

# Abstracts

## Oral Communications

( in numeric order)

### REPRODUCTIVE MEDICINE, CONTRACEPTION AND MENOPAUSE

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#### **Experimental study of the oxidant / antioxidant (ao) balance in ovariectomized female rats under hormone replacement therapy (HRT)**

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**Introduction:** The aim of our study was the experimental exploration of oxidative stress in surgically induced menopause and the effects of HRT (estrogens or estroprogestatives) on the uterine tissue and plasma antioxidant status in parallel to histological changes.

**Methods:** The researches were performed in white female Wistar rats. Bilateral surgical ovariectomy was performed, by the technique used for women, adapted for female rats. Seven days after ovariectomy, estrogen replacement drug therapy (estrogen monotherapy) and (combined) estroprogestative drug therapy was initiated for 14 consecutive days. The ovariectomized animals were divided into 3 groups, to which a fourth group of fertile animals was added: group 0—fertile control group. One day after the administration of the last HRT dose, blood samples were taken from all groups for biochemical determinations. Subsequently, the uterus was harvested on ice for the biochemical determinations and was kept in formol for the histopathological examination of menopausal endometrium, with and without treatment. Free malondialdehyde (MDA), lipoperoxides (LPx), carbonylated proteins CP), hydrogen donors (HD) were determined.

**Results and discussion:** Free MDA, LPx and CP as oxidative stress parameters have lower serum values in healthy animals, with an intact uterus, compared to ovariectomized animals. Free MDA, LPx and CP have lower serum values in ovariectomized animals receiving estrogen monohormone replacement therapy compared to ovariectomized animals without replacement hormone therapy or compared to ovariectomized animals receiving estroprogestative therapy, which demonstrates the AO efficacy of estrogen therapy. The tissue values of free MDA, LPx and CP are higher in ovariectomized animals with estroprogestative HRT compared to animals

with estrogen monohormone HRT, which supports the inclusion of monoestrogen HRT in AO therapy. Antioxidants, represented by HD capacity, have higher serum values in healthy animals with an intact uterus. HD have higher serum values in ovariectomized animals receiving monohormone estrogen replacement therapy, compared to ovariectomized animals without hormone replacement therapy or compared to ovariectomized animals receiving estroprogestative therapy. The short duration administration of estrogen HRT also induces proliferative endometrial effects in research animals. Estroprogestative HRT maintains endometrial atrophy, experimentally certifying the safety of the endometrium obtained by continuous combined HRT.

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#### **Respiratory problems in the offspring of hypertensive women: a role for oxidative stress?**

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**Introduction** Recent clinical studies suggest that respiratory distress syndrome (RDS) incidence is increased in infants of mothers with HELLP syndrome (Torrance J Matern Fetal Neonatal Med 2007 and Kim Yonsei Med J 2006). In line with these clinical observations, a recent study by our group showed that the L/S ratio is in fact significantly decreased in pregnancies complicated by HELLP syndrome (submitted).

RDS has been associated with oxidative stress and inflammatory processes (Buss Pediatr Res 2000), as has HELLP syndrome (Hubel Proc Soc Exp Biol Med 1999). Therefore, the present study investigated end-tidal carbon monoxide corrected for inhaled CO (ETCOc), plasma malondialdehyde (MDA) (markers of oxidative stress) and pro-inflammatory cytokine (IL-6, IL-8) production in infants of preeclamptic mothers with or without HELLP syndrome.

**Methods** All infants of preeclamptic mothers (GA <32 weeks) admitted to the NICU in 2003 were included in the study. ETCOc was measured at 0-12, 48-72 and 168 h postnatally using the CO-Stat™ End Tidal Breath Analyzer (Natus Medical Inc., San Carlos, CA). Simultaneously, blood was sampled for MDA, Il-6 and Il-8.

**Results** From the 36 infants, 19 had mothers with HELLP syndrome. At 0-12h, ETCOc, MDA and Il-8 values were significantly higher in the HELLP group (ETCOc  $2.4 \pm 0.7$  v  $1.7 \pm 0.7$ ,  $p < 0.02$ ; MDA  $2.3 \pm 0.7$  v  $1.6 \pm 0.7$ ,  $p < 0.02$ ; Il-8  $204 \pm 179$  v  $94 \pm 97$ ,  $p < 0.04$ ). MDA remained significantly higher during the first 7 days of life ( $2.6 \pm 1.2$  v  $1.5 \pm 1.0$ ,  $p < 0.02$ ). Il-6 did not differ significantly between groups.

**Discussion** Oxidative stress and pro-inflammatory cytokine levels are increased in infants of mothers with HELLP syndrome. These processes may cause inactivation of surfactant (Gitto Intensive Care Med 2001) and thus may explain the increased RDS incidence in infants from mothers with HELLP syndrome.

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### Increased 4-hydroxy-2nonenal expression in endometrial ovarian cysts

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Numerous studies have shown that oxidative stress may play a role in the pathophysiology of endometriosis as well as the disease-related infertility. 4-Hydroxy-2nonenal (4HNE) is one of the most reactive lipid peroxides, produced during oxidative modification of the lipid component. Therefore, measurement of its levels can be used to evaluate the level of oxidative damage. The aim of the study was to estimate the expression of 4HNE in ovarian endometrial cysts.

**Material and Methods:** Ten samples of endometriomas and ten functional follicle ovarian cysts were obtained during laparoscopy. Specimens were fixed in formalin and embedded in paraffin. Immunohistochemistry with specific antibodies was used to examine the 4HNE expression.

**Results:** 4-Hydroxy-2-nonenal expression was found in all examined samples. Mean ( $\pm$  SD) H score for 4HNE expression was significantly ( $p = 0.01$ ) higher in endometrial cysts ( $5.5 \pm 0.89$ ) as compared to functional cysts ( $2.0 \pm 0.33$ ).

**Conclusions:** Increased 4HNE expression suggests that oxidative damage occurs in ovarian endometriomas. On the basis of our findings we hypothesize that oxidative stress is an active participant in the pathogenesis of the endometriotic disease.

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### Evaluation of perinatal outcomes from pregnancies after assisted reproductive techniques

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**Introduction:** Infertility and its treatment are issues increasingly important in gynaecology practice. It is estimated that infertility affects 50 to 80 million couples in the world. In Portugal there are 10 to 16% infertile couples. These couples demand medical help for resolution of infertility and since 1978, when the first baby from in vitro fertilization was born in England, newborns from assisted reproductive techniques have greatly increased.

**Methods:** The authors made a retrospective observational study to evaluate perinatal outcomes of pregnancies after assisted reproductive techniques, between 1 January 1999 and 31 December 2006, at Department of Reproductive Medicine of Hospital de S. João. The authors evaluated pregnancies complications, incidence of preterm birth, average gestational age, weight at birth and neonatal outcome.

**Results:** A total of 266 pregnancies were included. Average women's age was  $31,7 \pm 3,86$  and time of infertility  $5,2 \pm 3,05$  years. The principal cause of infertility was male factor (48,1 %). Techniques used were intracytoplasmatic sperm injection (ICSI) in 56,4 %, in vitro fertilization (FIV) in 39,1% and intrauterine insemination in 4,1%. The type of infertility was mainly primary (73,3%). Perinatal outcomes were evaluated in 209 pregnancies where complete information was available. In this group, from this techniques resulted 73,2% singleton pregnancies, 23,0% twin pregnancies, and 3,8% multiple pregnancies. The mode of delivery was the cesarean section in 64,3% and vaginal birth in 35,7%. The average weight (in grams) at birth was  $3096 \pm 589,9$  in singleton pregnancies,  $2450 \pm 495$  in twin pregnancies and  $1625 \pm 462,8$  in multiple. Preterm birth occurred in 20,3%, half of the incidence (41%) in the same population between January 1999 and December 2003.

