnancy: a case report

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Diabetes Insipidus (DI) is a heterogeneous clinical syndrome of disturbance in water balance, characterized by hypotonic polyuria and polydipsia. There are two subtypes of dibetes insipidus: central or hypothalamic DI: due to relative (partial DI) or absolute lack of arginine vasopressin (complete) nephrogenic DI: due to partial or total resistance to the renal antidiuretic effects of arginine vasopressin. Diabetes insipidus is a rare complication of pregnancy and may be a prosecution of the syndrome discovered before pregnancy or it may appear for the first time in pregnancy, generally in the third thrimester, and remits spontaneously 4–6 weeks post partum. The physiological changes associated with pregnancy, such as decreased thirst threshold, enhanced vasopressinase secretion with reduced vasopressin secretory capacity, increased degradation of vasopressin by placenta-derived vasopressinase, may be predisposing factors for diabetes. Therefore, a subclinical central diabetes insipidus may become clinically apparent during pregnancy when vasopressin degradation by placenta occurs and adequate compensatory increase in vasopressin synthesis and release does not. The treatment of choice of DI is desmopressin. We present a case of Partial DI complicating pregnancy. A 32-year-old woman, affected by partial central DI since three years, was referred in the 38th week of her first single- gestation for polyuria and polydipsia. Her disease was welll controlled, until that moment, by DDAVP 160 mcg die. The fetus was well being . Laboratory data not revealed abnormal values. At 39 weeks of gestation we induce labour with dinoprostone 10 mg, because of a severe discomfort of the patient for the onset of insomnia and irritability caused by worsening polyuria. A cesarean section was performed because fetal heart rate monitoring revelead a loss of variability and persistent tachicardia. A male fetus weighing 3390 g was delivered, without complications.

P233 Gestational weight gain (GWG) is an independent risk factor for adverse pregnancy outcome in women with gestational diabetes (GDM)

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Introduction: Pre-pregnancy body mass index (BMI), obesity and gestational weight gain (GWG) are independent risk factors for an adverse pregnancy outcome. All these conditions are associated with a rising occurrence of Large for gestational age (LGA) babies and foetal macrosomia, a rising occurrence of Caesarean Sections and shoulder dystocia. The aim of the present study is to investigate if in women affected by GDM with an optimal glycaemic control the eGWG is a risk factor for adverse obstetrical outcome independently from pre-pregnancy BMI.
Materials and Methods: 3508 Women with a singleton pregnancy were followed in our tertiary referral centre. 283 Women had GDM with an optimal glycaemic control. Excessive GWG was defined according to the 2009 guidelines of the Institute of Medicine (IOM) for each pre-pregnant BMI class.
Results: Ninety-three women (32.9%) demonstrated an eGWG; they had a significantly higher incidence of LGA infants, macrosomia and hypertensive disorders of pregnancy. Furthermore, mean birth weight and mean birth weight percentile, were increased in this group respect to women with a normal GWG. By a multivariate logistic regression, both pre-pregnant BMI and eGWG resulted to be independent risk factors for macrosomia and LGA after adjusting for other risk factors.
Conclusions: Our principal findings about eGWG related to indices of a pathological fetal growth (rate of LGA, macrosomia). These data are novel in testing the importance of GWG in a population of women at high risk for the presence of GDM intensively managed during pregnancy. When a GDM occur, GWG could be the only modifiable risk factor. Our data suggest that an improved obstetrical outcome can be achieved using an intensive control of GWG for all women with diabetes, irrespective of antenatal BMI.

P234 Forming of neutrophil extracellular traps in cervical mucus of preterm labor patients

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Context: Neutrophils participate in the development of labor. Recently it has been found that stimulated neutrophils can produce extracellular structures called neutrophil extracellular traps (NETs). However, the role of NETs in the development of premature birth is not clear yet.
Objective: To study the ability of neutrophils to form NETs in cervical mucus of patients with threatening preterm labor in 23–34 weeks of gestation.
Methods: Cervical mucus was stained with Sytox Green and Blue Evans according to the manufacturer's instructions. Drop of the mucus staining was placed in the middle of a slide and covered with a coverslip. Neutrophils and NETs were visualized using a fluorescent microscope with fluorescent filter excitation 490 nm and emission 520 nm.
Patients: The main group consisted of 60 patients with singleton pregnancy and threatened preterm labor in 23–34 weeks of gestation. These group was divided into 2 subgroups: 16 patients whose pregnancy ended in spontaneous preterm birth in 34.6 (31.6–36.2) weeks (1a subgroup) and 44 patients with term birth in 39.2 (38.6–40.1) weeks (1b subgroup). The control group consisted of 20 female with normal pregnancy that ended in birth in 39.3 (38.4–39.6) weeks.
Main Outcome Measures: We counted 100 morphological units that included neutrophils and NETs and calculated the proportion of NETs.
Results: The percentage of NETs was significantly higher in cervical mucus of 1a subgroup [18% (13–20%)] compared to 1b subgroup [12% (8–18%), $p < 0.05$] and control group [10% (7–15%), $p < 0.05$]. Elevated NETs found in the present study may indicate their possible role in the development of premature birth.
Conclusions: Spontaneous preterm birth is characterized by the elevation of neutrophil extracellular traps in cervical mucus. Women with term delivery had no abnormalities in the percentage of neutrophil extracellular traps.

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P235 Education in pregnancy with diabetes (DBTG)

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Background: Women with gestational diabetes have an RR of 4.69 for developing type 2 diabetes at 5 years of pregnancy and doubles to 9.34 beyond 5 years postpartum. Eliminated the major risk factors could be envisaged ¾ load.
Objective: To establish the degree of recognition of women DBTG pathology.
Materials and Methods: 46 Patients diagnosed with DBTG: DBTG sample of patients was taken into the DBT and Nutrition Service of Hospital JR Vidal de Corrientes, Argentina, in 2012.
Patients – Intervention: We evaluated: perinatal outcomes, many patients who were retested at 6 weeks postpartum.
Main Measured Results: Age was evaluated insulin therapy, RN weight, weight gain during pregnancy, obstetric complications, complications of RN patients and retested. Average age: 25.6 years results ($R = 20–42$); 74% ($N = 34$) requiring insulin therapy, 26% ($N = 12$) diet only; average weight gain was 3 kg ($R = 1$ to 16 kg), 11% ($N = 5$) increased more than 9 kg and 89% ($N = 41$) increased from 1 to 9 kg; 2% ($N = 1$) presented eclampsia and 9% ($N = 4$) had induced hypertension; 19% ($N = 9$) they attended retesteo, while the remaining 80% ($N = 37$) did not: RN weight: 13% ($N = 6$) were APEG more than 4 kg, 15% ($N = 7$) were lower PEG pesos to 2.800 kg and the remaining 72% ($N = 33$) were PAEG; only 6.4% ($N = 3$) hospitalized in NICU, 93.6% ($N = 44$) rooming.
Conclusion: The lack of awareness of the disease to a woman with DBTG exposed, forcing us to implement a collaborative work, where we will try to improve the quality of care and perinatal outcomes in maternity hospitals in Argentina and get pregnant acquire knowledge, skills and attitudes in managing their condition.

P236 Subchorionic hemorrhage treatment with high-dose progestogens

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Objective: The objective of the study was to evaluate the efficacy of progestogenic therapy for the prevention of spontaneous abortions in patients with subchorionic hemorrhage.
Methodology: The study carried out in obstetric unit in Misurata maternity hospital over a period of one year from Jan 2013 to Dec 2013. One hundred pregnant women with bleeding and ultrasonographic evidence of subchorionic hematoma were treated with oral dydrogesterone 50 mg/day. Only cases in which the embryo was viable were included. The follow-up included ultrasonography and intravaginal examination.
Results: Of the 100 pregnancies, 90 had a favorable evolution with maintenance of pregnancy. The abortion rate was therefore 10%, as most cases had large-volume hematomas at the first visit and thus a poor prognosis. In conclusion, the marked immunomodulatory effect of dydrogesterone in maintaining a T helper-2 cytokine balance giving a substantial shift in the ratio of Th1/Th2 cytokines means that it is a good choice for preventing abortion in women suffering from subchorionic hemorrhage.

Keywords

Dydrogesterone, progestogens, subchorionic hematoma

P237 How do young type 1 diabetic females see conception?

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Context: Preconceptional management in type 1 diabetic patient is a crucial phase in diabetic pregnancy. Less than a half of diabetic pregnancies are programmed. Diabetes and materno-fetal mortality weighs heavily in our context. For that, prevention actions represent a priority.
Objective: The objective of the study is to evaluate the perception of conception in young diabetics female with a second aim to integrate pre-conception education at an early stage of education programs.
Materials and methods: A group of type 1 diabetic who are followed in our department were contacted by phone. Anthropometric data as well, diabetes history and opinions about diabetes pregnancy were collected.
Results: A sample of 33 patients have been contacted by phone. The mean age was 18.2 years, with an average duration of diabetes of 7.3ans. 96.6% of patients were nulliparous singles. The average of the last A1C was 9.8%. All patients had reported never having had information about conceptional preparation in a diabetic woman. 66.6% said that the congenital malformations are not potential complications of diabetic pregnancy. Only 43.7% knew that macrosomia is a potential complication of diabetic pregnancy. Preterm delivery was recognized as a complication of diabetes in 31.2% of cases. 100% said that neonatal diabetes is a possible complication when the mother is diabetic.
Conclusions: A huge lack of knowledge among our young diabetic patients had been noted. A potential reason could be the inertia of care providers to initiate conceptional question with this group of patient. Furthermore, the conception is still a taboo subject despite an average level of education. Such results will certainly have an impact on the evolution of practices.

P238 Life experience of gestational diabetic pregnant women during pregnancy: a phenomenological study

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Objective: This study was planned to better understand life experience of the gestational diabetic pregnant women and and to provide contribution to the literature.
Materials and Methods: This phenomenological study was conducted with 11 gestational diabetic pregnant women who presented for control to the antenatal polyclinic of a Medical Faculty. The data were collected through the depth interview technique using pregnant identification forms and semi-structured question forms. With written consents received from the pregnant women, the responses were recorded with a tape recorder.
Results: Mean age of pregnant women were 33.7 ± 4.6 years and no one took insulin. Five themes were defined in this study, including the reactions to the diagnosis of gestational diabetes (GDM), life style changes, causes of GDM, coping methods and looking to the future. Frequently reported reactions included fear, anxiety and confusion. All of them stated that they started a strict diet, they were nervous and stressful, experienced weight loss and their urinary frequency was increased. At the same time, they reported that they had to increase

monitoring of the fetal movements and frequency of control visits. The pregnant women reported that, to become pregnant in an advanced age, not to care too much to their nutrition and genetic factors were effective on gestational diabetes they developed. They stated that, they benefited from diet and walking, drinking plenty of water and frequent breathing exercises in order to cope with this situation. Again, all of them included in this study reported that, this complication will end with the delivery and post-pregnancy follow-up post-pregnancy is not necessary.
Conclusion: Health care professionals should inform pregnant women about the GDM during and after the pregnancy and support and psychologic support them.

P239 Pregnancy outcomes in patients with type 1 diabetes on insulin pump therapy, depending on the stage of nephropathy

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Objective: To evaluate the terms of delivery in patients with type 1 diabetes, depending on the initial state of the kidneys.
Materials and methods: The study involved 97 pregnant women with type 1 diabetes mellitus (DM 1), receiving insulin in a constant subcutaneous insulin infusion (CSII) using a portable dispenser (pump). Depending on the level of daily urinary albumin excretion, patients were divided into three groups: group 1 with normal urinary albumin excretion, group 2 – with microalbuminuria, group 3 – patients with proteinuric stage of diabetic nephropathy. Statistical significance of differences was assessed at $p < 0.05$. All patients had the same level of physical activity. The dose of basal insulin was titrated under the control CGMS. We estimated the dates of delivery, albumin excretion in daily urine before the pregnancy, and then up to 12 weeks, 22–24 weeks, 30–32 weeks of gestation. All patients were matched for age, weight, level of glycated hemoglobin, the degree of compensation of DM ($p > 0.05$).
Results: In the group 1, the term of delivery was 38 (37; 38.5 weeks) in Group 2 – 37.5 (35; 39) in Group 3 – 34 (31; 37) weeks. In group 1 and 2 the terms of delivery were comparable ($p = 0.26$). Statistically significant differences were found in the group 1 and 3 ($p = 0.00036$) and group 2 and 3 ($p = 0.017$).
Conclusion: The outcome of pregnancy in patients with type 1 diabetes who are on pump therapy depends on the stage of nephropathy.

P240 Conservative management of advanced cervical ectopic pregnancy in 12th week of gestation

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Context: management of an advanced cervical ectopic pregnancy is presented. The infertile patient was achieved pregnancy using ICSI, It was diagnosed by cervical examination, vaginal and abdominal ultrasound, then treated conservatively, using intra amniotic sac and intra muscular administration of methotrexat, injection of diluted vasopressin in the location of cervical vessels and distention of Foley catheter balloon, followed by evacuation of conception products by cervical curettage.
The utilization of various procedures in the treatment resulted in preserving the patient's uterus and her fertility potential.

Keywords
Cervical ectopic pregnancy, methotrexat, vasopressin, uterine preservation

P241 Selection of umbilical cord blood donor: midwife vs. Transfusionist: study investigating the ideal organizational model (Survey on ideal organization model).

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Background/Aims: The cord blood (CB) donation is to be considered a very important resource, since the use of hematopoietic stem cells contained in cord blood is well established for the treatment of many diseases (both hematologic or not). In order to make use of this important resource, the donated CB units need to be safe and suitable for the recipent: to this purpose the first essential step is to correctly evaluate the clinical history of woman/couple to assess whether that path is appropriate or not. The purpose of this study is to evaluate which is the best organizational model for most appropriate and cost-effective CB donor selection process, between one based on transfusionist and the other based on midwife's figure.
Methods: This study compares the activities in five hospitals: we have clustered four of them, based on transfusionist's figure in a so called 'Florentine area' (Nuovo S. Giovanni Di Dio, Santa Maria Annunziata, Borgo San Lorenzo and Empoli), while Pistoia's hospital is the only one based on midwife's figure. The survey covers a period of time from June 2010 to July 2012.
Results: According to data collected, midwife's figure based model proves to be successful, as more women are selected to participate to the process. Furthermore, the causes of women/couples' exclusion can be better traced and appear to be more standardized. Besides, midwife's based path is easier and cost-effective for internal managment; traditionally, midwife's figure is closer and assists woman from whole pregnancy to puerperium, hence being most suitable to easily advise women on CB's donation.
Conclusions: Evaluating and demonstrating midwives' importance in CB's donation path and specially in donors' selection, our study came to the conclusion that a new model is needed. We believe the midwife's figure based model, as is currently being planned in Pistoia's USL 3 hospital, is the ideal one, allowing the two figures, midwife and transfusionist, to fully coexist, integrate and collaborate.

P242 Vitamin D deficiency in pregnancy

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Context: Current data suggest maternal vitamin D deficiency during pregnancy as a significant risk factor for several conditions affecting fetal health.
Objective: Determine vitamin D levels in pregnant women in winter.
Method: The study is a prospective descriptive analysis. The electronic registration of clinical laboratory and medical records were used as database. Samples were taken between August 1st and September 30th, 2015.
Patients: 55 Patients between 18 and 45 years old were studied including pregnant women of any gestational age, parity and number of fetuses; 16 patients were tested in the first trimester of pregnancy, 23 in the second trimester and 16 in the third trimester. All patients receive prenatal care in Central Military Hospital.
Intervention: Determination of serum levels of 25-hydroxyvitamin D in pregnant women as part of the prenatal care tests. (Deficiency levels <20 ng/dl; Insufficiency levels 20.0–30.0ng/ml; Sufficiency levels 30.0–100.0 ng/ml)
Main Outcome: Hypovitaminosis was found in every patient.
Results: Results show deficiency levels below 16ng/dl in all cases. In terms of pregnancy complications, 13 patients suffer from these conditions at the time of the study: gestational diabetes (6),

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hypertensive disorders (4), hypothyroidism (2), and fetal malformation diagnosed in an ultrasound (1). In all these cases vitamin D levels were below 6ng/ml.
Conclusions: We observed a high incidence of decreased serum vitamin D concentration in pregnant patients in winter. According to this data, vitamin D supplementation should be prescribed to every patient included in this study. Lower serum vitamin D levels were found in patients with other conditions. Increasing the sample size and conducting a follow up study is mandatory to get accurate results; also, the analysis will be repeated during the summer months to complete the results.

P243 A case of intrauterine twins with a concomitant cervical pregnane our experience

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Aims: In this case report we have described the successful management of an intrauterine dichorionic twin pregnancy associated with a simultaneous cervical embryo implantation.
Methods: The improvements in *in vitro* fertilization techniques have increased the pregnancy rate in couples with reproductive problems, but have also caused a growing incidence of multiple pregnancies and pathological conditions such as ectopic cervical implantation. The cervical pregnancy was interrupted by intracardiac injection of 2cc of KC1 without embryo removing at 12 weeks and 4 days. Subsequent Shirodkar cervical cerclage was positioned at 2 weeks and 5 days.
Results: Healthy and viable twins were delivered in the third trimester by conservative caesarean section at 28 weeks and 5 days preserving patient fertility for future pregnancies.
Discussion: The occurrence of cervical pregnancy is potentially life threatening. In the past hysterectomy was the only available therapeutic option to save the woman's life. Currently pharmacological and surgical methods are available, with the possibility to preserve the fertility of the woman. Medical methods include local and/or systemic methotrexate treatment with or without chemoembolization or local KC1 injection. Alternatively, surgical interventions consist in cervical dilatation followed by curettage, aspiration without dilatation, Shirodkar-type cervical cerclage and resectoscopy. In our case, the presence of such a high risk condition and the desire of the parents to continue the pregnancy made the counselling and management challenging. Early diagnosis is crucial for treatment options. It reduces drastically the patient's morbidity and mortality and improves the outcome of the pregnancy. We hope that our experience in applying combined (medical and surgical) technique could be helpful when such an exceptional condition is diagnosed.

P244 Vitamin D supplementation in pregnancy

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Context and Objective: Low vitamin D levels during pregnancy have been associated by recent studies with pregnancy complications like preeclampsia, intrauterine growth restriction, gestational diabetes, primary caesarean section and preterm delivery. Despite this world wide problem, there is no consensus about optimal vitamin D levels and the international recommendations about Vitamin D supplementation during pregnancy vary widely, proposing between 400 IU/d and 2000 IU/d of Vitamin D3 independently of their geographical situation. This work compares the approaches in different countries on different latitudes and resumes the knowledge of clinical significance of vitamin D in pregnancy.
Methods: Comparison of recommendations concerning vitamin D supplementation in pregnancy of 7 european countries, USA, Canada, Australia, Marocco. Review of recent publications concerning vitamin D and pregnancy by pubmed research.
Results: The most recent (2012) Cochrane review on vitamin D supplementation for women during pregnancy reported a decrease of IUGR in supplemented women, but there is limited statistical significance and no evidence for prevention of other pregnancy complications was found. The authors conclude that further rigorous randomised trials are required to evaluate the role of vitamin D supplementation in pregnancy.
Conclusion: Vitamin D deficiency is a world-wide problem. Various pathologies have been associated with vitamin D deficiency, including adverse pregnancy outcomes. However, the benefit of supplementation concerning other organs than bone is not well established at present. Further studies are requested to evaluate the effects of vitamin D supplementation in pregnancy and to issue evidence-based guidelines.

P245 Effects of a lifestyle intervention during pregnancy and 1-year postpartum – results from the RADIEL study

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Context: Gestational Diabetes (GDM) identifies women with higher risk for type 2 diabetes (T2D). Lifestyle interventions have been effective in preventing T2D.
Objective: This study aimed to assess the effects of a lifestyle intervention (RADIEL) during pregnancy and 12 months postpartum on glucose metabolism, as well as body weight 1 year after delivery.
Methods: The RADIEL study was a multicenter randomized controlled trial that enrolled in early pregnancy women at high GDM risk, defined as having body mass index (BMI) $\geq$30 kg/m^2 and/or previous GDM.
Patients: Altogether 269 women were originally included. For the analysis of this study we included the 176 women who attended the 12 month postpartum visit.
Intervention: The subjects were randomized to either individual lifestyle counselling (n = 96) or control group (n = 80).
Main Outcome Measures: The primary outcome was glucose metabolism 6 weeks and 12 months postpartum, assessed by a 2-hour 75g OGTT.
Results: In the intervention group 1 (0.9%) of the participants had either impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or T2D 6 weeks postpartum compared to the control group, where 6 participants (7.0%) had abnormal glucose tolerance (IGT, IFG or T2D) (p = 0.026). 12 months postpartum 3 (3.5%) women in the intervention group and 7 (9.6%) in the control group had disturbances in their glucose metabolism (p = 0.188). Weight changes in both groups were similar and most women returned to their pre-pregnancy weight.
Conclusions: A lifestyle intervention aiming at prevention of GDM had a positive effect on glucose metabolism 6 weeks postpartum but although the results were similar in magnitude to those at 6 weeks postpartum, there was no statistical difference 1 year after delivery.

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P246 Application of 3D ultrasonography in analysis of fetal anomalies in Wolf Hirschhorn syndrome

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Background: Wolf-Hirschhorn syndrome is a rare chromosomal disorder caused by terminal deletion of the short arm of chromosome 4.
Objective: To present the results of morphologcal analysis by 2D/3D ultrasound of the fetus with multiple anomalies where Wolf-Hirschhorn syndrome was confirmed by amniocenthesis.
Methods: Pregnant woman aged 24 years was referred due to intrauterine growth restriction and suspicious multiple anomalies. Ultrasonographic examination was performed with transabdoiminal 4D 4–8 MHz probe at 22 weeks of pregnancy.
Results: Fetal biometric parameters were appropriate for 17 weeks and represented symmetric intrauterine growth restriction. Utilizing 3D and 3D multislice ultrasound, cleft lip and palate were detected on examination. On the right arm of the fetus, agenesis of radius and two fingers and thumb was detected. On the left arm, anomaly of fingers was detected. Fetal spine was normal. Due to decreased penetration of ultrasound only 4 chamber view of fetal heart was visualized and also fetal stomach and kidneys and bladder. Fetal right leg was hypoplastic, with short femur and tibia and club foot detected. Left leg showed shortened bones appropriate for 17 weeks. Club foot was also detected on left side. Fetus had male genitals. During fetal Doppler analysis, single umbilical artery was detected and in other fetal blood vessels hemodynamic parameters were normal. Wolf-Hirschhorn syndrome was confirmed later by amniocenthesis and pregnancy was terminated. Multiple fetal anomilies were confirmed after termination of pregnancy, on histopathological analysis.
Conclusion: Wolf–Hirschhorn syndrome was characterized by multiple fetal anomalies. In this case report we present a fetus which, besides standard facial anomalies had also marked anomalies on upper and lower extremities and also single umbilical artery.