**Conclusion:** Most newborns of this study have good neonatal outcomes although high incidence of preterm birth and multiple pregnancies could be associated with worst results. We hope better outcomes with actual policy in reducing number of embryos transferred.

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### **Sexual life changing in Women, partner of Men with Erectile Dysfunction treated with Viagra, measured by Index of Sexual Life (ISL).**

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**Objectives :** To investigate treatment responsiveness of the quality of sexual life specific questionnaire: Index of Sexual Life (ISL) for female partners of men with erectile dysfunction (ED). (ISL) questionnaire -an 11-item self-administrated questionnaire- has specifically been designed to document the impact of ED on the sexual life of female partners from their own perspective and had been validated previously.

**Design and Methods:** The ISL questionnaire was completed at baseline and at the end of the study by 57 female partners of 57 patients with erectile dysfunction enrolled in a 14 week, open label, multicentre, flexible dose sildenafil (50mg, adjustable to 25 or 100mg) study. The men were clinically diagnosed with ED using the International Index of Erectile Function (IIEF) recruited at 12 centres in France in 2006. Changes from the baseline score were analyzed using the paired t test. Correlations between the changes from baseline on the ISL and the Erectile Function domain of the IIEF and on the Sexual Relationship domain of the Self-Esteem and Relationship Questionnaire (SEAR) were examined. The statistical analysis of EDITS in men and female partners were presented.

**Results:** There was a statistically great increase ( $p < 0.0001$ ) in the primary domain partner Sexual Life Satisfaction score from baseline to Week 14. These data indicate moderate correlations between improvements in male erectile function (EF/IIEF) and female partner Sexual Life Satisfaction (SLS/ISL) with a Spearman coefficient = 0.527 and between improvements in male self esteem (SE/SEAR) and female partner sexual life satisfaction (SLS/ISL) with a Spearman coefficient = 0.519.

**Conclusions:** The ISL questionnaire is responsive to effective treatment of erectile dysfunction. These data suggest that the ISL questionnaire is a valid instrument for detecting sexual gains in female partners from beneficial intervention. Couples in a long-standing relationship should benefit from including partners in discussions of ED treatment for better treatments outcomes and continuation.

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### **Obesity and Reproductive Health**

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**Introduction:** Obesity has a negative impact on spontaneous conception, miscarriage, pregnancy and the long term health of both mother and child. PCOS is an important cause of subfertility. Several studies have shown that weight loss in women with PCOS improves the menstrual cyclicity and reproductive outcome for these women.

**Methods:** Retrospective audit of women with subfertility and increased body mass index (BMI) at the Waikato Hospital, Hamilton, New Zealand. The impact of obesity was measured with respect to its impact on subsequent management and outcome, modifications needed for the management of their subfertility and results of changes in the BMI of patients on their fertility and subsequent pregnancy.

**Results and Discussion:** Obesity was a common presentation at our clinic. These women were more likely to have anovulatory menstrual cycles and PCOS. Those who responded well to measures to decrease their BMI benefitted from improvements in their endocrine profile, menstrual cyclicity, rate of ovulation and likelihood of a healthy pregnancy. Measures to improve their fertility had higher success rates in patients who could lower their BMI. Multidisciplinary input and close supervision and support were critical in achieving these goals.

Those who had a high BMI had a higher incidence of miscarriages and needed closer monitoring and multidisciplinary input in the antenatal and intrapartum period. They also resulted in higher resource utilization including need for additional tests like ultrasound scans, Glucose Tolerance Tests (GTT), increased number of interventions in labor and a higher number of adverse outcomes.

**Conclusion:** Obesity has a negative but reversible impact on a woman's reproductive health. Preventive and timely corrective measures by multidisciplinary input, close supervision and support will have a major impact on their Reproductive health and quality of life.

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### **Laparoscopic treatment of ovarian endometrioma in infertile patients - our experience**

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**Introduction:** 14.5% of the infertile patients submitted to laparoscopy in our Unit between January 1999 and December 2006 presented ovarian endometriomas. The objective of this study was to determine the best surgical management with respect to recurrence and fertility outcomes.

**Methods:** We analyzed retrospectively the clinical files of 77 consecutive patients with a follow-up of at least 6 months. Four groups were considered: Group 1 - complete cystectomy (n=47); Group 2 - partial cystectomy and coagulation (n=8); Group 3 - drainage and coagulation (n=16); Group 4 - drainage (n=6). Recurrence and pregnancy rates were studied according to the laparoscopic treatment method, history of previous ovarian endometrioma surgery, number and characteristics of the endometriotic ovarian cysts. Recurrence was defined as the presence of cysts greater than 2 cm by ultrasonography.

**Results:** The mean follow up time was 21.6 months (6-84). Global recurrence rate was 22.1% (n=17). Patients of group 1 had a significantly lower recurrence rate

(14.9%; n=7) than those in group 2 (50%; n=4) and lower but not statistically different from groups 3 (25%; n=4) and 4 (33%; n=2). A history of previous ovarian endometrioma surgery (n=17) was associated with more frequent recurrence (41.2%; n=7). Multiple and/or bilateral endometriomas were not associated with a different recurrence rate. Endometriomas with dimensions between 2.0-4.0 cm (n=8) recurred in 44.4%; 4.1-6.0cm (n=7) 28% and  $\geq$  6.1cm (n=2) in 14.3% (differences not significant). Pregnancy occurred in 35 patients (45.6%): 9 spontaneously, 7 with ovarian hyperstimulation, 2 with IUI and 18 with ART. The pregnancy was obtained in average 12.4 months (5-58) after surgery. Cystectomy was associated with a higher pregnancy rate 31.9% (15/47) (no ART pregnancies included) than groups 2 (1/8; 12.5%), 3 (2/16) and 4 (0/6). Recurrence rate was lower in cases with post-operative non ART pregnancy - 14.3% (5/35) than in the no pregnancy group - 28.6% (12/42) but numbers do not reach statistical significance.

**Conclusion:** Cystectomy seems to be the most efficient technique in terms of recurrence and pregnancy. Previous ovarian endometrioma surgery is a negative prognostic factor.

## CANCER, BREAST, UROLOGY

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### Comparison of three novel "tension free" procedures to cure vaginal vault prolapse

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**Introduction:** this study was carried out to compare perineal ultrasonographic (US) findings and assess the efficacy of three different named "tension free" procedures: (a), IVS posterior; (b), TOT posterior and (c), TVM (Tension free Vaginal Mesh) in the management of patients with vaginal vault prolapse and associated pelvic floor defects.

**Materials and Methods:** 19 patients, 14 after vaginal and 5 after abdominal hysterectomy with  $\geq$  stage II cuff prolapse, who required surgical treatment, were enrolled in the study. Pre-operative evaluation included: history, urine culture, pelvic examination, US imaging of pelvic floor, urodynamics and quality of life (QoL) assessment. At regional anesthesia, 9 (a), patients underwent IVS

posterior procedure, 4 (b), females operated with TOT posterior and 6 (c), by TVM approach. All techniques provides apical as well as posterior wall support and additional reconstructive and anti-incontinence procedures were performed as indicated. Outcomes measures intra-operative complications, clinical prolapse degree, US evaluation of the bladder neck, apex of the vagina, anterior rectal wall, the tape or mesh position and width, it's distances from symphysis and bladder neck, healing abnormalities, QoL including dyspareunia, at last follow up after 1,3,6 and 12 months.

**Results:** the mean patient age was 65 (range 43-83 years), mean parity was 3 (range 2-6), there were no significant differences among groups with respect to demographic and clinical characteristics. At last follow up visit, mean total vaginal length was 7 cm (range 5-10), zero degree vault prolapse was restored in all patients, granulation reaction to the mesh occurred in 1 patient after TVM procedure, no tape or mesh ejection was found, no perineal hematoma, no pararectal abscess, no bladder and bowel perforation occurred, no pelvic discomfort, no buttock pain or dyspareunia was reported. Perineal US examination showed in all patients, no significant differences in the tape or mesh position among three surgical procedures, the apex of the vagina was located above the urogenital hiatus in the direction of the spread of any increase of the intraabdominal pressure.

**Conclusion:** perineal ultrasound helps us to understand the pathology of an individual patient and to analyze precisely anatomical outcome of three surgical procedures to cure vaginal vault prolapse. Overall optimal or satisfactory results in restoring vaginal anatomy were achieved in all patients undergoing three different safe "tension free" techniques

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### Long-term (11 years) Follow-up of the Results of the Tension-free Vaginal Tape (TVT) Procedure for Treatment of Female Stress Urinary Incontinence

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**Introduction:** The TVT procedure has become the most commonly performed surgical procedure for the treatment of female stress urinary incontinence. Intermediate time follow-up has shown high cure rates. We have prospectively been following a initial cohort of 90 women who had a TVT operation performed in the mid 90's. We here report on the eleven years results.

**Methods:** Ninety primary cases of urodynamically proven stress incontinence had a TVT operation performed in local anaesthesia between January 1<sup>st</sup> 1995 and August 15<sup>th</sup> 1996 at one centre in Finland and two centres in Sweden. Pre- and post-operative assessment included a cough stress test, a 24 hour pad test, post-void residual urine measurements, a visual analog scale for urinary symptoms (0-100). At the 11 years follow-up visit condition specific validated quality of life questionnaires were additionally utilized: IIQ-7, UDI-6, UISS, DIS. Patients Global Impression (PGI) of cure was asked and gynaecological examination performed to detect adverse reaction of the tape material or signs of erosion. Objective criteria of cure was a negative stress test and a negative 24 h pad test.

**Results:** Seventy three per cent of the initial 90 patients could be identified at a mean of 11.5 years after the operation. Fifty one of these could be evaluated at the clinics according to the protocol. Another 12 patients were interviewed by telephone. Six patients had died, six were severely disabled, seven are still scheduled for follow-up and 8 seems to be lost to follow-up. Objective cure was found in 85.4 % of the patients. By the PGI 78 % were subjectively cured with another 20 % improved and only 2 % regarded treatment as a failure. 90.7 % of the patients claimed they were dry on straining. No tape erosion was seen and 3.7 % reported some kind of voiding difficulties.

**Discussion:** The TVT procedure seems to have a good long-term durability in terms of both objective and subjective cure of stress incontinence. No long-term adverse effects of the operation were detected.

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### Comparative Study of *Inside-out* and *Outside-in* Transobturator Tape Procedures for the Treatment of Stress Urinary Incontinence

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**Objective:** To compare the clinical outcomes and safety of *inside-out* (tension free vaginal tape obturator-TVT-O) and *outside-in* (transobturator tape-TOT) transobturator isolated procedures for treatment of female stress urinary incontinence (SUI).

**Material and Methods:** Retrospective comparative study between 329 women who were submitted to TVT-O, performed according to *de Leval*, and 122 women submitted to TOT, performed according to *Delorme*, between 2004 and 2006. Surgical complications and outcomes at 3 months, 1 and 2 years after surgery were compared in both groups, using SPSS (Statistical Package for the Social Sciences) 15.0 for Windows. The choice of tape was primarily decided by the surgeon's preference.

**Results:** The two groups of patients were similar in terms of demographic criteria, associated diseases, clinical presentation and urodynamic characteristics. Surgery duration was longer in TOT group (21.8±7.0 min) than in TVT-O group (16.4±6.3 min; p<0,0001). Vaginal perforation was more common in TOT group (11.5% versus 1.8%; p<0,0001). Postoperative voiding difficulties were more frequent in TVT-O group, but with no statistical difference. The cure rate at 3 months of follow up was 88.4% for TVT-O and 76.3% for TOT (p<0,01), at 1 year was 79.3% for TVT-O and 58.5% for TOT (p<0,001) and at 2 years it was 82.5% for TVT-O and 56.9% for TOT (p=0,0001). Vaginal tape erosion occurred in 4.1% of cases of TVT-O and 13.9% of TOT (p=0,001). The rate of *de novo* urgency urinary incontinence was similar in both groups.

**Conclusion:** In this study TVT-O is a safer technique, with fewer intra and postoperative complications and tape erosions than TOT procedure. The efficacy of the *inside-out* technique is also better than *outside-in* technique, with superior cure rates.

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### Correlation between preoperative data and functional results after transobturator approach for surgical repair of female urinary incontinence

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**Background:** The complaint of any involuntary leakage of urine is an uncomfortable and embarrassing problem. TVT-O and TOT are minimal invasive techniques with promissory results in treatment of female urinary incontinence.

**Objective:** The objective of this study was to detect if preoperative variables (age, parity, body mass index, hormonal status, comorbidity, associated uro-genital prolapse, clinical and urodynamics characteristics of urinary incontinence, previous pelvic surgery, associated surgery and per or postoperative complications) predict the functional results after transobturator approach surgical techniques for treatment of female urinary incontinence.

**Material / Methods:** The present study included 359 women operated for urinary incontinence using transobturator tape procedures (TVT-O or TOT) at our institution, between January 2003 and May 2007. Those were divided in two groups: A- patients with positive results (cure or improvement of urinary incontinence) and B- patients with persistent postoperative urinary incontinence or appearance of de novo urge symptoms.

**Results:** Of the 359 women assessed, 273 were included in group A and 86 in group B. Median age at time of treatment was 54.4 vs 57.2 years. Multiparity, obesity (BMI<sup>2</sup>>30), menopause and associated morbidity were similar in both groups. Associated prolapse was present in 24.9% vs 20.9% (p=n.s.). Mixed incontinence (53.1% vs 77.9%; p<0,001), urethral hypotonia (2.6% vs 14%; p<0,001) and detrusor overactivity (1.5% vs 8.1%; p=0,005) were more frequent in group B. Other gynaecological surgery was associated in 25.6% vs 29.7% (p=n.s.) and 44% vs 50% (p=n.s.) had a previous pelvic surgery. Per or postoperative period complications arised in 13.5% vs 18.6% (p=n.s.).

**Conclusions:** The transobturator approach is an effective procedure for urinary incontinence. In our population, negative results were associated with the presence of mixed incontinence, urethral hypotonia and detrusor overactivity.

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### Invasive lobular carcinoma – pleomorphic variant

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**Objectives:** Characterization of pleomorphic invasive lobular carcinoma and comparison with classic invasive lobular carcinoma.

**Material and methods:** Retrospective analysis of invasive lobular carcinoma (ILC), diagnosed and treated in our department from January 2004 to December 2006.

**Results:** Histological diagnosis of 28 ILC revealed 10 pleomorphic variant (PV) and 18 classic variant (CV). Comparing PV vs. CV, mean age at diagnosis was 56 vs.59 (p=ns.), being 60% vs.78% post-menopausal women (p=ns.). Clinically, patients presented palpable lesion in 90% vs. 39% (p=0,003) and imaging alterations in 10% vs. 61% (p=0.003). Metastatic disease was found, at diagnosis in 50% vs. 5% (p=0.003), most frequently regional nodal metastasis. Histology described mixed invasive tumors (ILC and invasive ductal carcinoma) more often in CV (p=0.018). In-situ component had similar prevalence in variants, as well as Paget dissemination and multifocal lesions. G2 tumors were the most frequent, but G1 were only found in CV (p<0.005) and G3 in PV (p<0.005). Ganglionar invasion was present in 75% vs. 28% (p<0.005). Estrogen receptors (ER) were positive almost always, but presented as negative in 40% vs. 0% (p=0.001). Cerb2 was mainly negative. The authors found recurrences followed by death in two PV patients.