P247 Role of matrix metalloproteinases in the manifestation of earlu and late preeclampsia

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Background: early preeclampsia is characterized by an abnormal trophoblast invasion while a late one is based on secondary changes of microcirculation caused by a metabolic syndrome. In an area of a fixation of a blastocyst syncytiotrophoblastic complexes are formed producing zinkevicius matrix metalloproteinases.
Aim: to establish the influence of the level of MMP on the gestations in which took place manifestation of preeclampsia.
Methods: We determined the level of matrix metalloproteinases-2 (MMP-2) and metalloproteinase-9 (MMP-9) in serum enzyme-linked immunosorbent assay. The study was undertaken on 118 pregnant women with severe preeclampsia before 34 weeks of gestation ($n = 48$) – 1st group; after 34 weeks ($n = 50$) – 2nd group; control group ($n = 20$) with physiological pregnancy.
Findings and interpretation: early preeclampsia, time-limited prolongation of pregnancy ($p \leq 0.05$) and mean time to delivery in 1st group from 3 to 72 hours, in 2nd group- from 8 hours to 7 days. The level of MMP type in 1st group was in 2 times lower (12.72 $\pm$0, ng/ml) than in 2nd group ($p < 0.01$). MMP-9: 1st group the average value 16.88 in $\pm$0.72 ng/ml, in the 2nd group 10.41 $\pm$ 1.02 ng/ml ($p < 0.01$). Comparison of the level of MMP type 9 in two groups and the control one did not give any significant.
Results: Presented pattern suggests that the determination of the level of MMP determines the risk of early preeclampsia for the timely diagnosis of pregnancy complications and to improve perinatal outcomes.

P248 Mitochondrial dysfunction in early and late onset preeclampsia

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Context: PE, a severe pregnancy-specific disease, is a state of widespread mitochondrial dysfunction of the placenta. But its peculiarities in early (EOPE) and late (LOPE) PE is not clear yet.
Objective: To determine differences in the severity of placental mitochondrial dysfunction in EOPE and LOPE.
Patients: 90 Patients 18–43 yrs old were divided into 3 groups: 30 – with EOPE, 30 – with LOPE and 30pts – as control. Samples of placental tissue were obtained during C-section.
Methods: Fluorescent and confocal microscopy, differential spectroscopy, respirometry, gel-electrophoresis, WB-analysis.
Results: C-section was done at 31.5$\pm$3.1in EOPE, at 37.9$\pm$1.2 in LOPE and at 39.2$\pm$0.7wks in control group. The respiration rate in placental mitochondria was significantly higher in EOPE compared to LOPE and controls (11;9 and 7 nmol/min*mg protein, resp.) ($p<0.05$). ADP/O ratio equaled 8.88; 9.92 and 6.11, resp. Mitochondrial response to endogenous uncouplers decreased in both PE groups ($p<0.05$) and correlated with increased ROS production. The mitochondrial quantity detected by expression level of protein VDAC1 was almost similar in all groups. MT-ND5 core subunit expression was highest in EOPE (1.8; 1.1 and 1.0 a.u.,resp.) group ($p<0.05$) while the quantities of MT-ATP8 subunit of ATPase were almost similar (1.3;1.1and 1.0 a.u., resp.). The antiapoptotic protein Bcl2 expression decreased in EOPE compared to LOPE and control (0.6; 1.3 and 1.0 a.u., resp.) groups ($p<0.01$). But expression of antiapoptotic protein Bax was not changed: 0.8; 1.0 and 1.2 a.u., respectively.
Conclusion: In cases of EOPE there were statistically increase respiration rate and ROS production, lead to activation of apoptogenic factors and cause oxidative stress in placental mitochondria. These markers showed greater severity of oxidative stress in EOPE.

P249 Expression of beta-oxidation related genes in preeclampsia-like model under hypoxic condition in vivo and in vitro

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Context: Preeclampsia (PE) is a disorder of pregnancy characterized by high blood pressure and large amounts of protein in the urine. PE is thought in many cases to be caused by a shallowly implanted placenta that becomes hypoxic. The hypoxic condition during the pregnancy can result from a failure at any stage in the delivery of oxygen to the cells.
Objective: To investigate correlation between PE and beta-oxidation.

Methods: ACADVL, beta-oxidation related gene, was detected by gene-fishing technology using the placenta of human. *In vitro* and *in vivo* PE models were made by exposing the BeWo cells and mice placenta to hypoxic stress. The BeWo cells were cultured at 37°C under 1% O2, 5% CO2, and balanced with N2. Pregnant mice were maintained from GD 6.5 to GD 17.5 under 11% O2, 5% CO2, and balanced with N2. The expression of beta-oxidation related genes (ACADVL, EHHADH, HADH, ACAA1) were observed under hypoxic condition at mRNA and protein levels.
Results: The expression of genes known as biomarkers for hypoxia, HIF-1α, was increased in BeWo cells and mouse placenta which induced PE. The beta-oxidation related genes, ACADVL expression was significantly increased by hypoxic stress both BeWo cells and mouse placenta.
Conclusion: The elevated level of HIF-1α is indicating that our experimental conditions closely mimicked PE. These results indicate that changes of beta-oxidation related genes are correlated with PE induced hypoxic condition.

P250 Gestational diabetes mellitus – impact on bone mineral density changes 24 months postpartum

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Context: Previous studies have shown a detectable fall in bone mineral density (BMD) during pregnancy which subsequently recovers in the postpartum period. The impact of gestation diabetes mellitus (GDM) remains controversial.
Objective: To evaluate the bone mineral density (BMD) changes within 24 months after delivery and the relationship to GDM during pregnancy.
Methods: Patients diagnosed to have GDM during pregnancy (WHO 2006 criteria) over a period of 6 months were compared with uncomplicated singleton pregnancies. Standard BMD measurements using dual energy X-ray absorptiometry (DXA), and volumetric BMD of the distal limbs using peripheral quantitative computerized tomography (pQCT) techniques were performed within 4 weeks after the index delivery and then repeated between 21 and 24 months postpartum.
Results: A total of 17 women with GDM in pregnancy were compared with 77 normal controls. Significant gains in BMD were observed between the two assessments in both groups. There were no significant differences in the gain in BMD in the lumbar spine (L2-L4), (+0.0352 vs. +0.036 mg/ cm^2), but the GDM group showed less gain in BMD in the neck of femur (0.0406 vs. 0.0687 mg/ cm^2, $p = 0.024$) and Ward's triangle (0.0092 vs. 0.029 mg/ cm^2, $p = 0.036$), while the trochanter (0.34 vs. 0.37 mg/ cm^2, $p = 0.52$) showed no differences. There were no differences in the core or total volumetric BMD changes of the distal radius and tibia. No significant differences in the interval BMD changes were observed between those whose postnatal OGTT remained abnormal ($n = 3$) or not ($n = 14$).
Conclusion: There were significant gains in BMD within 24 months after delivery in both the GDM and control women. Previous GMD status during pregnancy apparently had some negative influence on the rate of BMD recovery in these women, but the clinical significance remains uncertain.

P251 Combined organ-spearing treatment of women with cervical ectopic pregnancy

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Context: Frequency of cervical ectopic pregnancy (CEP) is less then 1% of all ectopic pregnancies; 1.7 on 10 000 pregnancies.
Objective: To evaluate the effectiveness of combined treatment for preserving fertility in young nulliparous patients with cervical ectopic pregnancy.
Methods: Combined therapy with preoperative methotrexate chemotherapy and minimal invasive surgery for preserving fertility; in one case laparoscopic ligation of a.iliaca interna was performed.
Patients: 35 Patients with cervical ectopic pregnancies (CEP).
Main Outcome Measures: Clinical protocol included transvaginal ultrasound investigation with transducer for color Doppler mapping, magnetic resonance imaging to visualize gestational sac, definition of the boundaries between the chorion and stroma of the cervix; definition of the blood flow intensity in the chorion, the definition of β-subunit of human chorionic gonadotropin (β-hCG) in serum in dynamics, general clinical research: clinical parameters, biochemical blood tests and hemostasis in the dynamics, diagnostic hysteroscopy and followed resectoscopy with material removed
Results: The term of pregnancy on admission ranged from 5 to 9 weeks of gestation and the average term was 6.1 ± 0.9 weeks. Patients with cervical pregnancy received methotrexate at an average of 50 mg/ every 48 hours, leucovorin administered at a dose of 6 mg after 28 hours after methotrexate injection. The total dose of administered methotrexate ranged from 200 to 300 mg.
Conclusions: The results of this study suggest that resectoscopic removing of embryo with previous cytostatic therapy with methotrexate in combination with leucovorin allows to save fertility in young women with early cervical pregnancy, the effectiveness of organ-spearing treatment of cervical pregnancy is 93.1%.

P252 Pregnancy after IVF with preeclampsia and perinatal sucesss

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Kogj Prishtine

Aim: We present a case of pregnancy after IVF with preeclampsia. Acording to the literature of pregnancy after IVF, there is a high risk for gemelar pregnancy,prematurity and preeclampsia.
Case report: Patient L.K,20 years old as admitted to the OB/Gyn Department, 26 weeks of pregnancy, status post *in vitro* fertilization,Rh incopatibilia.She presents with sudden headache associated to epigastric pain with a blood pressure of 160/90.She was admitted to our hospital with severe preeclampsia.Doppler flowmetry with an increase in placental resistance and oligohydramnios. Laboratory analysis:AST:300U/l,ALT:255 U/L,LDH:800,total protein 5.7g/dl,creatinine:0.80 mg/L,PLT:50.000mm3,prothrombin time: 18 sec. On the day of adission, a 24 hour urine collection revealed 600 mg of protein that increased to 1000 mg the next day. The blood pressure was controlled by intravenoz hydralazine infuzion at rate 5–10 mg/hr. On the day of delivery serum AST was 1300 U/L and serum ALT 2400 U.L. She delivered a 800 gr baby girll SC. The newborn girl was discharged when she reached a weight 2000 gr.

P253 Prooxidant-antioxidant homeostasis in women with a first episode of miscarriage

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One of the priorities of modern medicine is the protection of motherhood and childhood. It is known that the system of lipid peroxidation is one of the key metabolic systems of the body, the state of which depend on the structure and function of biological membranes, their availability regulatory impact. The purpose of work – assessment of the state of prooxidant-antioxidant system in women with a first episode of miscarriage. The study involved 60 women: the control group consisted of 30 healthy pregnant women, the main

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group – 30 women with a first episode of miscarriage in I trimester. Determination of the concentration of diene conjugates (DC), malondialdehyde (MDA) and catalase levels were determined spectrophotometrically using a spectrophotometer ''SF-46'', ''Solar'' PV1251C. In assessing the performance of lipid peroxidation in women with a first episode of miscarriage had significantly decreased concentrations of DC and MDA in 1.3 and 1.4 times, respectively. According to our data, the average values of catalase activity in blood plasma of pregnant women in the control group made 33.18±1.92 mmol H2O2/min/g Hb. In women, the main group catalase activity was 21.66±1.82 mmol H2O2/min/g Hb was significantly reduced relative to the control group ($p < 0.05$). Thus, the trigger factor in the initiation of interruption of the first pregnancy is the change in prooxidant–antioxidant homeostasis, and the severity of metabolic disturbances in the process of implementation of the redox desynchronosis is the impetus for the formation of violations of biochemical processes at the cellular, tissue, organ and organism level, which calls for development new therapies.

P254 Suprarenal mass in mother and foetus – imaging and differential diagnostics

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Context: Adrenal hyperplasia in mother and the prenatally confirmed adrenal mass in fetus complicated by perinatal asphyxia and postnatal development.
Objective: Prenatal imaging have led to an increased rate of diagnosis of suprarenal tumors. It is important to differentiate benign from malignant adrenal lesions. MRI is the modality of choice for differential diagnosis.
Patient: 22-Year-old primipara referred for assessment of fetal suprarenal mass at 27 weeks of gestation. In her medical history at the age of 20 years CT scan confirmed bilateral adrenal hyperplasia. The diagnoses of late CAH was not confirmed.In foetus a suprarenal cystic mass was confirmed with no blood flow. MRI confirmed cystic formation with haemorhagic content. Planned follow-up sonography was not performed due to praemature delivery at 35 week of gestation. Labour was complicated by perinatal asphyxia,foetus was delivered by forceps Apgar scores of 6/9. Catecholamins replacement and corticotherapy was iniciated.CAH was supposed and the newborn was transferred to the perinatology center.
Outcomes: Postnatal USG confirmed the adrenal multilocular tumor,no clinical neither laboratory sign of CAH. The corticosteroid treatment was sequentially reduced,no medical neither surgical intervention was needed.The newborn is led in endocrinological medical care.
Results: As mother so the baby stays in the ambulatory medical care with no specific diagnosis,with confirmed mass in adrenal gland, with no hormonal patological laboratory screening.
Conclusions: Diagnosis of neonatal suprarenal mass depends on prenatal USG, clinical manifestations, MRI. Dynamic observation of suprarenal mass by MRI and USG is means of differential diagnosis. While conservative therapy is suitable for adrenal hemorrhage, adrenal tumors need surgical excision. An appropriate initial assessment and a close follow-up in a specialized center.

P255 Can activation of TLR3 induce apoptosis in patients with miscarriages?

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Context: Viral infection is capable to activate innate immune response through TLR3 (Lange M.J., Misfeldt M.L., 2009). In our previous study (Lebedeva O. et al., 2013) it was shown, that expression of TLR3 in endometrium is significantly higher in patients with early miscarriages.
Objective: To estimate influence of TLR3 activation on apoptosis proteins in endometrium in patients with miscarriages and missed abortions.
Methods: Endometrial tissue was received by uterine abrasion. Diagnosis was confirmed by histological examination. Expression of mRNA of Toll-like receptor 3 (TLR3), death receptors 4 and 5 (DR4, DR5), TRIAL, caspases (CASP) 1, 3, 8 and 9 was performed by quantitative polymerase chain reaction (PCR). Statistical analysis was performed by Mann–Whitney test and Spearman test by Statistica 10.0 (Statsoft, USA).
Patients: 22 Women with spontaneous abortion (group I), 22 – with missed abortion (group II), 57 – patients with medical abortion (group III, control) on 6–10 weeks of pregnancy.
Results: Expression of TLR3 in patients with missed abortion was 2.4-fold higher, and with spontaneous abortion – 1.7 fold higher, than in control group ($p < 0.01$). Also 10-fold increase of expression of DR4 was observed in both groups with miscarriages ($p < 0.01$). In case of missed abortion 3-fold increase of CASP-1 and 2-fold increase of CASP-9 ($p < 0.01$), and in case of spontaneous abortion – 18-fold increase of CASP-3 mRNA expression ($p < 0.01$) comparing with control group was observed. There were no significant differences between group I and group II in expression of proteins. Expression of TLR3 mRNA in cases of missed and spontaneous abortions had only moderate correlation with TRAIL ($R = 0.66$; $p < 0.05$ and $R = 0.44$; $p < 0.05$), but not with other apoptotic proteins.
Conclusions: Increased expression of TLR3 does not relate to activation of apoptosis through DR4/DR5.

P256 Can TLR3 influence to p53 and p63 apoptosis pathways in early miscarriages?

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Context: P53 protein activates apoptosis, while p63 can also promote cell-cell adhesion and epithelial proliferation. Toll-like receptor 3 responsible for recognizing double-stranded RNA of viruses.
Objective: To define the role of TLR3 in activation of p53 and p63 apoptotic pathways in patients with early miscarriages.
Methods: Endometrial tissue was received by uterine abrasion. Diagnosis was confirmed by histological examination. Expression of mRNA of Toll-like receptor 3 (TLR3), p63 and p53 was performed by quantitative polymerase chain reaction (PCR). Statistical analysis was performed by Mann–Whitney test and Spearman test by Statistica 10.0 (Statsoft, USA).
Patients: 22 Women with missed abortion (I group), 22 – with spontaneous abortion (II group), 57 – patients with medical abortion (III group, control) on 6–10 weeks of pregnancy.
Results: Expression of p53 and p63 was significantly higher in patients with missed abortion compared with control group. Expression of TLR3 had strong negative correlation with p53 ($R = -0.99$; $p < 0.05$). No significant correlation of TLR3 with expression of p63 was observed. In patients with spontaneous abortion only higher expression of p53 was observed. No significant correlation of p63 and p53 with TLR3 was discovered.
Conclusion: Thus, in patients with missed abortion TLR3 can influence to apoptosis, but not to cell-cell adhesion, through p53 pathway activation. In women with spontaneous abortions TLR3 does not influence to p63 and p53 pathways.
Supported by grant of Russian foundation of basic research №15–34–50467.

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P257 Obstetric and perinatal outcome in patients with thyroid dysfunction associated with pregnancy-induced hypertension

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Objective: Determine the obstetric and perinatal outcome in patients with Pregnancy-induced Hypertension (PIH) and its association with thyroid dysfunction.
Patients: We studied a group of 80 patients with the diagnosis of pregnancy over 20 weeks and PIH, which TSH, T3 and T4 where performed.
Methods: Descriptive study, cross-sectional and prospective study of 80 patients. They were divided into 2 groups; those with the diagnosis of thyroid dysfunction and Euthyroid
Main Outcome Measures: We evaluate the delivery, gestational age, Obstetric and Neonatal complications
Results: It was noted that the higher prevalence of PIH 41.25% (33/80) corresponded to Severe Preeclampsia. Of these patients affected by hypertensive disease, 15% (12/80) had thyroid dysfunction corresponding 10 with subclinical hypothyroidism, 1 with hypothyroidism and 1 with Hyperthyroidism. In relation of delivery, obstetric complications, gestational age there were not significant differences; however we found differences in birth weight in the group 1 with an average weight of 2.505 $\pm$ 0.62 kg. vs. group 2 with 2.822 $\pm$ 0.68 kg ($p < 0.01$); also we found that there were more newborns classified as Small for Gestational Age (SGA) in group 1 with 50% (6/12) vs. group 2, 25% (14/56) ($p < 0.01$) and in the maternal age group 1 with 27.5 years vs. 23.9 years group 2 ($p < 0.01$) .
Conclusions: The prevalence of thyroid dysfunction in was found outside the usual levels. There was no association in the maternal and fetal morbidity, however significant difference was found in the age of the patients, newborn weight and more SGA patients. This could mean that the thyroid dysfunction is associated with neonatal adverse results.

P258 Hereditary thrombophilia in the development of complications of gestation in pregnant women with pre-eclampsia

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Context: The risk of preeclampsia is primarily due to complications.
Objective: To determine the role of genetic thrombophilia in development gestation complications in pregnant with PE.
Methods: This prospective, cohort study looked at the association between hereditary thrombophilia and gestational complications on pregnant with PE. With PCR were detected genetic polymorphisms of coagulation factors and fibrinolysis (1691 G→A FVL, 20210 G→A prothrombin, 5G/4G PAI-1, 455 G→A fibrinogen β), endothelial dysfunction (192 Q→R PON-1, 677 C→T MTHFR), a regulator of blood pressure (235 M→T angiotensinogen II). Statistical analysis was performed using chi-square test, relative risk with 95% confidence interval.
Patient(s): 44 Pregnant women with PE and complications (premature detachment of normally situated placenta, eclampsia, HELLP- syndrome, FGR, antenatal fetal death, fetal distress) and 87 pregnant women with PE without complications (comparison group) were examined.
Result(s): Clinical and medical history factors developing obstetric and perinatal complications in pregnant women with PE include: first birth, symptoms of pre-eclampsia in the term less than 28 weeks of pregnancy, pre-eclampsia severe or moderate severity, duration of pre-eclampsia more than 5 weeks. Marker of predisposition to development of obstetric and perinatal complications in PE are the following genotypes: 1691 GA FVL – increases the risk in 2.9 times (95% CI 1.94–4.33); prothrombin 20210 GA – in 2.36-fold (95% CI 1.54–3.6); prothrombin 20210 AA – in 3.12-fold (95% CI 2.4–4.0); a combination of three or more pathological polymorphisms – in 2.58 times (95% CI 1.64–4.05).
Conclusions: These factors must be considered to determine the pregnant women at high risk of developing complications in PE.

P259 Pro-active follow-up of pregnant women with asymptomatic autoimmune thyroid disease

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Context: Maternal hormones are essential for normal fetal development during pregnancy. Autoimmune thyroid disease is a frequent pathology in our iodine-replete region.
Objective: Evaluating the occurrence of subclinical hypothyroidism (SCH) in cases with known autoimmune thyroid disease, but euthyroid state prior to pregnancy; assessing the association between supplemental treatments and the outcome of the pregnancy.
Methods: The study is a prospective interventional controlled study with two cohorts.
Patients: The interventional cohort consisted of 109 pregnant women with known autoimmune asymptomatic thyroid disease, without any previous LT4 treatment. The control group, with unknown thyroid disease, was age-matched.
Interventions: After the pregnancy was confirmed, monthly evaluation of TSH, FT3, FT4 was performed. Offspring evaluation was made at birth.
Main outcome measure: Monthly adjustments of supplemental LT4 doses (12.5 or 25 μg), depending on the most recent and previous TSH values
Results: 88.8% of the women developed SCH in the first 4 weeks of pregnancy. Average prescribed LT4 doses increased with pregnancy progression. When TSH values were in optimal range during the whole pregnancy, there were no significant differences regarding the number of gestational weeks, weight or length at birth between interventional group and controls. As a consequence of supplemental therapy, the incidence of pregnancy loss was very low (2 cases – 1.85%).
Conclusion: The correct evaluation of asymptomatic autoimmune disease is required in case of pregnancy. The prevalence of SCH in such cases is high, despite the euthyroid state before pregnancy. An individualized treatment is recommended, with a careful follow-up of hypothyroid pregnant women and a systematic testing of thyroid function. This pro-active approach ensures a positive clinical outcome for the fetus.

P260 Is there an association between subclinical hypothyroidism and preterm uterine contractions? A prospective observational study.

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Objective: We aimed to investigate the association between subclinical hypothyroidism and preterm contractions.

Methods: A prospective study evaluating parturients without know thyroid function abnormality, who presented with preterm uterine contractions. All patients underwent obstetrical evaluation as well as laboratory evaluation of Thyroid Stimulating Hormone (TSH) and Free Thyroxin (FT4). Women with preterm contractions were compared with women at the same gestational age without preterm contractions.
Patients: Parturients between 23 + 0/7 and 34 + 6/7 weeks of gestation without know thyroid function abnormality, who presented with preterm uterine contractions.
Main outcome measure: Thyroid function abnormalities and uterine contractions.
Results: No association was found between preterm contractions and sub-clinical hypothyroidism. Rate of spontaneous preterm delivery (PTD) were comparable between those with abnormal and normal thyroid function tests. However, when excluding indicated PTD, patients in the study group had a higher rate of spontaneous PTD (24.7% vs. 9.6%, $p = 0.03$). Patients with past PTD and preterm contractions had higher rates of hypothyroxinemia compared with patients with no past PTD (54.6% vs. 19.0% and 31.2%, $p = 0.001$), and patients with past PTD (regardless of the presence or absence of preterm contractions) had higher rate of sub-clinical hypothyroidism compared with patients with preterm contractions and no past PTD (59.1% and 66.7% vs. 31.6%, $p = 0.017$).
Conclusions: No association was found between preterm uterine contractions and subclinical hypothyroidism in the entire cohort, except for patients with preterm contractions and a history of past preterm delivery. This specific group of patients might benefit from thyroid function evaluation.

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P261 Gestational diabetes mellitus altered the relationship between maternal and fetal thyroid function

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Context: It is unknown if the relationship between fetal and maternal thyroid function in normal pregnancy is altered by maternal gestational diabetes mellitus (GDM).
Objective: To compare third trimester maternal and fetal thyroid function and the level of transthyretin (TTR), a carrier protein for thyroxine regulating transplacental thyroid hormone transfer, between normal and GDM pregnancies, and to determine if maternal-fetal thyroid function relationship is altered by GDM.
Method: In a prospective study, samples of maternal blood at recruitment, and cord blood at delivery, were collected for assessment of TSH, fT3, fT4, thyroglobulin (Tg), and TTR, and Spearman's correlation was used to examine maternal–fetal thyroid hormone relationship.
Patients: Clinically euthyroid women with GDM diagnosed by a third-trimester oral glucose tolerance test, and controls matched for age and parity (45 each), were recruited in the antenatal clinic for blood sampling. At delivery, cord blood was collected to assess fetal thyroid status.
Intervention: Diet/insulin treatment for GDM.
Main outcome measure: Maternal and cord blood thyroid function.
Results: The GDM group had higher booking BMI ($p = 0.006$), but no difference in maternal or fetal thyroid function. Significant positive maternal-fetal correlation in TSH ($p = 0.004$), fT3 ($p = 0.041$) and Tg ($p = 0.003$) were found only in the controls, whereas significant inverse correlation between maternal fT3 and fetal fT4 ($p = 0.042$), maternal fT3 and fetal TTR ($p = 0.026$), maternal fT4 and birth weight ($p < 0.001$), and positive correlation between maternal Tg and fetal TTR ($p = 0.012$), were found in GDM pregnancies.
Conclusion: Maternal–fetal thyroid relationship was altered in GDM, which might reflect enhanced transplacental transfer, and could have contributed to neonatal metabolic complications in the infants.

P262 Comparison of maternal iodine status and thyroid autoimmunity between gestational diabetic and normal pregnancies in euthyroid gravidae

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Context: Hypothyroidism is associated with gestational diabetes mellitus (GDM), and iodine insufficiency can cause hypothyroidism.
Objective: To compare maternal iodine status and thyroid autoimmunity between normal pregnancies and pregnancies with GDM.
Method: Gravidae were recruited in the third trimester to test for thyroid function and antibodies. Iodine intake was assessed using a food frequency questionnaire and spot urine iodine content (UIC) and iodine/creatinine ratio (I/Cr) assays.
Patients: Clinically euthyroid gravidae with GDM diagnosed by third-trimester oral glucose tolerance test, and controls matched for age and parity (45 each), were recruited in the antenatal clinic.
Intervention: Diet/insulin treatment for GDM.
Main outcome measure: Maternal levels of TSH, fT3, fT4, thyroglobulin (Tg), anti-thyroperoxidase (anti-TPO), anti-thyroglobulin (anti-Tg), TTR, maternal iodine intake, UIC and I/Cr.
Results: No difference in thyroid function or in incidence of thyroid autoimmunity (35.6% vs. 20.0%), daily iodine intake (1148.8 ± 2450.7μg vs. 1480.1 ± 2497.7μg), UIC (0.87 ± 0.50μmol/L vs. 0.92 ± 0.84μmol/L), or I/Cr (0.15 ± 0.98μmol/mmol vs. 0.17 ± 0.13μmol/mmol) was found between GDM and control pregnancies. Positive correlation between maternal UIC and anti-Tg ($p = 0.036$) was found only in GDM pregnancies.
Conclusion: Iodine insufficiency was not found in GDM pregnancies despite dietary treatment, which suggested that iodine intake was unlikely to play any role in thyroid function disturbances found in GDM reported previously.

P263 High-fidelity simulation in a shoulder dystocia scenario

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Introduction: simulation in obstetric has been demonstrated to be a unique tool to teach practitioner to face rare but potentially life threating events and it enhances the basic and complex technical skill, communication skill, multidisciplinary and team working. The aim of the study is to determine whether the use of simulation based-training (SimMom, Laerdal) in a shoulder dystocia scenario would improve the performance of obstetric practitioners.
Material and Methods: Thirty-eight six residents in Obstetrics and Gynecology are randomized in two groups. All of them filled a pre-assessment test. After that, an half are involved in an educational debriefing session and a subsequent shoulder dystocia simulation. The other group participates in an unanticipated simulated shoulder dystocia scenario. This module was repeated 3 weeks later. Each simulation was scored, based on standardized checklists, which focused on both technical action and communication tasks, by an external physician observer.
Results: Residents showed significant improvement in mean maneuver skill and communication scores after simulation training and debriefing session in comparison to naïve group. After 3 weeks, the first

group still presented better score even if also the naive group improved their technical skills.
Conclusion: The data are still preliminary but encouraging. High-fidelity simulation allows learners to practise new hands-on skills, the development of correct habits, and the ability of team working.

P264 Epidemiologia della preeclampsia in una realtà siciliana

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Scopo dello studio è stato valutare i fattori di rischio e gli effetti clinici che possono essere associati con la manifestazione clinica della preeclampsia. L'analisi è stata svolta su 4828 donne che hanno partorito presso l'Ospedale Buccheri la Ferla FBF, Palermo Italia, negli anni 2013 – 2014. Parametri considerati: età, BMI pregravidico, gemellarità,IVF,parità,etnia,presenza di ipertensione e diabete,parto pretermine, IUGR, distacco di placenta, atonia uterina, emorragia grave, ricovero in UTIR, isterectomia, basso peso alla nascita . I dati sono stati elaborati con un'analisi multivariata mediante regressione logistica. Risultati L'incidenza di preeclampsia (1.1%), aumenta con l'età ($p < 0.001$), aumenta in relazione all'aumento del BMI ($p < 0.001$), dell'incremento ponderale, ma non-significativamente,della scolarità, della gemellarità ($p < 0.001$), della IVF ($p < 0.001$),diminuisce con la parità (tendenza lineare al limite della significatività),è maggiore nelle donne straniere ma non-significativamente. Le donne ipertese nel campione erano il 2.7%,e il 21.9% ha sviluppato preclampsia, differentemente alle pz non-ipertese che soltanto nello 0.05% hanno manifestato una preeclampsia (OR = 54.79).Le donne diabetiche erano il 3.3% e la percentuale di preeclampsia è risultata 1.2% nelle diabetiche e 1.8% nelle non-diabetiche (OR = 0.54–5.67).La preeclampsia è significativamente associata ($p < 0.001$) a parto prematuro, ritardo di crescita intrauterina, distacco di placenta, atonia uterina, emorragia grave, ricovero in Terapia Intensiva, isterectomia e basso peso alla nascita . All'analisi multivariata mediante regressione logistica risultano fattori di rischio indipendenti età, BMI, parità e gemellarità. La preeclampsia è significativamente associata agli effetti clinici analizzati, confermandosi come una delle principali cause di morbilità materno-fetale.

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P265 Effects of maternal metabolism on fetal growth

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Objective: To study associations between maternal metabolic parameters and weight infants.
Subjects and methods: Prospective cohort study of 467 pregnancies. Maternal body mass index, gestational weight gain, serum lipids, glucose and insulin (fasting and 75 g oral glucose tolerance test) were analyzed.
Results: Prepregnant overweight with low insulin sensitivity, nondiabetic postprandial hyperglycemia, high serum cholesterol in pregnancy were associated with increased risk of macrosomia. Gestational weight gain was not associated with large for gestational age infants. Inadequate weight gain during pregnancy (lower in the 1-st trimester and excessive with low insulin sensitivity and relative hyperlipidemia in the 2-nd trimester) may include increased risk for small for gestational age infants. Third-trimester gestational weight gain was not associated with fetal mass.
Conclusion: This study has consistently linked increased risk of large-for-gestational-age infants with prepregnant metabolic disorders, increased risk for small for gestational age infants with lower gestational weight gain. Metabolic parameters in the first or second trimesters more strongly correlated with fetal growth.

P266 Carbohydrate and lipid metabolism in the pregnant patients depending on gestational weight gain

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Background: A significant proportion of women exceeds or does not meet the Institute of Medicine's gestational weight gain (GWG) guidelines (2009). It has been shown that inadequate and excessive gestational weight gain (GWG) are associated with adverse obstetric and neonatal outcomes. Related studies were mostly focusing on substantial effects. But for real prevention there is a need to determine the pathogenesis of abnormal GWG.
Aim: To elucidate the character of the relationship between gestational weight gain (GWG) and carbohydrate/lipid metabolism during pregnancy.
Objective and methods: This prospective cohort study enrolled 85 women with full-term sigleton pregnancy in the absence of signs of diabetes mellitus or severe somatic pathology including 15 ones with subnormal GWG, 35 with excessive GWG, and 36 with recommended GWG. Detection of gestational body weight gain, carbohydrate tolerance test, measurement of baseline and stimulated insulin secreation, lipidograms obtained in the first, second, and third trimesters. *Results*: The biochemical profile in the patients with pathological GWG has the following peculiarities in comparison with that of the women with recommended GWG during pregnancy. The women with excessive GWG in the second and third trimesters are characterized by enhanced levels of baseline and stimulated insulin secretion, high HOMO-IR index and LDLP concentration ($p < 0.05$). The women with subnormal GWG in the first trimester have a higher fasting blood glucose level whereas in the third trimester both fasting glycaemia and insulin concentration in response to standard carbohydrate loading decrease to below the respective normal values ($p < 0.05$).
Conclusion: The results of this study show that changes in sensitivity to insulin are in all probability the consequence of pathological enhancement of body mass rather than its cause.

P267 Giant ovarian mucinous cystoadenoma with borderline malignancy in an adolescent girl

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Context: Ovarian mucinous cystadenomas are epithelial tumors extremely uncommon in children, with the majority being benign.

Borderline tumors are very rare in puberty with only 11 sporadic cases being described. Tumor size ranges from 2.5 to 20cm.
Objective: We aim to report the rare case of a giant borderline ovarian mucinous cystadenoma (BOMC) in an adolescent girl, whilst reviewing the current literature and highlighting the controversies in treatment.
Methods: A search of the pubmed database was conducted using the keywords ''ovarian cystadenoma'', ''mucinous cystadenoma'', ''epithelial ovarian tumors'' in conjunction with ''borderline'', ''child'', ''adolescent'', ''puberty''.
Patient: Thirteen-year-old girl presented with abdominal pain. Medical history revealed progressive abdominal distention for at least 6 months. Clinical examination revealed a smooth palpable mass occupying the entire abdomen. Ultrasound examination demonstrated a giant cystic mass measuring $30.3 \times 24.3 \times 17.14$cm and hydronephrosis of the right kidney. CA-125 was elevated 52.6U/ml.
Intervention: Laparotomy was performed by midline incision. The mass originated from the right ovary. Unilateral salpingo-oophorectomy was performed. Examination of the peritoneal cavity showed no indication of metastases. A typical appendectomy was performed.
Results: 11 Cases of BOMCs in adolescents have been described, with our case being the second largest in diameter. Treatment varies, from simple cystectomy to unilateral oophorectomy, salpingectomy, appendectomy, peritoneal wash cytology and contralateral ovarian wedge biopsy.
Conclusions: BOMC is a very rare tumor in childhood. The limited number of cases, combined with the variety of surgical procedures performed does not allow for statistical analysis of the recurrence rate in this age group. However, fertility sparing surgery remains the standard of care in BOMC in childhood

P268 Differential expression of miRNAs associated in the development of preeclampsia detected in maternal serum

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Context: The abnormal remodeling of maternal spiral arteries by the cytotrophoblasts cells are the main cause in the development of preeclampsia (PE). In the National Institute of Perinatology in Mexico City the PE affects about 10% of all births. The pathogenesis of PE does not have biochemical markers that allow detection. Several miRNAs expressed in the placenta that coordinate its development have been detected.
Objective: The main purpose of this study was to determine the expression profile of miRNA-29a, -141, -153, -183, -200b, 210, and 376c in patients with PE.
Patients: One hundred ninety blood samples were obtained from pregnant patients who were divided into three groups: 1) PE ($n = 70$). The control group of healthy pregnant samples was divided into two categories: 2) at term without active labor ($n = 55$) and 3) at term with active labor ($n = 65$). Informed consent was obtained from all patients.
Interventions: Five milliliters of peripheral maternal blood were obtained. The total RNA was extracted from 500 μL of serum which were mixed with the same volume of Trizol reagent.
Main outcome measure: miRNAs expression was performed by reverse transcriptase (RT)-PCR using specific primers. Expression bands were visualized in agarose gels with RedGel reactive and its optical density quantified.
Results: The miRNA-29a, 141, -153, -183, 200b, and -376 were up-regulated, while miRNA-210 was down-regulated in patients with PE compared with patients without labor.
Conclusions: The results of this study suggest that the correlation of seven miRNAs can be used as molecular markers in developing preeclampsia.

P269 Impact of pregnancy on prognosis of thyroid cancer: clinical features

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Objective: Thyroid cancer represents the second most frequent tumor diagnosed during pregnancy only behind breast cancer. However, few data are available about the outcome of TC related to pregnancy, leading to conflicting *Results*: We analyze the presentation, follow-up and evolution of thyroid cancer (TC) detected during pregnancy.
Methods: 16 Women with TC detected during pregnancy were analyzed. Group I ($n = 9$) with TC was diagnosed in first trimester. Group II ($n = 7$) was diagnosed in second or third trimester. We performed neck ultrasound; TSH, free T4, thyroglobulin, and anti-thyroglobulin antibodies with and without treatment with levothyroxine; and RMN whole body scans. Histological diagnosis, lymph node metastases, tumor size and stage, complications from pregnancy, and TC evolution were evaluated.
Results: 100% of the patients had papillary thyroid carcinoma. Lymph node metastases were detected in 2 patients and we didn't detect any invasion of adjacent extrathyroid tissue. Tumor size was larger in Group II: 20.1 ± 10.7 versus 11.7 ± 4.3 mm; $p = 0.02$. No differences were found in the tumor stages between groups. 4 patients had abortions,3 spontaneous and 1 at the patients desire. The others patients had full-term pregnancies.
Conclusions: TC detected during pregnancy have in many cases a favorable evolution. Surgery may be postponed to the post-delivery period. Thyroid cancer seems not influence the good evolution of pregnancy.

P270 Perinatal outcome in fetuses diagnosed with unilateral ventriculomegaly: a systematic review and meta-analysis.

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Context: Ventriculomegaly (VM) is the most frequent brain abnormality diagnosed in fetal life. Even though fetal VM can be bilateral or unilateral, the majority of the studies reported perinatal and long-term outcomes in fetuses with antenatal diagnosis of bilateral fetal VM.
Objectives: The aim of this study was to undertake a systematic review and meta-analysis of the current literature to quantify the incidence of aneuploidy, congenital infections, progression, associated brain and extra-brain abnormalities and neurodevelopmental outcome of fetuses diagnosed with unilateral VM.
Patients: Unilateral VM was defined as an atrial measurement greater than 10 mm affecting only one side detected during the second- or third- trimester of pregnancy.
Methods: Medline and Embase were searched electronically utilizing combinations of the relevant MESH term for ''ventriculomegaly'' and ''outcomes''. Studies that reported data on the perinatal outcome in fetuses with unilateral VM were included in the analysis. Meta-analyses of proportions were used to combine data.
Main outcomes: A total of 17 studies were included in the systematic review out of the 2053 founded. The overall rate of abnormal neurodevelopmental status in children with a prenatal diagnosis of unilateral VM was 11.5% (95% CI, 6.7–17.5). In fetuses with unilateral VM the rate of chromosomal abnormalities and congenital infection was 1.7% (95% CI, 0.3–4.1) and 3.0% (95% CI, 1.3–5.4), respectively. The prevalence of MRI-detected associated brain abnormalities prenatally and postnatally was 6.7% (95% CI, 1.1–16.3) and 20.2%, (95% CI, 4.1–44.3), respectively.
Conclusions: The prevalence of chromosomal abnormalities, congenital infections and neurodevelopmental delay in infants with a prenatal

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diagnosis of unilateral VM is low. Large multicentre prospective studies are needed in order to confirm these results.

P271 Relationship between maternal Body Mass Index and neonatal anthropometric indices

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Background and Objective: Pregnancy outcomes and infant health is an important issue. An important factor affecting neonatal mortality and post it is neonatal birth weight. Considering the existing contradictions about the impact of maternal BMI on these outcomes, the present study was conducted the relationship of BMI with neonatal anthropometric indices in Guilan's pregnant women.
Materials and methods: This cross-sectional study was conducted based on existing data on 511 pregnant women in Guilan province, Iran, from March 2012 to March 2013. Data collection was based on their health record information in health centers. Neonatal anthropometric indices was studied on based mother's pre- pregnancy maternal Body Mass Index. The data was analyzed using descriptive and analytical statistics such as: T-test, ANOVA, and Chi-square tests, by SPSS 21 software. *Results*: In this study, the average of maternal primary BMI and newborn weight were 25/69, 3272/09±388/86 gram, respectively. Also the born babies were mostly male gender. There was significant relationship between mother's primary BMI and infant weight ($p < 0/05$). But there were not found significant relationship between mother's primary BMI and the variables of height and head circumference of new born and sex of infant($p > 0/05$).
Conclusion: According to the results and the effect of BMI on some of neonatal anthropometric indices, it is necessary that educational, advocacy and counseling programs for mothers to be done to ensure mother's good physical condition before pregnancy . Thus it is caused the promotion of the mothers' health and infants are provided.

Keywords
Body mass index, neonatal anthropometric indices, pregnancy

P272 Can inflammatory markers diagnosed in ultrasound examination during pregnancy regress after administration of vaginal treatment? A pilot study

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Context: Inflammatory markers in prenatal ultrasound are a heterogeneous group of images that can evolve during pregnancy, due to regression or exacerbation of infection in pregnant women.
Objective: The assessment if effective rebalancing of the bacterial flora of the vagina can lead to withdrawal of the symptoms of inflammation in ultrasound examination (US).
Methods: A retrospective pilot study.
Patients: Pregnant woman admitted to the Department of Prenatal Cardiology Polish Mother Memorial Research Institute in 2013–2014 in whom ultrasonographic signs of intrauterine infection were present.
Interventions: The analysis included 238 patients, 30 received antibacterial vaginal treatment, from 27 patients a complete follow-up (control ultrasound after 10–14 days and data on labor) were obtained. Electronic database were searched for key words'' infection, placentitis, tricuspid regurgitation, poly/oligohydramnion, IUGR, CRP, antibiotics, vaginal treatment''.
Results: The average age of patients was 29 years. In 22% of patients tricuspid regurgitation was observed and it was the most commonly recognized marker of infection. Regression of infection signs were observed in 21 patients (77.8%) after 2 weeks of vaginal treatment. 2 patients presented with ultrasound image stabilization, in 3 patients worsening of tricuspid regurgitation or cardiac hypertrophy were detected. Polyhydramnios, the second most common parameter (18.51% of patients) resolved after treatment in all studied patients. The delivery took place an average at 39th week of gestation (SD +/- 1.93).
Conclusions: Effective anti-inflammatory vaginal treatment improved ultrasound images in 21 out of 27 fetuses. These preliminary observations suggesting a beneficial role of the vaginal treatment on inflammatory markers in pregnancy ultrasound require further investigation.