**Conclusions:** PV seems to have more aggressive behavior than other ILC. Tumors presented more frequently as palpable lesions and with metastatic disease. PV was associated with G3 neoplasms, negative ER and ganglionar invasion.

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### Congenital forms of a thrombophilia in cancer patients with recurrent VTE.

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**Background:** High rate of the recurrent venous thromboembolism (VTE) as often complication in cancer patients has induced us to carry out association between congenital defects of a hemostasis system and the recurrent VTE in oncogynaecological patients.

**Aim:** Determination of the rate and structure of genetic forms of a thrombophilia in gynecological cancer patients with recurrent VTE.

**Methods:** 78 patients with VTE episodes in the past: 43 has ovarian cancer, 20 uterine carcinoma, 15 cervical carcinoma.

The control group includes 30 women with gynaecological cancer without any VTE episodes and has not family history of VTE.

Laboratory tests: Detection of FV Leiden mutation, prothrombin G20210A mutaton, gene PAI-1 G4/G5 polymorphism, gene MTHFR C677T mutation, genes of platelets glycoproteins polymorphism: GP IIb/IIIa, GP Ia/IIa, GPIb $\alpha$ , GP ADP.

**Results:** We have detected the incidence of FV Leiden mutation is 15 (19,2%); homozygous gene MTHFR mutation is 33 (42,3%); heterozygous gene MTHFR mutation is 40 (51,3%); prothrombin mutaton is 13 (16%); gene PAI-1 polymorphism is 23 (28,8%); platelets glycoproteins polymorphism is 35 (44,9%).

In control group FV Leiden mutation was in 3 patients (10%); homozygous gene MTHFR in 2 (6,7%), heterozygous gene MTHFR mutation in 5 cases (16,6%); gene PAI-1 polymorphism in 3 (10%) and platelets glycoproteins polymorphism is 3 patients (10%).

**Conclusions:** Presence of multigenic thrombophilia is the expressed trigger of VTE. So patients with multigenic thrombophilia should be permanently treated by anticoagulats (LMWH) under the control of thrombophilia markers, such as D-dimer, TAT complexes and platelet factor 4.

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### Invasive pT1 breast cancer with extensive in situ component

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**Introduction:** In situ disease surrounding invasive tumors is an important consideration in the management of patients with breast cancer. The objective of this study is to assess the influence of in situ disease including an extensive in situ component (histologic definition) on surgical treatment, margin, local recurrence and survival.

**Methods:** Analysis, in our Institution from January 1995 to December 2005, of 362 cases of ductal invasive pT1 breast cancer: one group of 318 cases of none or focal in situ ductal carcinoma and another group of 44 cases of extensive in situ ductal carcinoma.

**Results:** Average age at time of diagnosis was 55,1 years  $\pm$  12,1 (24-85). Most patients were post-menopausal. Statistically significant differences were found between the two groups for the histologic size of invasive component ( $p=0,001$ ), multifocal tumor invasion ( $p=0,005$ ), involved resection margin ( $p=0,002$  for margin with in situ tumor and  $p<0,0001$  for margin with invasive

tumor) and rate of re-excision ( $p<0,001$ ). No statistically significant differences were found between the two groups for treatment, local recurrence ( $p=0,746$ ), overall survival ( $p=0,865$ ) and for recurrence-free survival ( $p=0,178$ ).

**Conclusions:** An extensive in situ component predicts for a higher rate of multifocal tumor invasion, positive resection margin and re-excision. Nevertheless patients with extensive in situ component do not present a higher risk of local recurrence (re-excision with clear margins).

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### Impact of quadrivalent HPV (type 6, 11, 16 18) vaccine on HPV 18-related disease including adenocarcinoma of the cervix

Kevin Ault, for the FUTURE I and II Study Group

**Objective:** HPV 18 infection is responsible for approximately 70,000 cases of cervical cancer and 34,000 cervical cancer deaths worldwide annually. Although most HPV 18-related cervical cancers are squamous in morphology, HPV 18 causes approximately 50% of all cases of adenocarcinoma of the cervix, a cancer that is not well detected by Pap testing and is increasing in incidence in both developed and developing countries. Here we present combined, end-of-study data of the efficacy of a quadrivalent HPV vaccine against HPV 18-related disease, including adenocarcinoma of the cervix

**Methods:** 5442 and 12067 women were enrolled in 2 pivotal Phase III trials, named FUTURE I and FUTURE II, respectively. Women were assigned (1:1) to vaccine or placebo. Pap tests were taken at regular 6- (FUTURE I) or 12- (FUTURE II) month intervals and evaluated using The Bethesda System-2001. Comprehensive anogenital examinations were scheduled at day 1, month 3 (FUTURE I), and every 6 to 12 months thereafter. Colposcopy referral was algorithm-based. Biopsies were HPV typed. Histology slides were read by a blinded pathology panel. The endpoints reported here were HPV 18-related cervical intraepithelial neoplasia (CIN 1-3), adenocarcinoma *in situ* (AIS), and cervical cancer. Analyses were per protocol (received 3 doses, had no major protocol violations, were sero (-) at day 1 and DNA (-) day 1 to month 7 for HPV 18). Follow-up began at month 7. Anti-HPV 18 antibody levels targeting a single neutralising epitope (H18.J4) were measured using a competitive Luminex immunoassay (cLIA). The relationship between breakthrough disease and antibody titers measured by this cLIA method was determined.

**Results:** Subjects were followed through ~44 months post Day 1. The table below displays the results. Placebo recipients remained at risk for HPV-18 related disease throughout the 4 year study period. A single case of HPV-18 CIN 1 was observed among vaccine

recipients. This subject was positive to HPV 56 in swabs taken at day 1 and month 35 and in the CIN 1 biopsy at month 37. HPV 18 was detected in the CIN 1 biopsy only. There were no cases of HPV-18 CIN2/3 or AIS observed among vaccine recipients, in spite of an observed decrease in seropositivity over time. This confirms that an anamnestic response following exposure can mediate vaccine-induced protection. This has been evidenced in a separate study in which administration of an antigen challenge to subjects years after vaccination resulted in a rapid and higher antibody response than right after vaccination. Even amongst subjects who were seronegative at month 60, over 93% seroconverted (measured one week post-challenge), demonstrating robust immune memory.

	Quadrivalent vaccine (N =7382)	Placebo (N =7315)	Efficacy (95% CI)	% of subjects seropositive at given time point
<b>HPV 18 CIN (any grade) or HPV 18 AIS</b>	<b>1</b>	<b>61</b>	<b>98% (91, 100)</b>	<b>NA</b>
<i>By time interval</i>				
Day to <Month 12	0	1	—	99.5% at month 7
Month 12 to Month 24	0	9	—	71.1% at month 24
Month 24 to <Month 36	0	20	—	Not measured*
Month 36 to <Month 48	1	26	—	60.2% at month 44
Month 48 or Beyond	0	5	—	Not measured*

\*Not measured in the FUTURE I and II studies.

**Conclusions:** There were no HPV 18 related cases in subjects who received quadrivalent vaccine that could be related to circulating antibody levels. Administration of quadrivalent vaccine results in 100% protection against HPV18-related CIN2/3 or HPV 18-related AIS years after vaccination.