P273 Normal pregnancy in patients with acromegaly

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Context: Acromegaly is a rare disease that is usually caused by a GH secreting pituitary tumor. Reports of pregnancy occurring in acromegalic patients are uncommon, due to the fact that acromegaly is frequently associated with subfertility, menstrual irregularities or amenorrhea.
Objective: We report 2 cases of acromegaly patients who obtained spontaneous pregnancies.
Patients:
Case 1: A 34 year old female presented with a 3 year old history of gradual change in appearance, acromegaly facies, headache, increase in shoe and ring size, secondary amenorrhea and persistent galactorrhea after her last pregnancy. After cabergoline administration, she underwent transcranial removal of a GH secreting pituitary adenoma, but a large residual tumor and elevated IGF1 and GH levels remained. One year after initiating octrotide and cabergoline treatment, with a partial decrease in tumor size and function, the patient became pregnant. All treatment was discontinued and the pregnancy ended with the full term caesarian delivery of a normal infant. Postpartum, medical treatment was resumed.
Case 2: A 39 year old female complaining of asthenia, fatigue, a renewal of intense and generalized headaches, dysarthria, postoperative loss of sight in the left eye and left leg paresis was seen in our clinic 5 months after her third surgery for acromegaly. She was initially diagnosed 6 years prior with a GH secreting adenoma and had undergone 2 previous surgeries. Despite having experienced secondary amenorrhea since before the initial diagnosis, the patient obtained a spontaneous pregnancy between the first two surgeries and delivered a full-term normal infant. Her management later included conventional radiation therapy, followed by medical treatment.
Conclusions: The improved management of pituitary adenomas has led to an increasing number of pregnancies being reported in acromegaly.

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P274 Labor induction with transcervical catheter versus oral prostaglandin-E1 treatment in primiparous women and women with an unripe cervix

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Objective: To compare labor induction with transcervical catheter to oral prostaglandin-E1 treatment in primiparous women and women with an unripe cervix, who are at high risk for unsuccessful labor induction resulting in prolonged labor and cesarean section.
Methods: The WHO International Classification of Diseases (ICD)-10 diagnoses and the obstetric records for women who had labor induced with transcervical catheter ($n = 314$) or oral prostaglandin-E1 ($n = 265$) at the Department of Womeńs and Childreńs Health, Karolinska University Hospital, Solna, Sweden during 2012 and 2013 were examined. Primary outcomes were vaginal birth within 24 hours and the cesarean section rate. Secondary outcomes were the induction to vaginal delivery interval, and the rates of chorioamnionitis and neonatal asphyxia.
Results: Vaginal birth within 24 hours was obtained more frequently after catheter compared to oral prostaglandin-E1 in primiparous women ($p < 0.001$) and women with Bishop scores 3–4 ($p < 0.001$), but not in women with Bishop scores 0 – 2 ($p = 0.07$). The cesarean section rates were comparable with the methods in all subgroups ($p > 0.05$). The induction to vaginal delivery interval was 8 – 12 hours shorter after catheter ($p < 0.001$). The rates of chorioamnionitis and newborns with an Apgar score < 7 at 5 min did not differ ($p > 0.05$).
Conclusion: Labor induction with transcervical catheter resulted in a higher rate of vaginal birth within 24 hours and an 8–12 hours shorter induction to vaginal delivery interval compared to oral prostaglandin-E1 treatment. This was obtained without increasing the rates of cesarean section, chorioamnionitis or neonatal asphyxia.

P275 Diagnosis and management of pregnant women of early reproductive age with anemia and endocrine-dependent gestational complications

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Objectives: The aim of this study has been to investigate the effectiveness of therapy of pregnant women of early reproductive age with anemia and interrupted pregnancy.
Design and Methods: 56 Pregnant women, aged 18–19, with menstrual disorders in puberty (primary and secondary amenorrhoea, dysmenorrhoea, abnormal pubertal uterine bleeding) have been examined. The obstetric and gynaecological status and results of clinical-laboratory indices (with the hormonal pattern) were studied, the state of the foetoplacental complex was assessed (ultrasonography with dopplerography).
Results: It has been established that obstetric and perinatal complications are likely to occur more frequently in patients with pubertal disorders than in women with physiological puberty. It has been revealed that the most common complication of the gestation process is the threat of interrupted pregnancy (67.8%), in the majority of patients accompanied by anaemia (60.7%). The main clinical symptoms are bleeding, pain, weakness. Considerable hormonal imbalance has been established: hypoestrogenia, progesterone insufficiency and a lower level of placental lactogen and leptin. Dydrogesteronum (DUPHASTON) was the main drug for treatment.
Conclusion: Using the Duphaston in a complex with hyperbaric oxygenation, antianemik therapy and the drugs which normalize the placental blood flow has allowed to prevent miscarriage in all patients.

P276 The effects of fetal growth restriction (FGR) on the umbilical cord blood (UCB) hematopoietic progenitor stem cells: a prospective case-control study

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Background: UCB has emerged as a viable source of allogeneic hematopoietic stem cell for related or unrelated transplantation. Various maternal and fetal factors are known to influence the UCB volume and its HSC yield.
Objectives: To determine the nucleated cell count (NCC) and CD34+ hematopoietic progenitor stem cell count in UCB of fetal growth restriction (FGR) babies compared to normally-grown babies and factors that influence these outcome.
Methods: A case-control study was conducted at the UKM Medical Centre, a teaching hospital in Kuala Lumpur. UCB was procured at delivery of FGR and normally-grown babies. UCB volume was measured and NCC and CD34+ cell count were derived using TrucountTM tube-based stem cell enumeration kit (BD biosciences) on BD FACSCaliburTM.
Result: Maternal age, parity, gestational age at birth, mode of delivery, fetal sex, and UCB pH at birth were similar in both groups; FGR ($n = 20$) and control ($n = 20$) . Interestingly, the FGR group had significantly lower values of UCB volume (mean + SD: 93.12 + 18.87 versus 122.82 + 13.73 ml), nucleated cell count (mean + SD: 3.99 + 2.20 versus 11.1 + 3.27 $\times$ 106 cells/mL), total nucleated cell count (mean + SD: 3.74 + 2.25 versus 13.63 + 4.38 $\times$ 108 cells), CD34+ cell count (11.55: IQR 0.65–53.29 versus 22.19: IQR 10.11–73.38 cells/μL), and total CD34+ count (1.23: IQR 0.6–7.3 versus 2.93: IQR 1.13–9.42 $\times$ 106 cells). There were no correlation observed with maternal age, gestational age, mode of delivery and fetal gender.
Conclusion: FGR has a negative impact on the yield of HSC (UCB volume, NCC, total NCC, CD34+ and total CD34+ cell count) procured from CB at delivery. As adequate CD34+ cell count is imperative in ensuring the proliferative capacity of stem cells, the cost effectiveness of UCB harvest from babies affected by FGR may be significantly compromised.

P277 The markers of diabetic nephropathy in pregnant women with type 1 diabetes with different terms of delivery

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Objective: To determine the level of urinary excretion of IL-1β, MCP-1, TGF-β1 in pregnant women with type 1 diabetes with the early delivery.
Methods: Laboratory testing for the quantitative determination of urinary IL-1β, MCP-1 and TGF-β1 in the daily urine was measured by enzyme immunoassay.
Patients: We study 21 pregnant women with type 1 diabetes, 19 to 36 years old (25 [22; 27] years) and with diabetes duration from 1 to 26

years (10 [5, 12] years). Pregnant women with type 1 diabetes matched for age, duration of diabetes and the degree of compensation of carbohydrate metabolism ($p > 0.05$). Term of delivery before 38 weeks of pregnancy was seen as early delivery ($n = 7$), including 2 pregnant women with normoalbuminuria (NAU) and in 2 women during pregnancy NAU turned into microalbuminuria (MAU); in 1 patient MAU turned into proteinuria; 2 pregnant women had diabetic nephropathy with proteinuria. Delivery at term was considered as birth at term 38–40 weeks ($n = 14$), all pregnant women in this group had NAU. Early delivery in the study group was not associated with obstetric indications.
Results: In pregnant women with type 1 diabetes with the early delivery we noticed more than a twofold increase in the excretion of TGF-β1, IL-1β, MCP-1 with a daily urine in all trimesters of pregnancy compared with their level of excretion in a group of pregnant women with type 1 diabetes, who delivered at term ($r<0.05$). The level of urinary excretion of IL-1β, MCP-1 and TGF-β1 in women with type 1 diabetes who gave birth at term comparable to the level of excretion in healthy pregnant women who gave birth at 38–40 weeks of pregnancy in ($r < 0.05$).
Conclusion: The elevated levels of pro-inflammatory cytokines (IL-1β, MCP-1) and TGF-β1, starting from the first trimester, may possibly serve as a predictor of preterm birth in pregnant women with type 1 diabetes.

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P278 The early reproductive losses: pathogenetic aspects and methods of correction

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Context: The high rate of complications of pregnancy and early reproductive losses demonstrates the relevance of the search for innovative approaches to diagnosis and treatment strategy of this pathology.
Objective: To reduce the frequency of early reproductive losses through optimization of diagnostic and therapeutic measures based on pathogenetic aspects.
Methods and Patients: The study included 310 pregnant women at 5–12 weeks of gestation: 200 women with threatened miscarriage, 80 women with missed abortion, 30 women with normal pregnancy. Complex examination included: clinical, laboratory, ultrasound, Doppler, hormonal and genetic studies (progesterone receptor gene (PRG), estrogen receptor (ESR1), multi-drug resistance gene (MDR 1)).
Main Outcome: In women with early reproductive losses the frequency of genotype T1/T2 of the gene PGR was – 52, 4%, and the 3435TT genotype of the gene MDR1 — 38.1%, which was significantly higher than in a comparison group of women – 27.5% and 11.8%, respectively ($p < 0.05$). If there are patients with a genotype in T1/T2 of gene PGR and genotype 3435TT of gene MDR1 the optimal is the intravaginal use of micronized progesterone at a dose of 200–300 mg per day for the correction of progesterone deficiency.
Results: The interruption of pregnancy in the period of 5–12 weeks is associated with the presence of women genotype T1/T2 of PGR gene and genotype 3435TT of gene MDR1. The differentiated approach to the choice of optimal hormonal drug for the treatment of threatened miscarriage of early gestation based on genetic characteristics of women contributes to the successful completion of pregnancy in 95% of women and reduce the frequency of early reproductive losses in 2.8 times.
Conclusions: This study confirmed the presence of genetic determination of hormonal disorders and early reproductive losses.

P279 Influence of uterine fibroids on fetal growths and neonatal outcomes

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Objective: To prospectively estimate effect of fibroids on fetal growths and neonatal outcomes.
Methods: Prospective cohort study comparing fetal growths and neonatal outcomes in pregnancies with and without fibroids, all of them discovered at routine first trimester obstetric ultrasonography between September 2012 and December 2014. A total of 3479 pregnant women were recruited (729 of them with at least on fibroid as the experimental group and 2750 of them without fibroids as the control group). Fibroids' characteristics, monitoring indices from 11–14weeks, 22–24weeks and 28–32 weeks ultrasounds and neonatal conditions were prospectively observed and recorded.
Results: Women with fibroids had higher crown rump length and nuchal translucency at 11–14weeks ultrasound and higher femur length/biparietal diameter at 28–32 weeks ultrasound compared with those without fibroid. A significant difference existed between the two groups with regard to pregnancy outcomes. Fibroids were associated with more abortion, preterm birth and less partus matures. However, other of fetal growths in early, middle and late pregnancy and neonatal conditions had no statistical significance between the two groups.
Conclusion: Fibroids were associated with increased risk for abortion and preterm birth. But women with fibroids are at low risk for fetal growths and neonatal outcomes compared with those without fibroids once they safely pass through pregnancy. These results may be useful for preconception counseling and prenatal management of women with fibroids.

Keywords
fibroids, pregnancy, fetal growths, neonatal outcomes

The study was supported by the Beijing Municipal Science and Technology Commission. Research Grants No. Z131107002213090.

P280 Deficiency of vitamin D and gestational complications according to research data in Saint Petersburg, Russian Federation

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Aim: Prevalence of vitamin D deficiency among pregnant women vary from 50 to 86%, which is the cause of different complications during pregnancy. The aim of this research was to estimate frequency of vitamin D deficiency and insufficiency in pregnant with preeclampsia, miscarriage, sterility and gestational diabetes mellitus.
Materials and methods: Present study was cohort, prospective. In the base of Federal Almazov North-West Medical Research Center there were examined totally 800 blood serum specimens of pregnant women in Saint Petersburg (mean age was 29 $\pm$2.1 years), at 12–14, 24–26, 34–36 gestational weeks from 2013 to 2015. Estimation of 25-OH-D level in blood serum was conducted with the use of electrochemiluminescent method on the analyzer Architect 2000.
Results: Frequency of occurence of vitamin D deficiency in pregnant with preeclampsia was 73%, insufficiency – 25%, normal ranges – 2%. In cases of threatening miscarriage vitamin D deficiency was 47.9%, insufficiency – 22.9%, normal level – 29.2%. Vitamin D insufficiency and deficiency were revealed in 100% women with sterility. In normal

pregnancy vitamin D insufficiency was 14%, normal level was in 86%, there were no women with deficiency. There was not found correlation between gestational diabetes mellitus and vitamin D deficiency. Thus, the received data allow to suggest possible role of vitamin D in miscarriages, as the prevalence of vitamin D deficiency in group with threatening miscarriage in the I trimester 4.3 times higher than in women with physiological pregnancy. Vitamin D insufficiency and deficiency occur in 100% women with sterility, in physiological pregnancy – 14%, with preeclampsia – 2.5 times more often than in physiological pregnancy. Pregnant women with the revealed vitamin D insufficiency and deficiency are involved in group of risks for the development of preeclampsia.

P281 Seasonal fluctuations of the levels of 25-hydroxycholecalciferol in pregnant women in Saint Petersburg, Russian Federation

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Federal Almazov North-West Medical Research Center

Context: According to different sources, from 50 to 86% of pregnant women have levels of vitamin D below the normal ranges. The aim of this study is to evaluate the intensity of vitamin D in different seasons of the year in pregnant in St. Petersburg.
Materials and methods: Present cohort prospective study was made at clinical and diagnostic department of the Institute of Perinatology and Pediatrics of Federal Almazov North-West Medical Research Center. The study finished 192 pregnant. Inclusion time is from 2013 to 2015. All pregnant women were divided in 4 subgroups depending on the season of the year while inclusion at the research. At 12–14 weeks there was the first blood sample. All women took daily 500 IU of colecalciferol in the composition of multivitamin complex from the first trimester of pregnancy till the delivery. During pregnancy serum 25-OH-D level was defined at 12–14, 24–26, 34–36 gestational weeks. For detection of 25-OH-D it was used electrochemoluminescent method with the use of analyzer Architect 2000 on the base of central clinical and diagnosis.
Results: It was found no significant differences between the initial average 25-OH-D level in all pregnant women (17.5; 21.3; 22.6; 19.9 ng/ml in accordance to the 1, 2, 3 and 4-th subgroups). It was found maximal saturation of vitamin D at I trimester of pregnancy at summer season and was 22.6 ng/ml, which corresponds to the criteria of insufficiency. Minimal concentration of 25-OH-D among subgroups was found at winter season and was 17.5 ng/ml, which corresponds to the criteria of vitamin D deficiency. Total concentration of 25-OH-D significantly do not differ among subgroups. Acceleration of 25-OH-D level from the Ist to IIIrd trimester is present regardless of the season of the year. Research showed no significantly dependent changes of 25-OH-D levels in blood serum from the season of the year in pregnant.

P282 The safety of myomectomy during cesarean delivery

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Objective: To evaluate the safety and feasibility of cesarean myomectomy among women with uterine fibroids.
Methods: A total of 2565 pregnant women with uterine fibroids who deliveried by cesearean section was collected, which is from 14 provinces and 39 different hospitals in 2011 in mainland China. Women were divided into two group by whether myomectomy during cesarean delivery: cesarean myomectomy and cesarean alone. Data were analyzed for clinical characteristics of pregnant women characteristics of uterine fibroids, and obstetric outcomes such as postpartum hemorrhage, neonatal weight and fetal distress.
Patients: A total of 2565 pregnant women with uterine fibroids who deliveried by cesearean section from 14 provinces and 39 different hospitals in 2011 in mainland China.
Interventions: Women were divided into two group by whether myomectomy during cesarean delivery: cesarean myomectomy and cesarean alone.
Main Outcome Measures: Cesarean myomectomy can be a safe procedure.
Results: 2344(91.4%) Women underwent cesarean with myomectomy, and 221(8.6%) women underwent only cesarean. There are more patients had subserous fibroids (1537[65.6%] vs. 109[49.3%]; $p = 0.0001$) and uterus corpsus (2210[94.3%] vs. 204[92.3%]; $p = 0.004$) in the cesarean myomectomy group than cesarean alone group. The diameter and number of uterine fibroids were not differ between the two group. The comparison of postpartum hemorrhage, neonatal weight and fetal distress showed no statistical significance.
Conclusion: Obstetricians were inclined to remove sebserous and corpus fibroids during cesarean. Cesarean myomectomy can be a safe and feasible procedure for some patient.

P283 Adverse obstetric outcomes in women with uterine fibroids in Mainland China

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Objective: To estimate the association between uterine fibroids and adverse obstetric outcomes.
Method(s): Retrospective survey.
Patient(s): A total of 112 403 deliveries from 14 provinces and 39 different hospitals in 2011 in mainland China.
Intervention(s): A cross-sectional, hospital-based survey was performed.
Main Outcome Measure(s): The prevalence of uterine fibroids in pregnant women in China and obstetric outcomes.
Result(s): Of 112 403 women who underwent routine obstetric survey, 3012 (2.68%) women were identified with at least 1 fibroid. By univariate and multivariate analyses, the presence of uterine fibroids was significantly associated with cesarean delivery (adjusted odds radio [OR] 1.8, 95% confidence interval [CI] 1.6–1.9) and breech presentation (AOR 1.3, 95% CI 1.2–1.5). 22.9% pregnant women with fibroids taken cesarean section just for maternal request, in which there are only 24.7% fibroids more than 5cm. During 37 weeks to 39 weeks, planned cesarean proportion of uterine fibroid group is significantly higher than no fibroid group.
Conclusion(s): Pregnant women with uterine fibroids are at increased risk for cesarean delivery and breech presentation. A more effective quality control for indication of selective cesarean section and termination of pregnancy for pregnant women with fibroids should be done in China.

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DOI: 10.3109/09513590.2016.1150635

Contraception

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P284 Sperm synthesize proteins during capacitation-a basis for male contraceptive development

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Context: It is widely assumed that ejaculated spermatozoa are translationally silent.
Objective: To prove that mature sperm can synthesize protein during sperm capacitation.
Methods and Results: Incorporation of [35S] Met-[35S] Cys is completely inhibited by D-Chloramphenicol (CP) but not by cycloheximide (CH), suggesting that the translation process depends on 70S ribosomes. We localized translation site by incubating permeabilized spermatozoa with lysyl-transfer RNA tagged with BODIPY, showing that nascent polypeptides were found mainly in the sperm midpiece and head. Purification of total RNA from spermatozoa and subject it to RT-PCR using specific primers, revealed the presence of mRNA for the sperm specific proteins CatSper and Na-K ATPase α4 as well as mRNA for other proteins like AT1 receptor and PKCα. Western blot analysis of proteins extracted from CP treated sperm cells incubated under capacitation conditions, revealed significant reduction in the amount of several proteins including AT1-R, PKCα, PKCβI, PKA and EGF-R. Moreover, immunoprecipitation of [35S] Met-[35S] Cys incorporated AT1-R, PKCα, and progesterone receptor revealed complete inhibition of their synthesis by CP, but not by CH. Incubation of sperm cells in capacitation medium in the presence of CP resulted in about 50% inhibition in sperm motility, complete inhibition of capacitation dependent actin polymerization and sperm ability to undergo acrosome reaction as well as 60% inhibition of in-vitro fertilization rate.
Conclusions: We demonstrate here that translation of nuclear and mitochondrial proteins do occur in mammalian spermatozoa during their maturation process called capacitation.Thus, inhibition of synthesis of sperm specific proteins during sperm capacitation would be a specific method for the development of male contraceptive.

P285 Impianto sottocutaneo con solo progestinico: la nostra esperienza risultati preliminari

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Introduzione: I Long-acting reversible contraceptives (LARC) comprendono tutti quei metodi contraccettivi che richiedono l'assunzione meno di una volta al mese, come dispositivi intrauterini al rame (DIU), anello vaginale e metodi ormonali a base di solo progestinico iniettabili, intrauterini medicati ed impianti sottocutanei. Poiché l'efficacia dei metodi barriera e dei contraccettivi ormonali combinati a base di estroprogestinici è strettamente dipendente dall'uso corretto e costante, i LARC non-essendo influenzati dal comportamento personale offrono un'efficacia maggiore dei COC ed hanno un tasso di continuità migliore ad un anno di utilizzo. Inoltre, i LARC con solo progestinico possono essere somministrati anche a donne che presentano controindicazioni all'uso di estroprogestinici come determinati fattori di rischio, quali l'età maggiore di 35 anni correlata all'abitudine al fumo, l'ipertensione arteriosa, un'anamnesi positiva per rischio tromboembolico venoso, l'immobilizzazione prolungata, cardiopatie valvolari complesse, diabete complicato, emicrania con aura ed allattamento.
Obiettivo: Lo scopo del nostro studio è stato quello di valutare il profilo di sanguinamento, gli effetti collaterali, l'accettabilità e il tasso di continuazione del metodo.
Metodi: Sono state arruolate volontarie sane di età maggiore ai 18 anni, che afferivano al Servizio di Pianificazione Familiare Dipartimento di Scienze Ginecologico-Ostetriche e Scienze Urologiche "Sapienza" Università di Roma, con richiesta di contraccezione a lungo termine con solo progestinico, da marzo 2012. Per ogni donna è stata raccolta l'anamnesi familiare, personale, ginecologica ed ostetrica. Nel corso della visita tutte le pazienti sono state sottoposte ad esame obiettivo generale e ginecologico. E' stato effettuato un successivo controllo a 6–12–24 mesi dall'inserimento, durante il quale le pazienti hanno compilato un questionario riguardante le modificazioni mestruali, della sfera sessuale, dell'umore ed eventuali effetti collaterali. Lo studio è ancora in corso.
Risultati: Ad oggi sono state arruolate 48 donne per un totale di 953 cicli di osservazione. L'età media del campione è 34.7 anni (mediana 36). La classe di età più rappresentata è stata quella compresa tra 30 e 35 anni (38%). I caratteri del ciclo mestruale precedentemente all'inserimento erano normali per RQD nel 76% dei casi. La maggioranza del campione ha riportato almeno una gravidanza precedente in anamnesi (81%). Riguardo alla precedente contraccezione, il 56% delle donne in passato faceva uso di COC, il 12% di DIU, il 12% aveva già utilizzato un impianto e il 18.7% non-aveva mai fatto uso di metodi anticoncezionali. Nessuna difficoltà è stata riportata dal medico al momento dell'introduzione e nessun particolare effetto è stato riferito dalle pazienti Nel nostro campione il tasso di continuazione del metodo del 93% ad un anno. Per quanto riguarda le caratteristiche del ciclo mestruali ad un anno, i tassi di amenorrea sono stati del 62.6%, di spotting del 30% e cicli regolari sono stati osservati nel 18.7% delle pazienti. Rimozioni anticipate sono state richieste da 3 pazienti; una dopo 7 mesi per amenorrea e due entro 12 mesi per spotting. Gli effetti collaterali riportati sono stati: variazione ponderale, ritenzione idrica, diminuzione della libido, acne e cisti ovariche. Per quanto riguarda il grado di soddisfazione ad un anno d'uso del metodo il 42% delle pazienti si è considerata molto soddisfatta, il 38% abbastanza soddisfatta ed il 20% poco o per nulla soddisfatta.
Conclusioni: Lo studio è ancora in corso, ma i dati preliminari concordano con quelli riportati in letteratura con un grado di soddisfazione in circa l'80% da parte delle pazienti. Le modificazioni del ciclo mestruale osservate sono state causa di abbandono del metodo in soli 3 casi entro 12 mesi. Va sottolineato come lo spotting sia stato riportato dalla maggioranza delle pazienti nei primi 6 mesi. E' evidente come a causa delle sue caratteristiche peculiari sia fondamentale un appropriato counselling nel proporre questo metodo.