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### Impact of a quadrivalent human papillomavirus (hpv) (types 6, 11, 16, 18) I1 virus-like particle vaccine on abnormal cytology due to high-risk hpv types 16 and 1

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**Background:** A quadrivalent HPV vaccine (Gardasil/Silgard, Merck and Co., Inc) has been licensed in over

80 countries for the prevention of cervical cancer and genital warts, as well as vulvar and vaginal precancerous lesions. HPV 16 and HPV 18 are associated with 70% of cervical cancers and high-grade squamous intraepithelial lesions. Here we present the first combined analysis of the vaccine's impact on the incidence of Pap diagnoses related to HPV 16 and/or HPV 18, compared with placebo, among women aged 16-23, years.

**Methods:** 3571 women aged 16-23 were enrolled in a phase III study of the safety, efficacy and immunogenicity of a quadrivalent vaccine (a substudy of protocol V501-013, FUTURE I). Women were assigned (1:1) to vaccine or placebo. Pap tests were taken at regular 6 month intervals and evaluated using The Bethesda System-2001 at a central laboratory (Diagnostic Cytology Laboratories, Indianapolis, IN). Comprehensive anogenital examinations were scheduled at day 1, month 3 (one month post-dose 2), and months 7-12-18-24-30-36-48 at which time endo/ectocervical swabs (one specimen) and a combined labial/vulvar/perineal plus a perianal swab (pooled to become second specimen) were collected. A Pap test was considered HPV 16 and/or HPV 18-related if the endo/ectocervical swab collected at the same visit was positive for HPV 16 and/or HPV 18 DNA. The analysis included women who were negative to 14 HPV types at day 1 and who had a normal Pap test result at study entry.

**Results:** The median follow-up time was approximately 3.6 years. At enrollment, approximately 36% were positive to at least one of 14 HPV types tested (6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59) and approximately 10% had an Pap test diagnosis of atypical squamous cells of undetermined significance (ASC-US) or worse prior to study entry or on day 1 (note a subject may appear in both exclusion categories). Among the 1021 vaccine and 1023 placebo recipients who were eligible for the analysis, vaccination reduced the combined incidence of HPV 16- related ASC-US (positive by high risk probe), low-grade squamous intraepithelial lesions, or worse, by 92% (95% CI: 84 to 97; 7 cases vaccine versus 90 cases placebo) and HPV 18-related Pap tests as above by 97% (95% CI: 82 to 100; 1 case vaccine versus 32 cases placebo)

**Conclusion:** Among a population of 16- to 23-year old women, prophylactic administration of quadrivalent HPV vaccine significantly reduced the risk for Pap test abnormalities most commonly associated with underlying high-grade precancerous squamous lesions.



## OBSTETRICS I

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### Area of Wharton's jelly as an estimate of the thickness of the umbilical cord and its relationship with estimated fetal weight

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**Purpose:** The objective of this study was to construct a reference curve for the ultrasonographic measurement of the area of Wharton's jelly (WJ) in low-risk pregnancies of 15-40 weeks and to investigate the relationship between the area of Wharton's jelly and estimated fetal weight.

**Methods:** A prospective study was carried out between June 2005 and December 2006 in 2,189 low-risk pregnancies to determine the area of Wharton's jelly in a cross-section of the umbilical cord. The area of WJ was calculated by subtracting the areas of the umbilical vessels from the total area of the umbilical cord and calculating the 10<sup>th</sup>, 50<sup>th</sup> and 90<sup>th</sup> percentiles using a third-degree polynomial regression procedure. Fetal weight estimated by ultrasonography was correlated with the measurement of the area of WJ.

**Results:** The estimated area of WJ increased according to gestational age ( $R^2=0.64$ ,  $p < 0.0001$ ), stabilizing, however, from the 32<sup>nd</sup> week onwards. This relationship may be expressed by its regression equation of  $\text{Log}_{10}(\text{WJ}) = -1.4307 + 0.2986 \cdot \text{GA} - 0.008 \cdot \text{GA}^2 + 0.00008 \cdot \text{GA}^3$ . There was a significant linear correlation between the area of WJ and estimated fetal weight up to 26 weeks ( $R=0.782$ ), values of WJ then remaining practically constant from that time until delivery ( $R=0.047$ ).

**Conclusion:** The reference curve constructed for the area of WJ indicates that it increases according to gestational age, showing, however, a tendency to stabilize at around 32 weeks of gestation. It is also linearly correlated with estimated fetal weight only up to 26 weeks of gestation.

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### Expectant Management of first trimester incomplete abortion

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**Introduction:** About 15% of woman with a clinically recognised pregnancy will miscarry spontaneously during the first trimester. There are three options to solve

incomplete abortion: surgical evacuation, medical treatment and expectant management. Our objective was to evaluate and compare the effectiveness, safety and acceptability of expectant management, in the treatment of incomplete abortion with gestational age d" 12 weeks.

**Methods:** A prospective observational trial was conducted in our department between June 2006 and August 2007. Eighty eight women who had incomplete abortion with gestational age d" 12 weeks were included. Women were divided in two Groups A - expectant management after medical treatment with misoprostol (n=60) and Group B - expectant management (n=28). Weekly surveillance (clinical evaluation and transvaginal ultrasonography) for 45 days or until complete abortion was made. Groups were reviewed concerning success rate (complete abortion without surgery), time to resolution, duration of bleeding and pelvic pain, infection, observations in urgency room, degree of satisfaction. For statistical analyses  $\chi^2$  and Fisher's exact test were used. Statistical significance was considered when  $p < 0.05$ .

**Results:** The incidence of complete abortion was 86.7% and 85.2% in Group A and B respectively at day 14 and 100% in both groups at day 30. The number of days of pelvic pain (2,8 and 2,9) and bleeding (6,4 and 5,2) in Group A and B, respectively were not significantly different. Both groups showed 100% satisfaction, nevertheless the incidence of anxiety around the 90%.

**Discussion:** Expectant management may be a practical option in the management of incomplete abortion in women who gives consent. Expectant management is effective and well tolerable although it may increase the anxiety inborn to the abortion, because of repeated observations at the hospital.

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### Placental Gene Expression In Severe Preeclampsia

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**Introduction:** The aim of our study was to investigate global gene expression profile in placentas from pregnancies affected by severe preeclampsia (PE), defined as blood pressure  $\geq 160/110$  mmHg and proteinuria  $\geq 2+$  on dipstick or HELLP syndrome.

**Materials and Methods:** Placental samples (chorionic tissue) were collected after delivery from 16 patients

who had severe PE and 50 normotensive women who had uncomplicated pregnancies (after accounting for parity, 16 of these were randomly chosen to match with each PE patient). Global gene expression profile was evaluated by the Human Genome Survey Microarray v.2.0 (Applied Biosystems), containing 32,878 probes for the interrogation of 29,098 genes. The series composed of 32 hybridizations in a one channel detection system of chemiluminescence emitted by the microarrays. An empirical Bayes analysis was applied in order to find differentially expressed genes.

**Results:** A total of 18811 genes met our quality criteria. Genes that were  $\geq 2$ -fold up- or down-regulated and had a p-value  $\leq 0, 01$  were considered differentially expressed. In PE placentas 205 genes were significantly up-regulated and 81 genes were down-regulated, compared to normal placentas. These genes clustered to groups of biological processes related to cell proliferation and differentiation, immunity and defence, cell structure, lipid metabolism, and cell transport and protein traffic. Groups of differentially expressed genes were associated with angiogenesis, Notch-, PDGF-, TGF $\beta$ - and VEGF-signalling pathways. Leptin (37-fold), laeverin (10-fold), different isoforms of  $\alpha$ -chorionic gonadotropin (3 to 6-fold), endoglin (4-fold), FLT-1 (3-fold), and FLT-4 (2-fold) were up-regulated. PDGF-D was 2-fold down-regulated. Twenty genes were found to best predict PE, following supervised clustering by predictive analysis of microarrays. Moreover, subgroup analysis of PE placentas obtained before and after 34 weeks of gestation resulted in 38 differentially expressed genes, which suggests that early- and late-onset PE might have different pathogenesis.

**Conclusion:** Among 286 differentially expressed genes in PE placenta, 20 were found to be the best predictors of the disease. Early- and late-onset PE appear to have a different genetic signature.

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## Epilepsy and pregnancy – psychopathologic aspects

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**Introduction:** It is frequent to find psychopathological disturbances in an epileptic patient, as well as emotional and relational symptoms, anxiety, affective changes, psychomotor slowing, aggressive behavioural disturbances, psychosis, personality changes and sexual disturbances. Pregnancy affects the women physically and frequently creates unpleasant symptoms which also provoke fears and insecurity in relation to their children.

**Material/methods:** A structured clinical interview including a "Questionnaire about epilepsy and pregnancy",

elaborated by the authors, was used for assessment of the epileptic pregnant woman who were assisted in our department from Jan2004 to Set2007. The same questionnaire was answered by a control group, composed of 40 pregnant women without any pre-existent pathology, matched for age and gestational age, selected among pregnant women who, during the same period of time, attended the Outpatient Consultation.

**Results:** Among the epileptic women, 71% referred that the pregnancy was desired and only 47.6% was planned, numbers significantly lower than in the control group (100 and 65%, respectively). The psychological aspects analysed through the questionnaire responses didn't show significant differences between the groups except for higher references to sadness (76.2%), panic or terror disturbances (23.8%) and suicide thoughts (23.8%), as well as more difficulties in facing the everyday problems (23.8%) among the epileptic group when compared to the controls (47.5, 2.5, 5 and 2.5%, respectively). These results are independent from age and educational level, except for the difficulties in facing daily problems which differences are particularly more significant between the 30-35 years.

**Conclusions:** We concluded that the psychological and psychopathological aspects of the epileptic pregnant women are relevant, when compared with the non-epileptic pregnant ones. Epileptic pregnant women must be always sent to a referral centre, where they have access to a multidisciplinary team composed by specialists on Maternal-Fetal Medicine and Epilepsy, as well as a specific psychiatric support, so that their gestation might have a good outcome both in medical and psychiatric terms.

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## PHigfbp-1 vs FFN test in the evaluation of the risk of preterm delivery in symptomatic patients.

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**Introduction:** A potential clinical use of insulin-like growth factor binding protein's phosphorylated isoform (pHIGFBP-1) on endocervical secretions to predict delivery was supposed first in 2001. In this study we analyzed the fFN and pHIGFBP test as markers of preterm delivery in symptomatic patients.

**Methods:** 210 caucasian women with symptoms of preterm labor between 24 and 34 g.w., singleton pregnancy and

intact membranes. We tested the cervical-vaginal pHIGFBP-1 and fFN test.

**Results:** Of 210 symptomatic women, 16.2% delivered before 37 g.w. and 6.7% before 34 g.w. The pHIGFBP-1 qualitative test was positive in 17.6% symptomatic patients and 48.6% of them delivered before 37 g.w., also fFN test was positive in 20.9% symptomatic patients and 45.4% of them delivered before 37 g.w. Sensitivity, specificity, positive and negative predictive (NPV) values of pHIGFBP-1 test reported are 52.9%, 89.2%, 48.7% and 90.2% respectively.

**Discussion:** pHIGFBP-1 test seems to be a valuable tool in predicting preterm delivery in symptomatic patients. pHIGFBP-1 and fFN have a high NPV instead pHIGFBP-1 test seems to decrease the false positive ratio respect to fFN. The cost of pHIGFBP-1 test is much lower than fFN test and it is also unaffected by urine, seminal plasma and vaginal explorations. We think that the use of pHIGFBP-1 in the prediction of preterm delivery might be more advantageous than fFN.

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### Maternal treatment with allopurinol diminishes fetal cardiac oxidative stress following repeated episodes of ischemia-reperfusion in sheep

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**Introduction:** The prevention and management of perinatal asphyxia remain major concerns in obstetric practice today. Umbilical cord compressions (UCC) induce fetal asphyxia and ischemia-reperfusion (I/R). I/R increases reactive oxygen species, for instance via activation of the xanthine oxidase (XO) pathway, which may promote oxidative stress in the fetal circulation. While treatment with allopurinol of asphyxic human neonates reduced free radicals and improved cardiovascular status, treatment started postnatally was deemed too late to prevent oxidative damage (Benders *et al.* Arch Dis Child **91**:163, 2006). Consequently, in complicated pregnancy, recommendations to treat the fetus via the mother, rather than the neonate, with allopurinol are currently being entertained. This study investigated the effects of maternal allopurinol treatment on indices of oxidative stress in the fetal heart following repeated UCC in late gestation sheep.

**Methods:** Under halothane anaesthesia, 10 sheep fetuses and their mothers were instrumented at 0.8 of

gestation with vascular and amniotic catheters, an inflatable occluder around the umbilical cord, and a Transonic flow probe around an umbilical artery. At least 5 days later, all fetuses were submitted to an I/R challenge (produced by 5 x 10 minutes repeated UCC) under maternal allopurinol (n=5) or saline vehicle (n=5) infusion. Fetal hearts were collected 48h after I/R and snap frozen for measurement of (anti)oxidant proteins by Western blot. Hearts from 5 uninstrumented fetal sheep at 0.8 gestation served as controls. Statistical comparisons were made using one-way ANOVA.

**Results:** I/R episodes led to increased expression of cyclooxygenase-2 (COX-2), endothelial nitric oxide synthase (eNOS) and heat shock protein 90 (Hsp90), and decreased expression of manganese superoxide dismutase (mnSOD) and glutathione peroxidase (GPX) in the fetal heart, findings consistent with cardiac oxidative stress. Maternal treatment with allopurinol ameliorated these effects.

**Conclusion:** Repeated UCC promotes oxidative stress in the fetal heart. Maternal treatment with allopurinol offers potential therapeutic treatment against this effect.

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### Pregnancy and delivery in women with traumatic spinal cord injury

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**Objective:** To describe pregnancy outcome in spinal cord injured women. To expand the previous experience concerning this group of women, so as to allow appropriate counseling regarding the management and risks of pregnancy.

**Methods:** Over the past seventeen years thirty three women with spinal cord injury had forty five pregnancies at Stoke Mandeville Hospital. A retrospective review of the maternity and spinal records was performed. Seventeen women had lesions above T5 and sixteen at T5 or below.

**Results:** The mean age at delivery was 31.5 years and the mean time since injury was 11.6 years. Two women had sustained spinal cord injury during the second trimester of pregnancy. Road traffic accidents were the commonest mode of injury.

Urinary tract infection was the commonest antenatal complication. Four women developed pyelonephritis. Pressure sores occurred in five women with previous such history. Two pregnancies of the same woman were complicated by deep venous thrombosis.

All but one pregnancy progressed to term. In one case, maternal health was severely compromised by a respiratory tract infection at 29 weeks of gestation. An emergency caesarean section due to subsequent fetal distress was performed the following day.

The onset of labour was spontaneous in 17 out of 45 pregnancies; augmentation for prelabour rupture of membranes was performed in five patients. Twelve pregnancies were induced for various reasons.