P286 The therapeutic possibilities of continuous mode of COCs for military women in terms of continued Russian–Ukrainian conflict

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Modern Ukraine is a military time society, where in the Russian-Ukrainian conflict, according to the Ministry of Defense, from 9.10.2015, 938 women took part. Totaly, at present time, approximately 14.5K military women and 30.5 thousand workers of Armed forces serve for Armed forces of Ukraine. Taking into the consideration the fact, that mainly, these are young women, questions concerning

their reproductive and somatic health in conditions of the conflict which is taking place are becoming precisely actual. The study involved 17 women combatants, aged from 21 to 33 years who were staying in the conflict zone from 3 to 12 months. Of these, 15 (88.2%) had painful periods and irregular bleedings, 12 (70.6%) – have had increased symptoms of premenstrual tension and other cyclic complaints while being in the zone of conflict. At the same time, 94.1% of the patients didn't have an information about the possibility of drug suppression of menstruations. Taking into consideration the results of a survey of women in the armed forces, a memo about the features and benefits of using a continuous mode of hormonal contraception in terms of execution of their professional tasks has been written. The adoption of this category of patients an informed decision about the hormonal suppression of menstruation, will allow to ensure them not only to contraceptive, but a therapeutic effect as far, which is conditioned by decrease of clinic manifestation, related to menstruation, decreased blood loss and improved personal hygiene. Contraceptive use in this mode will not only improve the quality of life and reduce the risk of dyshormonal disorders of the reproductive system, but will increase the level of personal and social adaptation of female soldiers, which according to the literature, is much more inferior to that of military men.

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P287 Non-hormonal versus hormonal intrauterine contraception: survey of patients' perceptions in four Latin American countries

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UFMG

Objective: Understand consumer's perceived impediments to intrauterine contraceptive devices (IUD) use in Latin America.
Methods: We developed an online survey for women open to contraception in four Latin American countries.
Patients: Women aged 20–30 years seeking contraception in Argentina, Brazil, Colombia and Mexico
Interventions: Questions aimed at evaluating patient awareness of negative stories and statements and how women perceived barriers to copper IUD and the levonorgestrel intrauterine system (LNG-IUS) use.
Outcome measures: Method safety, efficacy, and side effects.
Results: The survey was mailed to 2300 women and 19 253 responses were obtained in Argentina ($n = 465$), Brazil ($n = 380$), Colombia ($n = 613$) and Mexico ($n = 495$). More women reported having heard negative stories about the copper IUD than LNG-IUS and perceived that the former was suitable only for women who have already had children when compared to the LNG-IUS. More women reported weight gain (14.3% × 38.2%; $p < 0.001$), mood swing (14.1% × 38.7%; $p < 0.001$) and infertility (16.3% × 19.9%; $p < 0.001$) as possible side effects for the LNG-IUS. Women assumed abortion (36% × 22.7%; $p < 0.001$), pelvic infections (42.1% × 15.7%; $p < 0.001$) and ectopic pregnancy (43.5% × 23.5%; $p < 0.001$) as side effects more associated to the copper IUD which was believed to cause with less pain during placement and removal in comparison to the LNG-IUS (42.8% × 31.2%; $p < 0.001$). The perception of increased risk of contracting sexual transmitted diseases did not differ between the devices (21.7% × 20.3%; $p = 0.388$).
Conclusion: In spite of the proven benefits of intrauterine contraception, these Latin American women still hold misperceptions regarding adverse effects and risks which may hamper the use of such safe and efficient contraceptive methods. Our findings provide insight into areas where additional counselling may be of value

P288 Contraccezione orale e long-acting (LARC): qualita' della vita e funzione sessuale della donna risultati preliminari

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Introduzione: Obiettivo dello studio: determinare l'impatto della contraccezione orale e della contraccezione reversibile a lunga durata d'azione (long acting reversibile contraception- LARC) sulla qualità della vita (QoL) e sulla funzione sessuale della donna.
Materiali e Metodi: Studio prospettico su 75 donne richiedenti contraccezione ormonale (CO).Criteri di inclusione: età tra i 18 e 45 anni, BMI >20 e ≤ 24, vita sessuale attiva (4 rapporti/mese), stato di buona salute. Criteri di esclusione: gravidanza,e/o allattamento e/o aborto nei 4 mesi precedenti; contraccettivi nelle precedenti 4 settimane; caratteristiche clinico-anamnestiche appartenenti alle categorie 3 e 4 della classificazione WHO ''medical eligibility criteria for contraception''.
Contraccettivi: 3 Formulazioni diverse di estroprogestinici (E/P) orali (E2 2.5 mg+Nomogestrolo 1.5 mg, EE 30 μg+ Dienogest 2 mg, EE 20μg+ Lovonorgestrel 100μg); 3 sistemi LARC a rilascio di progesterone: impianto sottocutaneo (Etonogestrel 68 mg), LNG-IUD (Lovonorgestrel 52 mg) e LNG-IUD (Lovonorgestrel 13.5 mg). Al tempo 0 e a 6 mesi dall'assunzione del contraccettivo, sono somministrati i questionari validati ''Female Sexual Function Index'' (FSFI) e ''Short form-36'' (SF-36), e dosati su plasma testosterone (T), testosterone libero (free T), SHBG e prolattina (PRL). L'analisi statistica è realizzata mediante il test T D Student e del test esatto di Fischer. La significatività è posta per valori di probabilità $p < 0.05$.
Risultati: I dati preliminari non-rilevano differenze statisticamente significative nei punteggi FSFI e SF-36 e nei valori plasmatici di T, free T, SHBG e PRL ottenuti al tempo 0 e 6 mesi per nessuno dei contraccettivi in esame. Non-sono state riscontrate differenze significative tra il delta dei punteggi FSFI e SF-36 e dei valori plasmatici di T, free T, SHBG e PRL a tempo 0 e 6 mesi dei contraccettivi orali e LARC.
Conclusioni: Ad oggi la CO nelle diverse formulazioni in esame e nelle diverse modalità di somministrazione sembra avere effetto neutro sulla funzione sessuale e la QoL.

P289 Simple management of deeply fitted implants

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Context: 56 Women, 18–45 yo, fitted with an Implanon (2004–2011), referred during 2010–2012 to UNICERH from 35 different sites due to difficulties in locating the device. 11 (19.7%) came from other cities, 43 (76.8% came from a different health area within Santiago.
Objective: Describe a simple surgical management of non-palpable implants in an outpatient clinic.
Methods: Description of cases and clinical management.
Patient(s): 56 Women with deeply inserted contraceptive implants difficult to locate.
Intervention(s): Location of implants by palpation, ultrasound or MNR as needed, and ambulatory surgical extraction with a minimal invasive surgical procedure.
Main Outcome Measure(s): Location and extraction of the implant.

Result(s): 47 (84.9%) Fitted by a Midwife, 9 (16.1%) by Physician. 53 (94.6%) in the left arm. Using the device for 1–76 months. 2 (3.6%) had palpated the implant, now 1 (1.8%) implant was palpable, 4 (7.1%) barely palpable and 51 (91.1%) non-palpable. Location done by palpation, ultrasound and NMR. 1 previous unsuccessful removal attempt was done in 13 (23.2%) cases, 2 in 4 (7.1%) and 3 in 1 (1.8%) case. 14 (25%) cases had im fitting, of which none was pregnant, 3 needed an NMR. 9 (16.1%) NMR were done of which 8 had no implant fitted. There were 7 (12.5%) pregnancies, 6 with no implant. All cases of extraction were managed in office, with local anesthesia and a small longitudinal puncture or incision. An incision of less than 5 mm in length, was made in 20 (35.7%) cases; 1 cm in 18 (32.1%), and of 1.5 to 2 cm in 7 (12.5%) cases, all of which were in the cases of sub aponeurotic placements. Only 10 (17.85%) women came back after 7 days to control to UNICERH and all were OK.
Conclusions: Deeply fitted contraceptive implants can be easily managed with simple US location and surgical techniques at an outpatient clinic by the gynecologist.

P290 Oral contraception and female sexual dysfunction

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Context: Hormonal contraceptives can influence female sexual function
Objective and Methods: A Medline search was conducted using several terms related to and including the terms contraception, oral contraceptive, female sexual function, dyspareunia, libido, and sexual desire
Results: The analysis has shown that combined hormonal oral contraceptives had dimished sexual desire, frequency of intercourse, and arousal disorders in women of different ages. Also they cause genital anathomic changes that made this situation worse. The combination of anathomical and phisiological changes affects quality of life. A Preliminary study on the effect of four-phasic estradiol valerate and dienogest (E2V/DNG) oral contraceptive on the quality of sexual life shows new oral contraceptive containing the natural estrogen estradiol and a 19-nortestosterone derivate dienogest (DNG) in a four-phasic 28-day regimen may be used by women.Moreover, the E2V/DNG multiphasic extended regimen has been found to positively modify the sexuality of users.
Conclusions: The sexual side effects of hormonal contraceptives are not well studied, particularly with regard to impact on sexual desire. There appears to be mixed effects on desire, with a small percentage of women experiencing an increase or a decrease, and the majority being unaffected. Millions of users can show tha OC is a gret method to avoid pregnancy, but Healthcare providers must be aware that hormonal contraceptive can have negative effects on female sexuality so they can counsel and care for their patients appropriately.

P291 Effetti dei contraccettivi ormonali sulla sessualità: dati preliminari

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Introduzione: Fin dal primo momento della commercializzazione dei contraccettivi ormonali (CO) vi è sempre stata la preoccupazione per la possibile influenza degli stessi sul comportamento sessuale, in particolare sul desiderio sessuale. Le review condotte tra gli anni 60 e 70, sugli studi che analizzavano l'influenza dei contraccettivi ormonali combinati (COC) sul desiderio sessuale, hanno prodotto risultati contrastanti, sia per la difficoltà di confronto tra studi con disegni diversi ed i differenti dosaggi ormonali utilizzati, sia per la complessità della risposta sessuale nell'uomo. La conclusione a cui si era giunti all'epoca era che una riduzione della libido come effetto diretto dei COC era probabilmente presente in un piccolo sottogruppo di donne. A distanza di quarant'anni la situazione non si è di molto modificata. Una recente review, ha messo in evidenza come i risultati ottenuti siano inconsistenti, con alcuni studi che riportano un aumento del desiderio sessuale, altri una riduzione ed altri nessuna modifica nelle utilizzatrici di COC, rispetto alle utilizzatrici di nessun metodo ormonale Nonostante l'introduzione di nuove molecole e dosaggi inferiori ancora non è stato chiarito se ci sia veramente un effetto biologico della contraccezione ormonale sul desiderio sessuale, e soprattutto se tale effetto sia dovuto alla componente estrogenica, a quella progestinica o ad una interazione tra le due. Maggiore chiarezza si ha sugli effetti della CO sulla qualità della vita: le donne in terapia con la CO sembrerebbero avere una miglior qualità della vita rispetto alle donne che non-usano alcun tipo di contraccezione o usano metodi contraccettivi non-ormonali. L'obiettivo dello studio è determinare l'impatto di alcuni contraccettivi ormonali e della loro diversa modalità di somministrazione sulla qualità della vita e della funzione sessuale della donna, mediante la somministrazione al tempo 0 e a 6 mesi dall'inizio dell'assunzione del contraccettivo, dei questionari validati ''Female Sexual Function Index'' (FSFI) e ''Short form-36'' (SF-36).
Materiali e Metodi: Vengono arruolate donne di età compresa tra i 18 e 45 anni, sessualmente attive (4 rapporti sessuali nel mese precedente), desiderose di contraccezione ormonale giunte presso il Centro di Pianificazione Familiare del Dipartimento di Scienze Ginecologico-Ostetriche e Scienze Urologiche ''Sapienza'' Università di Roma, da Gennaio 2015. Il termine per l'arruolamento è Gennaio 2017. Per ogni donna sono raccolti i dati demografici e clinico-anamnestici, con particolare attenzione all'anamnesi ginecologica e ostetrica ed allo stile di vita. I contraccettivi ormonali in esame sono alcuni estroprogestinici orali combinati e estroprogestinici per via vaginale. Al momento della prescrizione e dopo 6 mesi dall'inizio dell'assunzione del contraccettivo, si valuta la funzione sessuale e la qualità di vita utilizzando la versione italiana validata dei questionari ''Female Sexual Function Index'' (FSFI) e ''Short form-36'' (SF-36). Il questionario FSFI comprende 19 domande suddivise in 6 categorie: desiderio sessuale, eccitazione, lubrificazione, orgasmo, soddisfazione sessuale generale, dolore durante il rapporto. I punteggi vanno da un minimo di 2 a un massimo di 36. Il questionario SF-36 comprende 36 domande suddivise in 8 categorie: attività fisica, limitazioni di ruolo dovute alla salute fisica, limitazioni di ruolo dovute allo stato emotivo, dolore fisico, percezione dello stato di salute generale, vitalità, attività sociali, salute mentale, e una singola domanda sul cambiamento nello stato di salute. I punteggi vanno da 0 a 100. Più alto è il punteggio, migliore è il livello di salute percepita.
Risultati: Ad oggi 51 donne hanno completato il controllo a 6 mesi. Al momento della prescrizione la media dello score totale del questionario FSFI è stata 27.8. Le medie dei punteggi del questionario SF-36 sono state: 92.6 per attività fisica, 78.2 per limitazione ruolo fisico, 65.5 per dolore fisico, 70.5 per salute generale, 51.6 per vitalità, 61.7 per attività sociali, 59.5 per limitazioni ruolo emotivo e 56.8 per salute mentale generale. Al follow up a 6 mesi la media del punteggio FSFI è stata 27.2. Le medie dei punteggi SF 36 sono state: 93.1 per attività fisica, 79.9 per limitazione ruolo fisico, 68.2 per dolore fisico, 73.2 per salute generale, 52.6 per vitalità, 62.3 per attività sociali, 60.1 per limitazioni ruolo emotivo e 57.2 per salute mentale generale.
Conclusioni: Lo studio è ancora in corso nell'intento di raggiungere un campione adeguato all'analisi statistica. I dati preliminari non-mostrano differenze staticamente significative dello score totale del questionario FSFI mentre è stato rilevato un miglioramento significativo dei punteggi al questionario SF36 sullo stato di salute generale, in particolare per quanto riguarda limitazioni ruolo fisico, dolore fisico e salute generale. Dato il campione ancora limitato di pazienti che hanno seguito il follow up a 6 mesi non è stato ancora possibile effettuare una analisi comparativa statisticamente valida fra i diversi tipi di CO presi in esami.

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P292 Can three-dimentional ultrasound predict risk of mirena expulsion? In evaluation [?]

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Aim of the study was to find 3D ultrasound criteria to predict risk of levonorgestrel-realising intrauterine system expulsion. 103 patients aged from 28 up 52 years old who underwent treatment by Mirena due to menometrorrhagia, endometrial hyperplasia and adenomyosis were included into the study. First, subgroup was formed by 86 patients who underwent mandatory 3D TV ultrasound with uterus coronal plane reconstruction before Mirena insertion; second subgroup – by 17 patients with Mirena expulsion who did not undergo preliminary 3D ultrasound. High frequency of expulsion was related to uterine cavity deformation (64.7% among second subgroup patients); increase of uterine cavity width on tubal orifices level in coronal view more than 4.5 cm (sensitivity of expulsion prediction – 58%, specificity – 98%); increase of uterine cavity area more than 9.0 cm^2 (sensitivity of expulsion prediction – 58%, specificity – 98%).

P293 Effects of levonorgestrel-releasing intrauterine system on cardio-metabolic risk factors in reproductive-age women: a 1-year follow-up study

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Aim: The aim of the research is to study the influence of the levonorgestrel-releasing intrauterine system (LNG IUS) on the development of the diagnostic parameters of the metabolic syndrome in fertile-age women.
Method: The participants of the study were 53 reproductive-age women who in the period from 01.01.2010 to 30.06.2013 wanted to start using contraception. At the beginning of the study as well as after 6 and 12 months of using contraception, all the participants had their abdominal circumference and body mass measured, as well as their body mass index and the arterial blood pressure determined. Blood samples were taken to determine the levels of triglycerides, high density lipoprotein and fasting glucose. Depending on the chosen contraception method, the participants of the study were divided into 4 sub-groups: group 1 – did not use hormonal contraception; group 2 – used COC; group 3 – used LNG IUS and their BMI was less than 25; group 4 – used LNG IUS, and their BMI was above 25.
Results: At the beginning of the study, there was determined a statistically significant difference between the groups with regard to the abdominal circumference, body mass and BMI – all these indicators were heightened in group 4.After evaluating the cardio-metabolic risk according to the presence of 5 MtS indicators in the study groups, it was determined that, during the 12-month period of using contraception, one MtS criterion was found in 25% of the participants of groups 1 and 2, 31.6% of the participants of group 3 and 35.8% of the participants of group 4. Two MtS indicators were found only in the participants of groups 3 and 4: 5.3% and 7.1% respectively, while 3 indicators were only found in the participants of group 4: 7.1%.
Conclusions: The use of LNG IUS affects the development of cardio-metabolic risk factors in reproductive-age women.

P294 Post partum IUD very effective and easy to implement

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Objectives: To demonstrate that PPIUD is a effective method of family planning,safe and with only few contraindication.The rate of expulsion depends by the skills of the medical staff,and by the time of insertion after delivery of placenta.
Materials and Methods: This is a progressive study.There are included datas from all clients,that choose PPIUD as a method of family planning,in Universitary hospitals obstetric-gynecology of Tirana ''Queen Geraldine'' and ''Koco Gliozheni''.These clients are followed by the medical staff in their periodic control.We tried to make comparisons with other studies in Cochrane library,but there were only few.
Results: We included in this study 136 patients that in post partum period accepted to insert IUD. The delivery was vaginal delivery in all patients and we found 5% after first pregnancy, 39% after the second pregnancy and 56% more than two pregnancies. The post partum period was normal and all patients did not have problematic complains. Expulsion rate was 2%.
Conclusions: PPIUD is a good choise for family planning.It is safe to insert, immediately effective,and doesn't affect breastfeeding.There are less contraindications for insertion, but higher expulsion rate than interval IUD.The best time for insertion post partum is inside 10 min after delivery of placenta.At this moment we found a 5% expulsion rate.It does not affect the amount of puerperal bleeding,and active management of third stage of delivery doesn't increase the expulsion rate.

P295 Benefits from Long-acting reversible contraceptives (LARC) use in adolescents and the role of paediatricians

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Context: The need for consistent and correct use of contraceptives in adolescents is crucial in order to prevent teenage pregnancy and sexually transmitted infections (STI).
Objective: Long-acting reversible contraceptives (subdermal progestin implants, Intra-uterine devices, and progestin injections) represent a cost-effective, accessible, and user-and-coitus independent option.
Methods–Patients–Intervention–Main outcome measure: Review of current literature.
Results: Added benefits include improvement in dysmennorrhoea, immediate return to background fertility, and suitability for special populations, such as adolescents with chronic illnesses, disabilities, obesity, and organ transplant recipients; HIV or immunosupression are also not contraindications. Lack of knowledge regarding mechanisms of action and female anatomy cause many adolescents to reject these methods. Paediatricians are ideally placed in order to educate and encourage teenage populations to consider such alternatives. They have the trust of their long-term patients and know the individual factors that may affect adolescents when choosing a contraceptive method, especially the ones that seek confidential advice with minimal embarrassment. In order to shape future attitudes paediatricians need to be adequately trained for the initiation of such methods and to maintain their skills. The use of condom must always be highlighted.

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Conclusions: Further studies need to be conducted on adolescents' views on LARCs to help healthcare professionals recommend the most appropriate contraceptive method for each one of them.

Menopause

P296 Menopause and HRT

Hayat Al-Harthy (SA)
PSMMC

The quality of life and the prevention became major objectives of medicine. In 2030 more than 45 million women will be postmenopausal (Hill K, 1996). Menopause is a normal, natural life event that usually occurs between ages 40 and 55. It becomes official after 12 months without a menstrual period. Some women reach menopause early or uprubtally, because of surgical removal of the uterus and ovaries, chemotherapy or medical treatment, or natural causes. Perimenopause, as its own name suggest, is the time in women's lives near menopause. It is important to keep the perspective that MHT is a tool that affects the care of menopausal women not only during their transition years, but also over the long-term given that they spend one third of their lives in menopause. Since a large proportion of menopausal women will suffer the consequences of cardiovascular disease and osteoporosis, further research regarding the role of MHT in these chronic medical conditions is needed. The science of MHT is evolving, and it is important to stay informed and keep an open perspective as our understanding about these agents improves. Age and years since menopause are important variables affecting the benefit-risk profile. For symptomatic menopausal women who are under 60 years of age or within 10 years of menopause, the benefits of MHT generally outweigh the risks. Systemic MHT initiated early in menopause appears to slow the progression of atherosclerotic disease, reducing the risk of cardiovascular disease and mortality.

P297 Vasomotor syndrome diagnosis (adapted Gerrie Gast scale)

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Context: The vasomotor syndrome is the main reason of consultation in menopausal women. It has been also associated with increase in cardiovascular risk. Thus the importance of its diagnosis. In 2008, Gerrie Gast et al described a questionnaire that assesses the vasomotor symptoms specifically.
Objective: Determine the vasomotor syndrome frequency using the modified Gerrie Gast scale in patients in transition to menopause and in post-menopausal women.
Methods: Observational, descriptive, cross-sectional, and prospective study of a group assessed with a measurement scale in the Climacteric Clinic of the Hospital Juárez de México, in Mexico City.
Patients: 201 Patients were assessed using the modified Gerrie Gest scale in the period from 30 June 2014 to 15 January 2015.
Interventions: None.
Main Outcome Measures: Modified Gerrie Gast scale.
Results: Vasomotor syndrome was detected in 172 patients (86%), 73 presented severe symptoms (36%), 37 moderate symptoms (18%), and 62 mild symptoms (30%). Hot flashes were present in 171 patients (75%), whereas night sweats were less frequent, seen in 108 patients (53%). Greater diagnostic frequency was detected when correlated to a prior study, compared with the Green scale, and resulting in diagnosis of 11% more cases.
Conclusions: The scale proposed by Gerrie Gast includes specific items to assess hot flashes and night sweats. Accordingly, using it in our population is recommended to obtain greater diagnostic accuracy and give timely treatment for vasomotor syndrome.

P298 Comparison of hematologic variables and NGAL levels of premenopausal overweight women with and without PCOS

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Context: Mean Platelet Volume(MPV), neutrophil to lymphocyte ratio(NLR) and platelet to lymphocyte ratio(PLR) are the new markers of the detection of inflammation. Neutrophil gelatinase-associated lipocalin(NGAL) is released from neutrophils and related with cardiovascular diseases. PCOS increases the risk of atherosclerosis by chronic inflammation.
Objective: To determine the chronic inflammation we compared the hematologic, metabolic parameters and NGAL levels of overweight premenopausal PCOS women with age matched overweight non-PCOS women.
Methods: This is a cross-sectional study.
Patients: Premenopausal women with BMI over than 25 kg\m2 were included. PCOS group was selected from women who fullfilled with 2 out of 3 Rotterdam criteria and non-PCOS group was selected from overweight otherwise healthy women who had regular menses and without a history of PCOS.
Interventions: Anthropometric measurements and blood tests.
Main Outcome Measures: BMI, NGAL levels,NLR, PLR, hemogram parameters, lipids, glucose and other biochemical markers.
Results: At PCOS group; NGAL=56.8±25 ng\dL, NL*R* = 1.83±0.76, PL*R* = 128.23±37.5, MPV=7.45±1.5fL, glucose=112.1±42.2mg\dL, cholesterol=211.2±43.1mg\dL, triglyceride=159.3±103.9mg\dL and at non-PCOS group; NGAL=71.22±100.1ng\dl, NL*R* = 1.96±0.73, PL*R* = 127.52±41.75, MPV=7.35±1.5fL, glucose=105±14.37mg\dL, cholesterol=217.7±32.1mg\dL, triglyceride=154.16±97.8mg\dL. No significant difference was observed for hematological variables and metabolic markers of two groups ($p > 0.05$).
Conclusions: We could not found any difference between metabolic and hematologic variables of PCOS and non-PCOS overweight premenopausal women which were useful for detecting chronic inflammation. As a result overweight women have the similar long-term cardiovascular and metabolic risk as PCOS due to chronic inflammation related vascular damage.

P299 Effect of partial light deprivation on vegetative, somnological, endocrine and psychoemotional status of women in perimenopausal period

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Context: Climacteric period in 60–80% of women in the population is associated with the development of disregulatory processes that occur on a background of involutional changes in the ovaries and the weakening of their hormonal function.
Objective, methods, patients and interventions: In order to study the nature of functional responses of the female body on the partial light

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deprivation we surveyed 184 women aged 41–60 years living in the Rostov region (Russia). All women with dysfunctional neuro-vegetative, endocrine, metabolic and psychoemotional disturbance carried out partial light deprivation using optical lenses with photochromic coating (mineral photochromic lenses ''Glare Control'' company ''Corning''). Usiing of sunglasses with light protective lenses was carried out daily in the conditions of stay in the sun, the course was at least 30 days during the period from May to October. Then, a re-examination was conducted. Women did not receive any medications or substitution hormonal correction.
Main Outcome Measures: We evaluated the level of 6-sulfatoxymelatonin in urine, hormonal status and neurovegetative and psycho-emotional changes.
Results: We found that under usual light regime the severity of vegetative, somnological and psycho-emotional changes in women in pre-and postmenopausal periods are largely determined by the expression of deviations of melatonin, FSH, luteinizing hormone, estriol, testosterone norm levels from the physiological level and as well – by the ratio of androgens and estrogens. We revealed that the use of partial light deprivation leads to increased levels of 6-sulfatoxymelatonin in urine and normalization of hormonal status in women with neurovegetative and psycho-emotional changes during menopause.
Conclusion: We showed that partial light deprivation has greater efficiency in premenopausal period compared to postmenopausal period.

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P300 Analysis of Framingham's score on postmenopausal women with and without metabolic syndrome

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Introduction: The menopause is defined as the permanent discontinuation of menstruation after one year of amenorrhea. The occurence of Hypoestrogenism during this period is marked by the worsening of climacteric symptoms, and also common emerging risk factors such as central obesity, hypertension, dyslipidemia and hyperglycemia which could lead to metabolic syndrome (MS).
Objective: To evaluate cardiovascular risk in the next 10 years through the Framingham's score in postmenopausal women with and without the diagnostic of MS on women treated at Hospital das Clinicas Samuel Libânio (HCSL) in Pouso Alegre/MG, Brazil within January 01, 2013 to June 01, 2015.
Methods: The sample included 121 postmenopausal women that were divided into two groups: the group with a diagnosis of MS ($n = 54$) and the Control group ($n = 67$) that didn't have the syndrome. It was used the data from clinical and laboratory examinations of patients contained in the medical record and applied to the Framingham's score that generated the cardiovascular risk of both groups.
Results: The Control group had a rate of 89.55% (60/67) low cardiovascular risk and greater statistical significance ($p = 0.001$) compared to the group with metabolic syndrome that obtained 60.25% low risk. In relation to the medium cardiovascular risk, the control group had a prevalence of 10.45% (7/67) compared to 31.50% (17/54) of the group with MS but without any significance ($p = 0.7$). The Control group have not showed any prevalence of high cardiovascular risk, and when compared to the MS group that have reached 9.25% (5/54) prevalence, a difference with statistical significance ($p = 0.013$) have occurred.
Conclusion: The women diagnosed with metabolic syndrome in postmenopausal period exhibit an increased risk of having a cardiovascular event over the next 10 years.

P301 Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty

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Osteoporotic vertebral compressive fractures (VCF) are an increasing health problem.They cause severe back pain and loss of physiological posture, functional disability and decreased quality of life.VCFs are usually treated conservatively with analgesics, bed rest and rehabilitation. However, if pain management fails, other treatments should be considered. Percutaneous Vertebroplasty (PVP) is a minimally invasive procedure to treat acute VCFs which don't benefit from medical therapy alone. This procedure restores vertebral height and produces significant relief from back pain. We report our experience of 73 osteoporotic patients (61 women, 12 men; mean age 77.3 $\pm$ 8.2 years; femoral neck BMD: 0.552 $\pm$ 0.103; BMD: 0.736 $\pm$ 0.137 g/ cm^2) who undergo PVP. PVPs were performed by our experienced neuroradiologists with bilateral transpedicular 10/13-gauge needle injection of polymetilmetacrilate (PMMA) cement under fluoroscopic guide. All patients presented almost a symptomatic VF with associated edema in MRI. Back pain was assessed before, 6 hours and 1, 6 and 12 months after procedure with Visual Analog Scale (VAS), a numeric scale from 0 to 10 in which 0 indicates absence while 10 maximum level of pain.VAS score was very low in all patients with VCF at baseline. VAS decreased significantly immediately after procedure and after 6 and 12 months ($p = 0.002$ vs. baseline). None patient reported clinical complications after PVP. All patients received an individualized antiosteoporotic treatment after PVP.Our results demostrate PVP is well tolerated and associated with significant improvement in back pain in osteoporotic patients with painful VCFs. They show great pain relief with early and sustained improvement in quality of life increasing many time after procedure. However, clinical follow-up experience of patients undergoing PVP remain controversial and should be better assessed.

P302 Involvement of pro- and anti-inflammatory adipokines in the pathogenesis of postmenopausal osteoporosis: data from a pilot study

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Context: A wealth of evidence suggests that increase in body fat may exert beneficial effects on bone health and prevent the onset of osteoporosis in postmenopausal women. However, the mechanism underlying the interplay between these two tissues is still unclear.
Objective: To evaluate if adipokines act as biological mediators of the protective role of fat on bone tissue.
Patients: Total sample (119 postmenopausal women, median age= 56 years, median BMI= 35.1 kg/m2) subdivided into 30 women with normal bone mass density (BMD), 45 osteopenic and 44 osteopenic.

Methods: Serum levels of adipokines including interleukin (IL)-6, IL-8, IL-1β, adipsin, lipocalin-2, tumor necrosis factor alpha, resistin, leptin and adiponectin were assessed in all study subjects.
Main outcomes: Waist circumference and BMI were positively correlated ($p < 0.01$ for all correlations) with BMD at all sites (spine, femoral neck, total hip trochanter). Concerning adipokines: leptin was positively associated with BMD at spine ($r = 0.24$, $p < 0.05$), femoral neck ($r = 0.22$, $p < 0.05$), and total hip ($r = 0.28$, $p < 0.01$), while adiponectin was inversely correlated with BMD at trochanter ($r = -0.23$, $p < 0.05$). Of note, the observed association were all influenced by systemic level of IL-6. Indeed, at high level of this pro-inflammatory cytokines they all disappeared, while they persisted (with strength comparable to that observed in whole sample) at low IL-6 levels.
Conclusions: Our data suggest that adiponectin and leptin might be biological determinants of bone health in postmenopausal women, with an effect that is likely abolished when frank inflammatory responses take place.

P303 Follicle loss and apoptosis in cyclophosphamide treated mice: what's the matter?

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With increasing numbers of young female cancer survivors following chemotherapy, fertility loss is the most common side effects. We showed that the alkylating agent cyclophosphamide (CTX) treatment could cause severe primordial follicle loss and follicles apoptosis, resulting in loss of ovarian reserve. SPF female C57BL/6 mice were treated a single dose of 120 mg/kg of CTX or saline as control, and both sides of the ovaries were collected 3 or 7 days after injection. After CTX treatment, the ovaries were mostly composed of collapsed oocytes, presented marked cortical fibrosis, with a reduced number of follicles especially primordial follicles, which were confirmed by primordial follicle counting and immunohistochemistry and western blot detection for DDx4/MVH. The follicle apoptosis was tested by TUNEL assay and the number of TUNEL-positive follicle cells increased obviously in CTX treated mice. Then analysis of the PI3K/Akt/mTOR signaling pathway showed that CTX increase phosphorylation of proteins Akt, APAF-1, cleaved caspase-3, mTOR and its downstream protein S6K1 without affecting total levels. These demonstrated that the CTX treatment leads to the hyperactivation of PI3K/Akt/mTOR signaling pathway in ovaries which may be concerned with follicle loss and apoptosis. Any medication that can prevent PI3K/Akt/mTOR signaling pathway activation may own the potential as an ovarian-protective agent, which may be able to apply in female cancer patients for fertility preserving.

P304 Reasons for abandoning hormone replacing therapy (HRT) in menopausal women in Zhejiang province of China

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Objective: Hormone replacement therapy (HRT) has shown benefits for menopausal women, but it has low rates of acceptance and compliance in China. Our current survey was aim to analyze the reasons for abandoning the use of HRT in Zhejiang province of China.
Patients: We invited 716 women, aged from 40 to 65, at Women's Hospital School of Medicine Zhejiang University.
Intervention: The patients participated in a telephone survey about HRT practices. A total of 623 eligible questionnaires were included in the analysis. All participants had used or were using HRT with a doctor's prescription.
Main Outcome Measure: The age, degree of education, HRT type, Menopausal status, Years of HRT use, postmenopausal symptoms before and after HRT and the reason for discontinuation of HRT was questioned.
Results: The remedies were categorized as estradiol tabletes+ dydrogesterone/cyproterone acetate(383/623, 61.4%, included 82 taking complex packing tabletes), estradiol patch+dydrogesterone(78/623, 12.5%), tibolone(123/623, 19.7%) and estradiol valerate tabletes/estradiol patch alone for women after hysterectomy(39/623, 6.3%). A total of 209 (33.5%) women discontinued treatment. The main reasons for abandonment included, fear of breast and uterus cancer (64/209, 30.6%), menopausal symptoms decreased (42/209, 20.1%), inconvenience in taking pills or seeing a doctor (36/209, 17.2%) and doctor advised against HT(20/209, 9.6%). No relationship is found between any remedy types and the symptoms relief. However, taking two kinds of medication (estradiol tabletes/patch+ dydrogesterone/cyproterone acetate, not complex packing) is associated with the complain of inconvenience of medical treatment (OR 1.27, 95% CI 1.08–2.34).
Conclusion: The incidence of abandoning HRT was still high. The risks of HRT were over-concerned among Chinese menopausal women. HRT education should be promoted.

P305 The pattern of lipids and lipoproteins during the menopausal transit in Chinese women

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Background: The changes of lipids and lipoproteins during perimenopause and postmenopause have not been extensively studied in Chinese people.
Objective: For further understanding the characteristics of Chinese women during their menopausal transit from perimenopause to postmenopause, the changes of lipids and lipoproteins including Lp (a) during perimenopause and postmenopause have been investigated for the first time as primary study endpoints in Chinese women.
Methods: The retrospective study was carried out in perimenopausal and postmenopausal women from 20 provinces of China who visited Beijing Obstetrics and Gynecology hospital during 2008–2015. A total of 1015 women aged 34–76 years without hormone-replacement therapy were analyzed. Menopausal status was defined by the ''2011 Stages of Reproductive Aging Workshop criteria''. Metabolic patterns including total cholesterol (TC), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), lipoprotein (a) (Lp (a)), apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B) and hormones including estradiol (E2) and follicle-stimulating hormone (FSH) were assessed.
Results: TC, TG, and LDL-C increased significantly in the postmenopausal compared to the perimenopausal group, HDL-C decreased significantly (all $p < 0.05$). LDL-C and age had positive correlation, however, LDL-C and E2 had negative correlation; HDL-C and FSH had positive correlation; TC and FSH, age had positive correlation (all $p < 0.05$).
Conclusions: Some changes in lipids can be related to menopausal status, some to increasing age, some to both. Surprisingly Lp (a), despite known possible interference with estrogenic status, did not change neither with increasing age nor during the transit.

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P306 Metabolic patterns during perimenopause and postmenopause in Chinese women

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Context: The changes of metabolic patterns during perimenopause and postmenopause have not been extensively studied in China.
Objective: Whether menopausal stage and age are associated with the changes of metabolic pattern remains unclear. The study aimed to examine the changes of metabolic patterns during perimenopause and postmenopause in Chinese women.
Methods: Menopausal status was defined by the ''2011 Stages of Reproductive Aging Workshop criteria''. Metabolic patterns including body fat, resting metabolic rate, fasting plasma glucose (FPG) were assessed. Linear regression was used to evaluate the correlation between demographic information, metabolic patterns, and menopause status.
Patients: The retrospective study was carried out in perimenopausal and postmenopausal women from 20 provinces of China who visited Beijing Obstetrics and Gynecology hospital during 2008–2015. A total of 1015 women aged 34–76 years without hormone-replacement therapy were analyzed.
Intervention: No intervention.
Main outcome measure(s): Blood levels of FPG. Measurement of body fat and resting metabolic rate.
Results: Body fat and FPG increased significantly in the postmenopausal compared with the perimenopausal group, resting metabolic rate decreased significantly (all $p < 0.05$). Body fat had positive correlationship with age and BMI; FPG had positive correlationship with age and BMI; resting metabolic rate had positive correlationship with BMI, however, resting metabolic rate had negative correlationship with FSH (all $p < 0.05$).
Conclusions: Our data suggest that metabolic patterns are significantly different between perimenopausal and postmenopausal group. All changes in metabolic patterns are related to BMI. Some changes in metabolic patterns can be related to increasing age, some to menopausal status.

P307 Adherence in the vulvovaginal atrophy (VVA) treatment associated to psychological support

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Background: It is estimated that 40% of postmenopausal women experience discomfort due to vulvovaginal atrophy (VVA) treatment.
Materials and methods: A group was subjected to psychological support and a control group without it. In both, they were given medical treatment for VVA. All were informed that they would be incorporated into a research. The time taken for this job was a maximum of 20 sessions.
Patients: 50 Patients were taken. Both groups had similar characteristics. We worked with gynaecologist and psychologists.
Intervention: Assigning therapy was performed at random using numbers. The patients assigned to active intervention group, received the indication of medical treatment and referral to a psychologist. The control group received only medical treatment.
Main measured results: Randomized study, clinical trial with intervention and another group assigned to control. Evaluated age, marital status (MS), parity, occupation, time of onset of symptoms; required count sessions, adherence to treatment, gynecological evaluation, and perception of patient satisfaction.
Results: Average age 45 years; MS 28 married (56%), 22 single or divorced (44%); Parity 64% had children and 36% without; Occupation 36% ($N = 19$) housewives and administrative, and 64% ($N = 32$) professionals. The average time VVA symptoms, onset was 21 months. Of the 25 women assigned to the intervention, 88% required 15 or more sessions; 86% were treated with local treatment using óvulos and creams. In the intervention group 88% showed clinical improvement and semiological, in the control group 84% had clinical and semiological improvement. The perception, patients who received the intervention, 88% reported feeling very happy with psychological support. Control, 84%, group expressed the need for psychological support.
Conclusion: The two groups showed no significant differences.

P308 Gender-specific emerging cardiovascular risk factors and evaluation of the individual cardiovascular risk score

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Introduction: Cardiovascular disease (CVD) is still nowadays the main cause of death and disability among people worldwide, despite the efforts made for its prevention, it is actually more common in women. Besides the traditional CVD risk factor (CVDRF), new potentially independent sex-related CVDRF exclusive to women are emerging. Disorders of pregnancy like gestational hypertension and diabetes, endocrine pathologies such as PCOS and premature menopause, and rheumatic diseases such as rheumatoid arthritis and fibromialgia, are recognised by the literature to accelerate the development of CVD.
Materials and methods: Our observational study was conducted on 238 women without previous pathologic cardiovascular events in their life, aged 40–69 years, who attended the Menopause and Osteoporosis Centre of the University of Ferrara. We assessed their Individual CVD Risk Score (ICVDS) using Cuore.exe software, on the basis of their clinical history, anthropometric measures and latter blood cholesterol and glycemic values. Subsequently, we made a counselling about the significance of score, promoting a healthy lifestyle and organizing a follow-up.
Results: The sample was made of 238 patients, with mean age 57 years and mean ICVDS 1.77%. 67% were postmenopausal women, characterized by an average ICVDS of 2.2%, while the remnants premenopausal women had a mean ICVDS of 0.9%. The higher the body mass index (BMI) and abdominal circumference values, and the higher were their ICVDSs. The average ICVDS of patients affected by a rheumatic disorder (4.6%) was significantly higher than mean ICVDS of healthy women. Moreover 8.4% of patients were affected in the past by gestational diabetes mellitus or by pre-eclampsia and its average ICVS was slightly, even if not significantly, higher than that of people without obstetrics CVDRF.
Conclusions: A more favorable lipid profile and lower levels of blood glucose, mean blood pressure, BMI and ICVDSs than rational mean values characterized our sample. Postmenopausal patients and women who had obstetrics and rheumatic CVDRF, demonstrate to have a higher ICVDS than otherwise healthy patients, and the values were statistical significantly in the second subgroup.

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P309 The effects of soy isoflavones and conjugated estrogen on the aorta thickness of castrated rats

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Objective: To investigate the effects of soy isoflavones and conjugated estrogen on the aorta thickness of castrated adult Wistar mice (Rattus Novergicus).
Methods: Fifty four female albino rats were studied. The animals were castred 32 days before the gavage drug administration. They were divided into seven groups: Group A: control; Group B: isoflavone 46 mg; Group C: isoflavone 92 mg; Group D: isoflavone 120 mg; Group E: isoflavone 460 mg; Group F: conjugated estrogen 5 mcg and Group G: conjugated estrogen 50 mcg+Isoflavone 46 mg. The control (group A) did not receive any medication, but the groups B, C, D, E, F, and G received treatment for 32 days. All animals were sacrificed after 32 days. The aorta was extracted for histological analysis and was properly fixed and prepared according to the histology procedures for coloring with Hematoxilin-Eosin. Quantitative and qualitative evaluations were performed using morphometric method.
Results: When we compared the aorta thickness of castrated adult mice on Group D, E and F to Group C there was significant difference.
Conclusion: There was an increase in the aorta thickness using isoflavone 120 mg, isoflavone 460 mg and conjugated estrogen 5 mcg compared to isoflavone 92 mg.