The majority of women, including these with high level injuries, delivered vaginally

(34 out of 45 pregnancies). Malpresentation, maternal sepsis associated with fetal distress and pelvic contortion were the main indications for Caesarean section.

All women with Spinal Cord Injuries above T5 were offered epidural early in labour. Six of them developed symptoms suggestive of autonomic dysreflexia such as hypertension, headache and sweating. In all cases the symptoms were recognized and managed appropriately.

The puerperium was complicated with perineal infection in two cases.

Sadly there was one maternal death three months postpartum. This case was complicated by pre-pregnancy cachexia, pressure sores, asthma requiring steroids, anaemia during pregnancy and intrapartum sepsis. She underwent a laparotomy for suspected peritonitis eight weeks postpartum and she died from widespread amyloidosis.

Neonatal outcome was uniformly good. All neonates were appropriately grown for their gestation. There were no stillbirths or neonatal deaths.

**Conclusions:** Pregnancy outcome in women with spinal cord injuries is favorable.

Women and medical personnel should be aware of the overall good prognosis.

A multidisciplinary approach is essential for the provision of appropriate care and early recognition of potential complications.

Optimal bladder care is essential in order to prevent urinary tract infections. Prompt treatment of them is equally important.

Women with high level lesions can be allowed to deliver vaginally. However, close monitoring and early epidural analgesia must be provided to them, because they are at risk of autonomic dysreflexia. Awareness of the presenting symptoms and signs of this condition among the staff that is responsible for their care is of paramount importance.

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### **Placental M-CSF, GM-CSF and G-CSF alterations in Small for Gestational Age infants.**

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Small for Gestational Age (SGA) refers to two main groups of foetuses that have failed to achieve their growth

potential: foetuses that are constitutionally small for dates– (SFD), and those that have poor growth later in pregnancy, Intra uterine growth restriction–(IUGR). GM-CSF (Granulocyte Macrophage Colony Stimulating Factor) and M-CSF (CSF-1-Macrophage Colony Stimulating Factor) are haematopoietic cytokines expressed by decidual tissue, mediating placental growth, development and proliferation of myeloid haematopoietic cells <sup>1</sup>.G-CSF (Granulocyte Colony Stimulating Factor) is an essential cytokine promoting neutrophil proliferation and differentiation. There is evidence for expression of M-CSF, GM-CSF and G-CSF in the feto- maternal interface. Few studies have shown alterations in levels of M-CSF, GM CSF in placental tissue in intrauterine disease <sup>2</sup>.

We evaluated whether M-CSF, GM-CSF and G-CSF levels in placentas of SGA (Small for Gestational Age) differed from AGA (Appropriate for Gestational Age) controls. Our study is the first attempt to date to correlate alterations in these essential cytokines in placentas of SGA infants with an attempt at classifying the clinical phenotypes of IUGR.

**Methods:** Our subjects were 65 pregnant women of whom 14 had a SFD (Small for Dates) baby at term (>37 weeks), with 12 IUGR (Intrauterine Growth Restriction) at term, 5 IUGR preterm (<37weeks), 32 controls who had AGA infant at term and 2 with AGA infants preterm. Placental tissue cut after delivery, suspended in PBS, homogenised and centrifuged with separated supernatants stored for subsequent analysis at -80°C. Sandwich ELISA used to quantify cytokines in the stored supernatants and cord blood serum.

**Results:** Statistically significant lowering of placental M-CSF in IUGR (p=0.007) and SFD (p=0.090) as well as combined SGA group (0.006) compared to AGA infants. No significant differences in GM-CSF or G-CSF between groups. No significant difference found in Cord blood M-CSF between groups.

**Conclusion:** This is the first report distinguishing clinical phenotypes of SGA (IUGR and SFD) and correlating M-CSF, GM-CSF and G-CSF levels in these conditions. The reduced M-CSF in placenta of IUGR and Small for Dates infants in our study probably reflects poor placental development and function in these babies. Increased M-CSF in maternal serum has been noted in IUGR pregnancies <sup>3</sup>. One explanation to correlate our findings in placental explants and cord serum with that of maternal serum could be that an increased level of maternal M-CSF down regulates the placental and fetal production of M-CSF.

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### Maternal and perinatal outcome of first subsequent pregnancy after completing chemotherapy for gestational trophoblastic neoplasia in Brazilian women

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**Objective:** To evaluate maternal and perinatal outcomes in Brazilian patients who conceived after chemotherapy for gestational trophoblastic neoplasia (GTN).

**Methods:** This observational, retrospective study included 252 women who conceived after chemotherapy for GTN between 1960-2005. The women were assigned into 3

groups according to the interval between completion of chemotherapy and first subsequent pregnancy (<6 months; between 6 and 12 months; and >12months). Maternal and perinatal outcomes were compared among groups.

**Results:** Adverse maternal outcomes were more frequently observed <6 months than 6 – 12 months (76,2% e 19,6%; p <0, 0001; OR = 13,12; CI 95% = 3,87 – 44,40) and > 12 months (76,2% e 21,6%; p < 0, 0001; OR = 11,56; CI 95% = 3,98 – 33,55) after chemotherapy. Spontaneous abortion frequency was higher < 6 months (71.4% ) than 6 – 12 months (17.6%; p < 0, 0001; OR = 11.66; CI 95% = 3.55 – 38.22) and >12 months (9.4%; p <0. 0001; OR = 23.97; CI 95% = 8.21 – 69.91) after chemotherapy.

**Conclusion:** Adverse maternal outcomes and spontaneous abortion were more frequent among patients who conceived within 6 months of chemotherapy. Pregnancy should be avoided for at least 6 months after completion of chemotherapy.

**Keywords:** Gestational trophoblastic neoplasia. Chemotherapy. Subsequent pregnancy outcome.

## GYNAECOLOGY

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### Obstetrics & Gynecology: evaluation of the portuguese scientific activity based on bibliometric indicators

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**Introduction:** The bibliometric analysis of the Portuguese scientific production in the field of obstetrics and gynecology (OG) since 1997 to 2006 provides an overview on the developed scientific activity on this subject and allows the characterisation of some relevant features as well as its evolution along the studied period.

**Material and Methods:** Documents collected in 2 databases (DB), Medline, Science Citation Index journals were studied. We applied quantitative and qualitative bibliometric indicators to the found number of articles and the journals where they were published

Quantitative indicators based on the n<sup>o</sup> of published articles illustrate Portugal position in the area of OG within the international scientific community; it also allows the identification of the participation of the different institutions, allocated by geographic areas, in scientific production as well as the establishment of international collaboration. Qualitative indicators were used to investigate influence and impact of the scientific production. These are indicators based on the journal classification where the articles were published and also the citations they received. N<sup>o</sup> of citations obtained by

articles collected in the performed search was determined, based on the Science Citation Index and the Impact Factor (IF) of the journals in the Journal Citation Reports (JCR).

**Results:** During evaluated period, the Portuguese scientific production in the selected area showed an increase of 75%. We analysed 846 documents published in the selected international DB. The distribution of article production is as follows: 52% in Oporto, 29% in Lisbon and 15% in Coimbra, 4% in others. The national institutions with a higher rate of publishing in renowned international journals are IPATIMUP, IPO Oporto, IPO Lisbon, Hospital de São João. The international journals selected by the national scientists present a high IF. In the whole of the 846 articles selected in the international DB, 260 obtained a total of 3.120 citations (average of 12,4 % per article).

**Conclusions:** An increase of the investigation in OG is observed, this being illustrated by the increase in the n<sup>o</sup> of articles published in well-recognized international journals. It is also noticed a trend to publish in journals with a higher IF as well as an increasing role of co-authorship and international collaboration.