Keywords

Aorta, artery wall, conjugated estrogen, isoflavones

P310 Innovations in treatment of climacteric syndrome. Experience of human placental extract in perimenopausal women

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Problem statement: Menopausal hormone therapy is effective in correction of climacteric symptoms, but in some women its use is limited due to its adverse events and contraindications. Our objective was to evaluate placental extract clinical efficacy when compared to placebo in correction of menopausal symptoms in perimenopausal women.
Methods: We performed randomized, blind, placebo-controlled prospective study in parallel groups. Forty premenopausal women with climacteric syndrome symptoms, menstrual disorders (amenorrhea) and FSH $\geq$20 mIU/ml were recruited at Scientific Center for Family Health And Human Reproduction Problems (Irkutsk, Russian Federation) in the period from 2013 to 2014. All patients were randomized in 1:1 ratio by the envelopes method. Twenty women (group 1) used placenta extract Melsmon® (Japan) 2ml (100 mg) SQ every second day for two weeks, then two times a week. Twenty patients (group 2) comprised a placebo group (2 ml SQ, similar regimen).
Results: After 4 months of treatment, the significant decrease of modified Kupperman menopausal index (mMI) were registered in both groups: from 48.31$\pm$10.79 to 26.33$\pm$7.39 points in the group of women who used Melsmon®, and from 48.21$\pm$9.65 to 33.11$\pm$12.29 points in the placebo group ($p = 0.0001$ for both groups). Statistically significant improvement of general health self-assessment, registered after 4 months of psycho-emotional symptoms after intervention was reported only in the first group. In this group, the symptoms of depression were observed before treatment in 15 (78.9%) patients, while after treatment only in 4 (21.1%) women ($p = 0.002$) (in the second group in 15 (78.9%) and in 11 (57.9%) women, respectively, $p = 0.14$).
Conclusion: Using placental medicine, in contrast to placebo, leads to significant decrease of incidence of psycho-emotional disorders associated with the menopausal transition.
Disclosure of interest: None declared

P311 Efficiency of estrogen-gestagen preparations in the treatment of osteopenia in postmenopausal women depending on the level of vitamin D

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In the presence of estrogen deficiency in postmenopausal women resorption prevail on bone formation, that leads to osteoporosis. The use of estrogens is the main pathogenetic method of treatment of osteopenia, associated with hypoestrogenemia. But in some women hormone-replacement therapy does not have the desired effect. Combined use of calcium and calciferol slow down the decrease of bone mineral density (BMD). The aim of this study was to define the efficiency of estrogen-gestagen preparations in treatment of osteopenia (daily continuously for 12 months) in postmenopausal women depending on the level of vitamin D in blood serum, who used sex steroids and calcium (1000 mg) and vitamin D3 (400IU) in I group ($n = 12$, mean age 53.7 + 0.8, vitamin D level 53.4 + 0.2 ng/ml) and in II group-($n = 11$, mean age 55.2 + 0.4, vitamin D level 29.7 + 0.4 ng/ml). BMD was defined by dual-energy X-ray absorptiometry on apparatus Lunar (USA). There were defined biochemical markers of bone metabolism in blood serum, which significantly changed during the first three months of therapy: the increase of osteocalcin level, the decrease of ß-cross-laps. During the treatment, BMD raised in all skeletal parts: I group: in lumbar spine, by 5.7 + 0.6%, in the proximal femur, by 4.0$\pm$0.5%, in the distal forearm, by 2.9 + 0.6%; decreased osteoresorption marker (48.3 + 0.9%) and increased marker of osteosynthesis (15.7 + 0.7%). In II group, BMD increased less than in I group: in lumbar spine, by 3.4 + 0.6%, in the proximal femur, by 2.3 + 1.1%, in the distal forearm, by 1.8 + 0.4%; osteoresorption index decreased by 41.3 + 0.7%, osteosynthesis index increased by 11.2 + 0.7% in comparison with baseline. Thus, high efficiency was found in the treatment of osteopenic syndrome with estrogen-containing preparations with the use of calcium and vitamin D in postmenopausal women depending on the level of vitamin D in blood serum.

P312 Estrogen replacement regulates vaginal innervations in ovariectomized adult virgin rats: a histological study

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Context: Vaginal dysfunction during menopause is generally assumed to occur because of diminished estrogen mediation of vaginal nerves.

Our previous Gräfenberg spot findings confirmed that the distal-third areas of the anterior vaginal wall bore a significantly greater number of nerves and sexual hormone may have certain degree of influence on these significant differences. However, the role of estrogen in vaginal innervations remain controversial.
Objective: To investigate whether hormonal–neural interactions occur in the vagina.
Methods: Sixty rats were randomly divided into six groups: the Sham-operated (SHAM) group, the ovariectomy (OVX) group, and 4 Estradiol treatment groups. After 2 weeks of treatment, biopsies were drawn from the distal- and proximal-half areas of the vagina, and the total number of PGP9.5-ir neuronal profiles was quantified using immunohistochemistry. Main Outcome Measures. The effect of estrogen lies on vaginal qualitative density. Results in SHAM group rats, the density of small nerve fibers in the lamina propria and muscularis was significantly higher in the distal-half areas of intact vaginal walls than the proximal-half areas ($p = 0.001$). In contrast, the overall PGP 9.5-ir fiber innervation density was significantly decreased in both the distal- ($p < 0.001$) and proximal-half ($p = 0.001$) areas in the OVX rats subjected to surgical menopause. Sustained estrogen administration for 2 weeks resulted in nerve fiber proliferation, with values reaching normal levels in the low-dose estradiol valerate group.
Conclusions: Our findings indicate that systemic hormonal therapy with low-dose estradiol valerate is effective and safe for treating deficient vaginal innervation caused by low level of estrogen activity in menopausal women, and may aid studies to identify an optimal estradiol dose to provide relief from vaginal discomfort.

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P313 Bone turnover alternations across the menopausal transition in southeastern Chinese women: the correlations with endocrine hormone levels

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Context: Menopause-associated osteoporosis is a global health problem affecting millions of women worldwide with an increased risk of fracture.
Purpose: To explore the serum levels of bone turnover makers in Chinese women across menopausal transition and the correlation between follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol with the bone turnover markers.
Methods: A cross-sectional study was conducted on 400 healthy Chinese women, separated into pre-, peri- and post-menopausal groups based on their menstruation changes. The serum levels of CTX, P1NP, FSH, LH, and estradiol were detected. Written informed consents were obtained from all participants.
Results: The serum levels of CTX and P1NP were significantly evaluated in peri- and post-menopausal status. Both serum FSH and LH were positively correlated with serum CTX in peri-menopausal women and post-menopausal women. Estradiol was inversely correlated with CTX in peri-menopausal groups. Multiple linear regression models shows that the serum FSH levels were independently related to the bone turnover marker CTX and P1NP after adjusting with age or estradiol levels.
Conclusions: The elevated serum levels of FSH were independent risk factors of bone loss in peri- and post-menopause, and measurement of the serum hormone levels in mid-age women with irregular menses could be used in early diagnosis of postmenopausal osteoporosis.

P314 Clinical efficacy and tolerability of dropsordry in Spanish women with urge urinary incontinence

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Context: Urinary incontinence (UI) is a significant health problem with considerable social and economic impact. An estimated 30% of women aged 30–60 years have urinary incontinence (UI), while more than 50% of community-dwelling older women have the condition.
Objective: To examine the effect of the supplementation of tablets containing dropsordry in women with urge urinary incontinence (UUI).
Method: A single-center, not randomiized open prospective study was carried out in 82 women with UI $\geq$45 years and were enrolled in this study (45–62 yrs old age). Items related to UI symptoms, were previously collected (T0) and these ítems were reviewed at the final of the study, 8 weeks (T2). The presence of UI was previously diagnosed using the International Continence Society standards (ICS).
Measures: Relationships between presence of UI and potential related factors as diabetes were also explored. Daily urinary test control was performed during the 8 weeks of treatment. Daily dosage was 1 g/day (500 mg twice per day) from 0 to 4 week (T1), following a 500 mg/day daily intake from 4 to 8 week (T2).
Results: Urgency grade score was reduced to 24.7%. The total urge episodes was reduced to 46%. Nocturia was reduced to 69.35%. Strenght Urinary Incontinence (SUI) was also tested showing a remarkably 52.17% reduction. The use of daily pantyliners was reduced to 66.25%. The panel test ICIQ-SF quest (Spanish versión) revealed 96.2% of subjective satisfaction and a 85.8% objective score in the improvement of quality of life.
Conclusion: the combination of High genistin isoflavones and pumpkin seed pyrogallol in dropsordry tablets seems to be a safe and highly effective supplementation to relieve the urinary incontinence symptoms

P315 The impact of menopause on the quality of sexual life

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Introduction: Menopause is a physiological process that affects women in many ways. The sex life of a woman continues during and long after the menopausal transition. The impact of menopause on the quality of sexual life is an important issue in today's society.
Methods and patients: From September 2014 until August 2015, we conducted a multicenter clinical trial aiming to determine the impact of menopause on the quality of sexual life. We assessed 469 women aged 45–60 years, belonging to all socioeconomic classes and being in natural menopause. Women with surgical menopause, systemic diseases, hormone replacing therapy, and mental or physical illnesses were excluded. All patients completed a questionnaire regarding their sexual activity and sex-related quality of life, recording the occurrence of five side effects of the menopause (low libido, difficulty in achieving sexual fulfillment, vaginal dryness, dyspareunia, and decreased

frequency of sexual intercourse), rating each with values ranging from 0 (no side effect) to 5 (severe).
Results: 59.28% of the patients had low or absent libido, 67.16% declared rarely achieving sexual fulfillment, 62.90% of the patients complained of vaginal dryness, while 80.17% complained of moderate to severe dyspareunia. 74.84% of the patients observed a decline in the frequency of sexual intercourse, due to alteration of libido and physical discomfort.
Conclusions: Although the menopause generates severe alterations in every woman's life, its impact on the quality of sexual activity is often underrated. A better understanding of the women suffering in their sexual life during menopause is needed in order to improve its quality.

P316 Influence of treatment of vulvovaginal atrophy with intravaginal prasterone on the male partner

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EndoCeutics

Context: Vulvovaginal atrophy (VVA) is caused by thinning of the epithelial lining of the vagina and lower genitourinary tract, with decreased lubrication and a loss of elasticity of the vaginal wall. The decrease in vaginal tissue strength and the increased friability increases the risk of epithelial damage with pain at sexual activity, dryness, burning, irritation, and bleeding after sex.
Objective: The aim was to analyze the opinion of the male partner of women treated for VVA with intravaginal 0.50% prasterone (DHEA), thus providing information to the couple.
Methods: On a voluntary basis, in a prospective, randomized, double-blind and placebo-controlled phase-III clinical trial, the male partner filled a Male Partner Exposure Questionnaire at baseline and at 12 weeks stating his observations related to his penis and intercourse before and after VVA treatment.
Patient(s): A total of 100 partners in the male population answered the Male Partner Exposure Questionnaire.
Intervention(s): Postmenopausal women with moderate to severe dyspareunia were administered daily for 12 weeks intravaginal 0.50% (6.5 mg) prasterone or placebo.
Main outcome measure(s): The administration of intravaginal prasterone to women was considered to have no significant negative adverse effect on the male partner if at least 80% of male partners from the prasterone-treated group had a global score ≤ 1 for changes from baseline to week 12.
Result(s): Thirty-six percent of men having a partner treated with prasterone did not feel the vaginal dryness of the partner at the end of treatment compared with 7.8% in the placebo group. In the prasterone group, 38% of men scored very improved compared with 18% in the placebo group.
Conclusions: The male partner had a very positive evaluation of the treatment received by his female partner.

P317 Evaluation of the acceptability of intravaginal prasterone ovule administration using an applicator

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Context: Atrophic changes of the epithelial surface of the vaginal mucosa are responsible for the best known symptoms of vulvovaginal atrophy (VVA), namely vaginal dryness, pain at sexual activity and irritation/itching. The correct use and acceptability of local therapies by women, has a great influence in the effectiveness and adherence to the treatment.
Objective: The objective of the study is to evaluate the acceptability of the intravaginal administration of prasterone vaginal ovules for the treatment of VVA in women with moderate to severe dyspareunia who were administered daily for 12 weeks intravaginal 0.50% (6.5mg) prasterone or placebo.
Methods: On a voluntary basis, in a phase III, placebo-controlled, double-blind, prospective, and randomized study women were asked to fill a 7-item self-report Usability Questionnaire at week 12.
Patient(s): There was a total of 373 women who responded to the Usability Questionnaire for both treatment groups.
Intervention(s): Postmenopausal women with moderate to severe dyspareunia were administered daily for 12 weeks intravaginal 0.50%(6.5mg) prasterone or placebo.
Main outcome measure(s): It was considered before start of study that the applicator was suitable if at least 80% of participants had a global score ≤ 2 (mean score from Questions 1 to 5) and a score ≤ 2 for Question 7.
Result(s): 99% and 100% of participants had a score ≤ 2 units in the placebo and prasterone groups, respectively, for the global score (mean of 5 questions). When asked about like and dislike of the technique of drug administration, 284 comments were positive, while 114 women gave no comment. From 92–94% of women indicated that they were very confident to be able to use the applicator successfully in the future.
Conclusions: The survey shows a high degree of satisfaction and of confidence to use the applicator successfully in the future.

P318 Prevalence of overweight and obesity in Brazilian postmenopausal women

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Context: The association between obesity and menopause have been studied by several authors. In fact, during this period there is a fat redistribution to the android type that is associated with metabolic syndrome.
Objectives: Study the prevalence of overweight and obesity in Brazilian postmenopausal women and determine whether there is an association between BMI weight classification and two variables: type of menopause (natural or surgical) and time elapsed since menopause (early or late postmenopausal).
Methods: A prospective study involving 930 postmenopausal women treated at the Climacteric Ambulatory at Irmandade da Santa Casa de Misericórdia de São Paulo Hospital between June 2013 and April 2014 was performed.
Patients: Postmenopausal women with amenorrhea >_one year and FSH>_ 30mUI/mL.
Interventions: Data like age, BMI, type of menopause and time elapsed since menopause were collected from medical records. Overweight was defined by BMI of 25–29.9kg/m2 and obesity by BMI>_30kg/m2.
Main Outcome Measures: A bivariate analysis was performed using the chi-square test. It was considered statistically significant at $p < 0.05$.
Results: An overall prevalence of overweight and obesity of 70.75% was detected. The overweight prevalence was 39.14% and obesity 31.61%. There was no statistically significant association between BMI weight classification and type of menopause ($p = 0.53$) or time elapsed since menopause ($p = 0.75$).
Conclusions: The high prevalence of overweight and obesity detected is an important outcome given the strong correlation between obesity and increased morbimortality. Perhaps the absence of analysis of other variables such as parity, use of hormone replacement therapy and practice of physical activity influenced the result of no statistical difference between BMI weight classification and type of menopause or time elapsed since menopause.

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P319 Effects of Hormone Replacement Therapy on the Breast Density: Transdermal Estrogen vs. Oral Administration Estrogens in Postmenopausal Patients. Systemic Review.

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The Hormone Replacement Therapy (HRT) reverses symptomatology and improves the metabolic and cardiovascular profile during the climacteric. Previous studies have shown that the HRT increases the breast density, which is a risk factor of breast cancer.
It is known that the way of administration of the estrogens, influences on their pharmacokinetics and this can generate different clinical effects.
The objective of this systemic review is to evaluate the effects of the breast density of transdermal estrogens vs. of the oral administration.
Materials and methods: A systemic review was made of the Literature based on the PUBMED EMBASE, CENTRAL and LILACS data, using the MESH terms and the terms DeCS for LILACS .
Results: A primary selection was made of the articles and 10 studies were selected by title and summary. Two studies met the inclusion criteria and were chosen for complete text reading and statistical analysis. Out of this Systemic Review of the Literature, it is evidenced that estrogens administered via transdermal vs. oral have a protector effect for any increase in the breast density (Peto OR 0.37; 95% IC 0.21 to 0.67), and likewise in changes of at least 15% (Peto OR 0.25; 95% IC 0.12 to 0.50).

P320 Brain and serum cholesterol metabolism during perimenopausal transition: a risk factor for Alzheimer's disease?

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Context: Perimenopause is a transitional state in women's life characterized by reproductive and neurological senescence most likely related to alteration in lipid metabolism. Furthermore, several climacteric symptoms like depression and memory impairment are associated with increased risk of Alzheimer's disease(AD).
Objectives: The present study was focused on the investigation of brain and serum cholesterol (Chol) metabolism during perimenopause transition in order to better understand how it potentially relates with neurodegeneration.
Methods: Chol metabolism was evaluated in rat models with main characteristics of human perimenopause. Gene and protein expression involved in lipoprotein transport and Chol metabolism were evaluated in rat brain cortex. Moreover, serum Chol profile was compared with data from 231 women in different menopausal stages.
Results: Gene expression analysis indicated two distinct aging programs: chronological and endocrine. Chronological aging was characterized by activation of genes involved in Chol synthesis, transport, and efflux mainly before perimenopause. Conversely, endocrine aging was characterized by repression of the same pathway. Similarly, serum-lipid profile analysis showed an age-dependent increase of total Chol and triglycerides levels, whereas endocrine aging was not correlated to modification of the same markers. Serum-Chol profile data in the animal model were comparable to that observed in humans.
Conclusion: Both chronological and endocrine aging impact Chol metabolism in rat cerebral cortex. The age related increase in Chol metabolism was unanticipated and suggests activation of pathways involved in myelin or steroid pathways. A reduction of Chol levels in cortex and hippocampal areas in AD patients. Moreover, the increase of serum Chol due to chronological aging appears not to be influenced by estrogen decline in humans and rats.

P321 Prevalence of climacteric symptoms comparing perimenopausal and postmenopausal Chinese women

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Objective: To understand the characteristics of Chinese women during their menopausal transit from perimenopause to postmenopause, the study aims to compare the prevalence of climacteric symptoms in Chinese women.
Methods: Menopausal status was defined by the ''2011 Stages of Reproductive Aging Workshop criteria''. The climacteric symptoms were investigated.
Patients: The retrospective study was carried out in perimenopausal and postmenopausal women from 20 provinces of China who visited Beijing Obstetrics and Gynecology hospital during 2008–2015.A total of 1115 women aged 34–76 years without MHTwere analyzed.
Main outcome measure(s): Calculation of the prevalence of climacteric symptoms.
Results: The most frequent five symptoms of 1115 women were fatigue (75.97%), insomnia (70.59%), irritability (66.40%), palpitation (62.11%), and depression (61.71%). The most frequent five symptoms of 808 perimenopausal women were fatigue (73.28%), insomnia (67.77%), irritability (63.77%), depression (59.92%), and palpitations (57.02%), however, the most frequent five symptoms of 307 postmenopausal women were fatigue (83.33%), insomnia (77.90%), palpitation (75.72%), irritability (73.19%), and dizziness (66.67%).The prevalence of fatigue, insomnia, irritability, palpitation, dizziness, muscle and joint pain, vaginal dryness, hot flash, sweat, pain during intercourse, and myrmeciasis was significantly higher in postmenopause compared with the perimenopause status group (all $p < 0.05$).
Conclusions: The prevalence of climacteric symptoms we investigated were different from Western countries' reports. The most frequent five symptoms of 1115 women were fatigue, insomnia, irritability, palpitations, and depression, nearly the same in perimenopausal and postmenopausal women.

P322 Acidity level (pH) of vagina as alternative diagnostic marker for menopausal women in remote areas

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Introduction: Indonesia is an archipelago country with many remote areas which is not covered by medical/laboratory facilities. Moreover, the average level of education and economy in Indonesia is still low, affecting the availability and affordability of medical examination. Many Indonesian women are still uninformed about menopause and often assumed that they had already experienced menopause even without adequate serum hormonal examination. Compared with

serum hormonal examination, vaginal pH examination is relatively easy to perform, and inexpensive as an alternative method to diagnose menopause definitively.
Method: Analytical study of diagnostic tests performed in the clinic of obstetrics and gynecology of Hospital in Samosir Regency, Sumatera Utara, began in August 2015 with the case was menopausal women and the control was non-menopausal women who met the inclusion criteria. Vaginal pH was measured using a pH meter strip, then 3 cc of blood was drawn to measure the level of FSH.
Result: The subject of study is 45 menopausal women and 45 non-menopausal women, with menopause group results most of them are 50–59 years old, the highest parity is 3–4, most BMI of obese, and duration of menopause is generally above 4 years. While in the non-menopause group; most of them are 30–39 years old, the highest parity is 3–4, and generally with a normal BMI. There are differences in the mean vaginal pH levels (menopause 6.07 ± 0.72 and non-menopause 3.80 ± 0.89; $p < 0.001$) and FSH (menopause 74.67 ± 35.47 mIU/ml and non-menopause 21.75 ± 25.34 mIU/ml; $p < 0.001$) that were significant. Vaginal pH has a good diagnostic value with AUC value of 95.7% (95% IK 91.7–99.6%); $p < 0.001$. Vaginal pH cut-off point is ≥ 5.5 with sensitivity of 77.8% and specificity of 93.3%.
Conclusion: Vaginal pH value can be used as an alternative diagnostic tool in enforcing the menopause in women in remote areas.

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P323 Glutathione peroxidase (GPX) level as one of diagnostic tools of menopausal complaints severity degree among paramedics women in Medan, Indonesia

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Background: During menopause, recurrent vasomotor disturbance episodes resulted in an increase in long-term metabolic problems and demonstrated the contribution to the formation of oxidative stress in disturbing antioxidants function to neutralize ROS (Reactive Oxygen Species).
Objective: Determining the characteristics of postmenopausal paramedics, the relationship, the average difference, the degree of menopausal complaints, cut-off levels of Glutathione Peroxidase (GPx) as a marker of menopausal complaints severity degree, measuring the sensitivity and specificity, positive predictive value, negative predictive value and accuracy of GPx levels.
Methods: This analytical study using the diagnostic tests design, carried out in Haji Adam Malik Hospital. Sample recruitment began in December 2013 until the sample size of 50 people. The study population was postmenopausal patients aged 45–56 years who worked as paramedics.The degree of menopausal complaints are assessed by Menopause Rating Scale (MRS).
Results: We obtained five paramedics with no menopausal complaints, 19 with minor complaints, 18 with moderate complaints and 8 with severe complaints. There is a significant difference between the levels of GPx against the severity of menopausal complaints ($p = 0.0001$). Negative correlation ($r = -0.641$) was observed in the relationship between the levels of GPx and the severity of menopausal complaints. Cut-off value of GPx levels of paramedics menopausal women can be used as a marker of the severity of menopausal complaints are at levels of 533.33 mU/ml with the degree of severity of moderate to severe menopausal complaints obtained sensitivity value of 87.5% and specificity value of 80.8%, positive predictive value of 80.8%, negative predictive value of 97.5%, and accuracy value of 84%.
Conclusion: Glutathione Peroxidase (GPx) can be used as a diagnostic tool to assess the severity of moderate to severe menopausal complaints.

P324 The associations of carotid artery intima-media thickness, magnetic resonance imaging of brain artery, and atherosclerosis-related factors in postmenopausal women

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Objective: The purpose of this study was to investigate the relationships between carotid artery intima-media thickness (IMT) and severity of cerebral infarction, lipid profile, blood glucose, blood pressure, bone mineral density (BMD), and physical and age-related factors in postmenopausal women.
Design and methods: The subjects were 311 postmenopausal Japanese women aged 48–82 years (mean age 62.2 ± 6.5 yrs) who visited our menopause clinic. Magnetic Resonance Imaging (MRI) examination of brain artery was made and hyper intensity of deep and subcortical white matter density was classified into five grades after Brain dock guideline of Japan. Carotid artery IMTs were measured by the ultrasonography. Levels of serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), blood glucose (BG), HbA1c, blood pressure (BP), and BMDs at the lumbar spine (L2–L4) were measured. LDL-C/HDL-C ratios were calculated, respectively. The relationships among max IMT, severity of cerebral infarction, and these atherosclerosis-related factors were analyzed.
Results: Significantly apparent correlations were found between max IMT and severity of cerebral infarction. Significant correlations were found among max IMT and age, years since menopause (YSM), habit of tobacco smoking, and BP. Significant correlations were found among severity of cerebral infarction and age, YSM, habit of tobacco smoking, HbA1C, and BP.
Conclusion: Measurement of thickening of IMT of carotid artery can be useful in predicting severity of cerebral infarction. Age, habit of smoking, hypertension, and hyperglycemia may be mainly responsible for the atherosclerosis and cerebral infarction in these postmenopausal women.

P325 The effectiveness of FRAX for osteoporosis in postmenopausal women in Beijing

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Context: The FRAX tool has been developed by WHO to evaluate fracture risk of patients. It was used for prevention and treatment of osteoporosis in USA and China.
Objective: To evaluate whether FRAX is appropriate screening tool for osteoporosis in postmenopausal Chinese women.

Method: This study was a cross-sectional design. The subjects administered the DXA and then were given the 10-year probability of fracture through FRAX.
Patients: All subjects were community-dwelling postmenopausal women living in Beijing, which have never received any pharmacologic therapy for osteoporosis and have never been classified by past diagnosis as a secondary osteoporosis.
Intervention: Basic information was collected by structured interview. No other intervention in this study.
Main outcome measures: Data analysis was performed using SPSS for windows 18.0. The following values were calculated for screening test: sensitivity, specificity, and Youden's index.
Results: A total of 759 subjects were included. The median 10-year probability of hip fracture was 0.6% (range 0–10%) and the median 10-year probability of a major osteoporotic fracture was 2.7% (range 1.4–16%). 10-year probability of fracture in osteoporosis were 0.95% (range 0.2–8.6%) and 2.75% (range 1.8–11%), respectively.
As the cut-off value of 10-year probability of fracture increased, sensitivities decreased and specificity increased. But, all of the Kappa values were $\leq$0.4. As cut-off value of 10-year probabilities of hip fracture risk was 0.6%, we had the maximum Youden's index which was 31%. At this point, sensitivity was 81.9% and specificity was 49.1%.
Conclusion: The results calculated through FRAX underestimated the 10-year probability of fracture in post-menopausal women in Beijing. FRAX was not adequate screening measure for osteoporosis in the same population.

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P326 Effect of lemon balm on postmenopausal sleep disorder: a triple blind randomized controlled clinical trial

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Sleep disorder rate in menopausal women are high, and must be prevented by using safe pharmacologic or complementary therapy.
Objectives: To assess effect of lemon balm on postmenopausal sleep disorder.
Material and methods: In the first phase of this triple-blind randomized controlled clinical trial, 270 healthy volunteer menopause women with age group 50–60 yrs had been visited in one of the clinics of Tehran University of Medical Sciences. Study had two questioners: demographic characteristics and Petersburg Sleep Quality Index (PSQI). Regarding PSQI cut of point, 100 volunteer, who had sleep disorder, after filling in informed consent in the second phase of study randomly divided to two groups and received 250 mg lemon balm oral capsules or 50 mg starch oral capsules as placebo in the same shape capsules, two times in a day for one month. PSQI were checked again after one month intervention. Descriptive and inferential statistics were used. Study was approved by ethics committee of TUMS.
Results: Most of the women were in the age group of 50–52 yrs (62%). A total of 20% of participants in intervention group and 8% in placebo group showed improvement in the quality of sleep. There was significant difference between average of PSQI in intervention and Placebo group, and significant decrease of PSQI had been seen in lemon balm group. ($p < 0.05$)
Discussion: Use of 250 mg lemon balm oral capsules two times in a day for one month had effect on improvement of sleep quality. There was no side effect after its use but need more study in this field.
Acknowledgment: Received grants from research department of Tehran University of Medical Science, Year 2011–2013.

P327 Predicting the presence of psychoemotional disorders in perimenopausal women.

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Context: The development of reliable criteria for predicting the presence of psychoemotional disorders in perimenopausal women allows the doctor and the patient in a timely manner carrying out a complex of measures aimed at maintaining the health of women, form risk groups that require special attention on the part of gynecologists and psychotherapists.
Objective: The purpose of the study is to define the criteria for predicting the presence of psychoemotional disorders in perimenopausal women.
Methods: Modified menopausal Kupperman–Uvarova index (MMI), Greene Climacteric Scale (GCS) and a statistical module "Classification Trees" (CT) were used in the study.
Patients: The study involved 127 perimenopausal women and was conducted at "Gynecological City Hospital", Belarus.
Main outcome measures: The algorithm of the module "CT" allowed reducing the number of significant analyzed parameters, allowed determination of their threshold values and ranges, as well as a sequence of incremental assessment to predict the presence of psychoemotional disorders in patients.
Results: Six factors were emphasized which were associated with the presence of psychoemotional disorders in perimenopausal women: age, severity psychoemotional component of the MMI, anxiety and depression by GCS, the lack of sex, reduced sexual desire. According to the "CT" 5 classes of perimenopausal women with psychoemotional disorders were singled out: moderate to severe psychoemotional component of the MMI; 45 years of age and decreased sex drive; the age of 46–50 yrs; age>50 years, absence of sexual relations, while maintaining sexual desire; depression by GCS>5 in conjunction with anxiety by GCS$\geq$7 points.
Conclusions: The proposed algorithm will improve the quality of diagnostic procedures for assessing the risks of psychoemotional disorders in perimenopausal women during gynecological examination.

P328 Exercise patterns and postmenopausal health

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Introduction: Menopause is an inevitable component of ageing. Menopausal symptoms, osteoporosis, and cardiovascular disease are the major consequences of postmenopausal estrogen decline. Exercise may aid in the management of menopause-associated pathology.
Purpose: To investigate the association of exercise with parameters of physical and mental health in a sample of postmenopausal women who engage with exercise regularly.
Methods: 51 women aged 54 years, 5.2 years postmenopausal, answered a questionnaire about their habits concerning their physical activity. These data were compared with self-reported parameters on physical and mental health.
Results: 72.2% of women exercised at least three or more days per week, at least 45 min per day. The most frequent types of exercise were swimming by 65.4% and walking by 55.8%. 44% of women started exercise after 40 years of age. The reason to start exercise was medical prescription in 25% of women and encouragement by friends in 40% of women. Regular exercise improved sleep in 83% and mood in 66.7% of women. Concerning menopausal symptoms, 13.9% of

women showed improvement in hot flushes, 27.8% were helped in weight management and 33.3% mentioned improvement in muscle aches. 28% of women reported improvement in serum glucose and lipids after they had started exercising.
Conclusion: Swimming and walking were the most frequent types of exercise in our sample of healthy postmenopausal women. Regular exercise is associated with multiple health benefits in postmenopausal women, specifically concerning sleep, mood and muscle functioning.

P329 Menopausal osteoporosis in a patient with compressive goiter and untreated seizures: from fall to the risk of fracture

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Context: Osteoporotic fractures risk includes low Bone Mineral Density (BMD) at central DXA (diagnosis of osteoporosis based on menopausal T-score), but also the risk of fall (based on muscle strength, vitamin D deficiency, neurological or hypoglycemic conditions).
Objective: We analyze the relationship: from fall (caused by medical conditions) to the risk of fractures (due to the diagnosis of osteoporosis).
Methods: Menopausal bone metabolism is assessed, as well as thyroid and general biochemistry parameters.
Patient: This is a case report of a menopausal women evaluated in different tertiary centers of endocrinology and gynecology from Romania.
Intervention: A 59-year old Caucasian non-smoking female is known with goiter since the last two years. She developed compressive symptoms so thyroidectomy was recommended but she delayed it. Her medical history includes symptomatic menopause since age of 51 with no hormone therapy. She is mildly hypertensive. She complains about a lack of appetite during the last weeks which she believes to be related to her goiter.
Main Outcome Measure: On admission, a body mass index of 16.5 kg/sqcm is found. Thyroid ultrasound revealed a 2.8 cm nodule with intact trachea. She suffered a short seizure while she was admitted and, later, she remembered a few similar episodes since last year. A psychiatric exam confirmed depression.
Result: Computed tomography scans found skull lesions after previous contusions, lumbar fractures. DXA found osteoporosis: lumbar BMD of 0.83 g/sqcm, T-score of −2.9, Z-score of −0.8. Weekly alendronate, vitamin D/ca supplements together with anti-depressives and anti-epileptic drugs were started.
Conclusions: Depression might mimic menopause symptoms and also the goiter-associated dysphagia. An osteoporotic patient with seizures and low weight has a higher risk of fractures because of fall risk.

P330 A prospective case-control study on the lipid profile and the cardiovascular risk of menopausal women on oestrogen plus progestogen therapy in a northern Italy province.

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Context: Tertiary-care academic center.
Objective: To evaluate the effects of oestrogen plus progestogen therapy(EPT) on the lipid metabolism in menopausal patients.
Methods: Prospective study.
Patient(s): 223 patients with clinical and biochemical diagnosis of menopause, eligible for hormone therapy and with a follow-up period of at least 5 yrs.
Intervention(s): 178 patients were included in the study group (EPT Group) and 45 in the control group (N-EPT-Group). The control group was composed of patients who had declined for personal reasons. Patients attended annual or 6-monthly visits for the duration of the 5-year follow-up period.
Main outcome measure(s): Modification of Serum values of total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride in both groups during the follow-up, from the recruitment (measurement I) to 5 years (measurement II).
Result(s): At the first visit, comparing EPT-Group versus N-EPT-Group, the median values were: cholesterol 240 versus 226 mg/dL, LDL-cholesterol 169 versus 174 mg/dL, HDL-cholesterol 60 mg/dL in both groups, triglyceride 125 versus 92 mg/dL[p:n.s]. Five years later EPT-Group were characterized by significantly lower total cholesterol (225 versus 236 mg/dL), and lower LDL-cholesterol (125 versus 184 mg/dL). No significant difference was observed between groups for HDL-cholesterol (64 versus 68 mg/dL) and triglyceride (72 versus 94 mg/dL). No adverse effects of EPT were observed.
Conclusions: Our data clearly show that EPT positively impact on the lipid profile of menopausal women. In particular when started early, initially with low doses and without rigid cutoffs, EPT could represent a valid instrument for cardiovascular prevention.

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P331 Benefits of isoflavones, calcium, vitamin D and insulin in postmenopausal woman: clinical and metabolic aspects, quality of life and sexual function.

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Context: The onset of menopause heralds an opportunity for prevention strategies to improve health and quality of life.
Objective: To evaluate the effects of isoflavones, calcium, vitamin D, and insulin preparations in menopausal women.
Methods: Patients were randomly divided into two group. Several aspects were investigated: clinical (vasomotor disturbances), metabolic (body composition, bone depletion, lipid profile), quality of life, and sexual function. The t-test was employed to compare the two groups.
Patients: 50 menopausal women with a mean age 52.6±3.69 years and an average of 3.32±1.62 years since menopause were enrolled. Intervention: women were randomized to receive either oral preparations of isoflavones (40 mg), calcium (500 mg), vitamin D (300 UI), and insulin (3 g) (group A) or placebo (group B).
Main outcome measures: Assessment of quality of life and sexual function were carried out through the Menopause-Specific Quality of Life Questionnaire (MENQOL) and the Female Sexual Function Index (FSFI). Evaluations of anthropometric indicators, body composition through bioelectrical impedance analyser, lumbar spine, and proximal femur T-score and lipid profile were performed.
Results: After 12 months, a significant reduction in MENQOL vasomotor, physical and sexual domain scores ($p < 0.05$), and a significant increase in all FSFI domain scores ($p<0.05$) were observed in treatment group. Laboratory tests showed a statistically significant increase in serum levels of HDL ($p < 0.05$). No statistically significant changes in lumbar spine and femur neck T-score ($p > 0.05$) and body composition were found.
Conclusions: Isoflavones, calcium, vitamin D, and insulin exert favourable effects on vasomotor symptoms, lipid profile, sexual function quality of life and a protective effect against bone mass depletion. No effects on body composition have been demonstrated.

P332 Effect of menopause and hormone therapy in postmenopausal women on visceral fat: a meta-analysis

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Context: Menopause causes changes in the distribution of fat, particularly visceral fat, which is a predictive factor for cardiovascular risk. Hormone replacement therapy (HRT) can improve menopausal symptoms and reduces visceral fat area in postmenopausal women. However, reports on the association between visceral fat area in pre- and post-menopausal women and use of HRT are inconclusive.
Objective: To investigate the association of visceral fat area and menopause as well as the relationship between hormone therapy and visceral fat area in postmenopausal women.
Methods: MEDLINE, EMBASE and CNKI were searched through July 2014, and six studies met the eligibility criteria.
Patients: Postmenopausal women.
Interventions: HRT.
Main outcome: Effect of menopause and HRT on visceral fat.
Results: This meta-analysis was performed involving 479 premenopausal and 278 postmenopausal women. Visceral fat area was significantly increased in postmenopausal compared with premenopausal women (mean difference=−20.54, 95% confidence interval: −39.07–2.00, $p = 0.03$). HRT was associated with significantly decreased visceral fat area and low-density lipoprotein and increased triglyceride and high-density lipoprotein (visceral fat area, hormone therapy vs. controls, mean difference=−18.39, 95% confidence interval: −22.52–14.27; low-density lipoprotein, mean difference=−18.56, 95% confidence interval: −32.28–4.84; triglyceride, mean difference=13.65, 95% confidence interval: 8.90–18.41; high-density lipoprotein, mean difference=6.32, 95% confidence interval: 1.92–10.72). Visceral fat area showed no significant difference between pre- and post-HT in postmenopausal women (mean difference=0.08, 95% confidence interval: −9.42–9.59).
Conclusions: Hormone therapy reduces visceral fat area and may have beneficial effects on serum lipids in postmenopausal women.

P333 Microbiota of vagina in postmenopausal women

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At the moment there is enough information about peculiarities of vaginal microbiota in women of reproductive age. But there are single reports concerning vaginal microflora (VF) in postmenopause(PM).
Objectives: To study qualitative and quantitative vaginal microbiota in postmenopausal women.
Materials and methods: The study included 136 postmenopausal women aged from 45 to 75. All patients underwent cytological assessment of vaginal wall with the following estimation of epithelium maturation index. In accordance with the results, all patients were distributed into the groups: group1 included 84 patients with VA, 52 patients without VA made up group2. PCR–RT was used to study VF.
Results: Total bacterial mass (TBM) in postmenopausal women makes up with median10 6.6 genomic equivalents/sample that is lower than in women of reproductive age.While the duration of PM progresses TBM slowly reduces as well as the number of VF representatives, and Lactobacillus spp.(Lb spp.) all dramatically to complete elimination. Simultaneously with lactobactarial fall a number of anaerobic flora increases with Prevotella bivia/Porphyromonas spp. and Eubacterium spp. prevailing. TBM was less in group1 compared with group2 ($p < 0.0001$). We also noted the decrease of Lactobacillus ($p < 0.0001$), Gardnerella vaginalis($p = 0.005$) and increase of Enterobacteriaceae, Prevotella bivia/Porphyromonas spp., etc. ($p < 0.005$). In spite of the decreased TBM and low share of lactobacteria in VF normocenosis (NC) (Lb spp. more than 80% relating to TBM) was found in some postmenopausal women. NC rate was significantly lower in women with VA and it reduced while the duration of PM progressed. L.iners, L.Crispatus and L.gasseri of lactoflora were most common in postmenopausal women.
Conclusion: TBM in PM is less then in reproductive women. Incendes of NC is lower in women with VA, and it was reducing with the duration of PM.

P334 Vulvovaginal atrophy: symptoms, impact on emotional well-being, quality of life and sexual function

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Objective: 40–57% of postmenopausal women have such vaginal atrophy (VA) symptoms as vaginal dryness, pruritus, stinging pain, and dyspareunia. The purpose of the present research is study of VA symptoms impact on emotional well-being, quality of life, sexual function of postmenopausal women.
Materials and methods: 136 postmenopausal women from 40 to 75 years have participated in the medical research. Cytological screening of vaginal paries with further assessment of maturation index of epithelium has been applied to all the patients, which resulted in grouping of women depending on VA presence or absence. Patients answered the questionnaire according to the results of which VA impact on emotional well-being, quality of life, sexual function was investigated.
Results: The study group (group1) included 84 patients who had the diagnosis "VA", the control group (group 2) of 52 women. VA symptoms were present in two groups and statistically did not differentiate. Dryness appeared to be the most frequent complaint mentioned by 63% of respondents. Our respondents felt embarrassed because of the feeling of discomfort in the vagina (in group1–42.9%, in group 2–50.0%, $p = 0.418$), which in turn had negative influence on women's emotional status. Both in groups1 and 2, women experienced discomfort during sexual intercourse: pain, dryness and postcoital blood discharges. Group1 observed pain and dryness in the time of sexual intercourse more frequently. It may show that the patients of this group turned to be less sexually active. Patients of both groups marked that VA symptoms caused refusal from intimate life, libido decrease that had negative impact on interpersonal relationships between partners.
Conclusion: Vaginal dryness, pruritus, stinging pain and dyspareunia often disturb women in postmenopausal period and impact on emotional well-being, quality of life and sexual function.

P335 Influence of estrogen-gestagen preparations on elastic properties of vessels and ventricular arrhythmias in postmenopausal women

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Estrogens not only regulate important aspects of cardiovascular(CV) system functioning, but also influence on risks for the development of CV diseases. Significant stature of CV pathology rate caused by changes in elastic properties of vessels(EPV), electrophysiological mechanism disturbance of impulse formation in myocardium and atherosclerosis is one of the consequences of estrogen-deficient conditions in postmenopause.
Aim: To estimate the influence of MHT on EPV and on characteristics of idiopathic ventricular arrhythmias without structural cardiac changes in 64women with vascular risk factors in postmenopause (mean age 52.8 + 2.8). Group I ($n = 18$, mean age 52.4 + 2.5) used oral forms of MHT, II-transdermal ($n = 24$, mean age 55.2 + 0.4 года), III-control group ($n = 22$, mean age 53.2 + 4.6). Holter monitoring was conducted to estimate rhythm disturbances. Pulse wave velocity, augmentation index were measured by sphygmography. The study lasted six months.
Results: Favorable effect of MHT on EPV in early postmenopausal women, more marked in II group. In receiving antihypertensive therapy women with hypertension (1–2st) the use of CRHT showed the decrease of pulse wave velocity (on 38.3 + 5.7%) and improvement of vascular stiffness parameters, but the increase of augmentation index (on 13.3 + 0.9%), probably, connected with interaction of antihypertensives. In early postmenopause in patients with idiopathic rhythm disturbances prevalence of single, paired and group ventricular arrhythmias, that can be explained by electrophysiological features of women myocardium work. Management of MHT leads to authentically significant decrease of idiopathic rhythm disturbances amount. Thus, management of MHT can decrease CV-risks in women with vascular risk factors in postmenopause due to the improvement of EPV and stabilization of electrophysiological mechanism of impulse formation in myocardium of ventriculus.

P336 Investigation on the prevalence of climacteric symptoms and its influencing factors of women in Southeastern China

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Objective: To investigate the influence of living environment, education level, economic level and occupation condition on menopause symptoms in women during menopause transition.
Methods: The questionnaire survey was carried out on 2000 menopausal women in Women's Hospital, School of Medicine, Zhejiang University, from May 2011 to May 2015. Chi square test was used to analyze the data. Written informed were obtained from all participants.
Results: 1. Among all 2000 participants, the average age was 46.63±7.66 years, and the average Kupperman score (KI) was 14.02±4.40; 2. KI of menopausal women living in the city (14.57±4.23) was significantly higher than the rural (12.07±4.56) ($p < 0.05$); 3. The women with higher educational level had more severe symptoms, KI of those with university education was 14.79±5.32, high school education was 14.50±4.99, middle school and lower was 13.78±4.46; 4. There were no significant differences among the postmenopausal women with different economic levels; 5. Women working full-time suffering from the menopause symptoms (KI=13.01±4.27) were the lowest among the those working part time (14.26±4.87) and the those retired or unemployed (15.88±5.33). The statistical difference between full-time group and retired/unemployed group was significant ($p < 0.05$).
Conclusion: The living environment and occupation condition may be associated with the prevalence of menopause symptoms, but the level of culture and economic income may not be associated with symptoms of menopause.

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