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## Minilaparotomy Hysterectomy: Another Option For Minimal Invasive Surgery

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**Introduction:** Minilaparotomy approach is defined as a transversal abdominal incision into the pubic hair no longer than 6 cm, in which is placed a circular elastic retractor that enables better exposure of the surgical field. The aim of this paper is to compare the results obtained using Minilaparotomy technique, Pfannenstiel approach and laparoscopy in the hysterectomy procedure.

**Methods:** A retrospective data analysis was performed on 165 patients who underwent hysterectomy for benign disease from 2004 to 2006 in our center. 81 patients (49.1%) had undergone Minilaparotomy procedure, 46 (27.9%) Pfannenstiel laparotomy and 38 (22%) were laparoscopic approaches.

**Results:** Postsurgical bleeding (mean value) rounded 2 gr/dl for the three procedures analyzed. Surgical timing statistics revealed the Minilaparotomy option as the fastest mean time of 73.4 minutes (67.85-78.94). Pfannenstiel and laparoscopy procedures respectively required 101.96 (92.40-111.51) and 159.34 (140.23-178.46) minutes to be performed. In the other hand the laparoscopic hysterectomy consumed the less number days of hospitalization: 3.24 days (2.86-3.61) nearly followed by Minilaparotomy with 3.89 days (3.66-4.12). Pfannenstiel approach consumed 5.07 days (4.60-5.53) All these differences were significant, after performing Kruskal-Wallis test ( $p < 0.001$ ). Considering the global percentage of intraoperative complications we found Minilaparotomy surgery as a more secure option (1.2%) than Pfannenstiel surgery (8.6%),  $p < 0.05$  after Chi-square test performing, but not significant than laparoscopy (2.6%).

**Discussion:** Based in our results, we consider Minilaparotomy surgery (on selected patients) as a fast performing technique in experienced hands that offers the advantages of a minimal invasive procedure (low morbidity, quick reincorporation to normal life, good cosmetic results) as well as the benefits of traditional approach (mastered in reasonable manner quickly with conventional instruments) without expensive technology requirements facilitating the minimal invasive surgery in the places with limited resources.

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## Pretreatment % increment in hCG within 48 h: New predictor variable for therapeutic success of methotrexate in ectopic pregnancy

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**Objective:** To evaluate pretreatment % increase of  $\hat{\alpha}$ -hCG levels over 48 h as a predictor of success in the treatment of ectopic pregnancy with methotrexate.

**Study Design:** A prospective study at Federal University of São Paulo with 65 patients with ectopic pregnancy treated with a single dose of methotrexate, IM application (50 mg/m<sup>2</sup>). Predictor factors were evaluated: the level of  $\hat{\alpha}$ -hCG on day of MTX and pretreatment % increase of  $\hat{\alpha}$ -hCG over 48 h.

**Results:** Success occurred in 49 cases (75.4%), with a lower  $\hat{\alpha}$ -hCG level (1928.9 mUI/ml), lower variation within 48 h (13.1%) as compared with failure:  $\hat{\alpha}$ -hCG (4828.6 mUI/ml;  $p < 0.01$ ), variation within 48 h (36.3%;  $p = 0.01$ ). The level of  $\hat{\alpha}$ -hCG on day of MTX  $< 2685$  mUI/ml has demonstrated sensibility (79.6%) and specificity (75%) for the therapeutic success. Pretreatment % increase of  $\hat{\alpha}$ -hCG over 48 h  $< 11.1\%$  showed 61.7% sensibility and 81.3% specificity.

**Conclusions:** The  $\hat{\alpha}$ -hCG level on day of MTX and pretreatment % increase of  $\hat{\alpha}$ -hCG over 48 h reflect the intensity of the ectopic pregnancy hormonal activity. Thus, variation in  $\hat{\alpha}$ -hCG levels is an important predictor for medical treatment of ectopic pregnancy. Methotrexate may be used with a higher safety margin when the level of  $\hat{\alpha}$ -hCG on day of MTX is lower than 2685 mUI/ml and its variation within 48 h is lower than 11.1%.

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## The effect of exercise on menstrual pattern

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Normal menstruation involves the breakdown, remodeling and repair of the functional endometrial layers.

Disturbances of menstrual bleeding and dysmenorrhea are a major medical problem not only for adult but also for teenagers and health services.

**Objective:** The main objective of this research was to determine the effects of exercise on menstrual pattern in high school girls.

**Study Design:** This study was a randomized clinical trial of 150 students that they were separated in two "exercise" and "non exercise" groups.

Then all of them were studied in a accordance to the prospectus, from the character of the menstruation

pattern such as duration and amount of bleeding and the frequency for two periods. The exercise group were given some exercise and the results of two periods after the exercise were registered.

All after in all the study took four periods in each groups. The descriptive statistics, repeated measure design and the least significant different way were used for analyzing the statistical information.

**Results:** The duration of bleeding in the exercise group declined from 6.49 days to 5.32 days in the third period and 4.12 days in forth period, hence the difference is  $p < 0.01$  in two groups.

The average of using sanitary pad also decreased from 10.15 to 7.34 in the third period and 6.21 in the forth period.

Also the variation rang of frequency in non exercise group was  $27 \pm 6$  days and  $29 \pm 3$  days in exercise group.

**Conclusion:** The planned exercises will be decreased the duration and amount of menstrual flow and regulate the interval of menstrual period

**Key Words :** dysmenorrhea . menstrual pattern . exercise

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### Single-Dose Methotrexate For The Treatment Of Tubal Ectopic Pregnancy: Centro Hospitalar De Gaia 5.5 Years Experience

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**Objective:** The purpose of this study was to determine our institutional success rate with single-dose intramuscular methotrexate (MTX) therapy for ectopic pregnancy treatment and to compare with results of published studies.

**Methods:** A retrospective chart review of 26 patients diagnosed with ectopic pregnancy and treated with single-dose MTX ( $50 \text{mg/m}^2$ ) from January 2002 to June 2007. Successful treatment was defined as the resolution of the ectopic pregnancy without surgical intervention.

**Results:** The mean pre-treatment level of human chorionic gonadotropin (hCG) was  $2538 \pm 2085$  mIU/ml. Twenty-two (84.6%) patients were successfully treated with a single dose of MTX. Four patients (15.4%) required a second dose one week after the first injection. Twenty five patients (96%) were successfully treated with MTX. Only one patient was submitted to laparotomy after a single-dose MTX, as a result of suspected ectopic rupture. There was no difference between the mean pre-treatment serum hCG level in patients that needed a second MTX injection and patients who were successfully treated with a single injection of MTX ( $2263 \pm 1196$  vs.  $2588 \pm 2226$  mIU/mL respectively,  $\tilde{n} > 0.05$ ).

The mean time to resolution of hCG was 37 days (14 to 96 days). Twelve patients had side effects minor (mild pain, nauseas and vomits). There was no symptomatic or biochemical evidence of toxicity using this low dose regime.

**Discussion:** Our success rate with methotrexate for treatment of ectopic pregnancy is comparable with other published results. This study showed that medical treatment of ectopic pregnancy with systemic single-dose methotrexate seems to be a good option for patients with unruptured tubal pregnancy.

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### Is lung function associated with levels of female sex hormones in a general population?

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**Introduction:** Lung function and asthma appear to vary according to hormonal status in women. We wanted to examine whether lung function was association with levels of female sex hormones among women in the reproductive age.

**Methods:** Women aged 24 to 45 years from general populations in 13 centres from Spain, France, Switzerland, Iceland, Estonia, Sweden and Norway, who participated in the European Community Respiratory Health Survey, went through an examination including lung function tests and hormone measurements in serum. Pregnant women, OCP users and HRT users, and women with amenorrhoea > 6 months or delivery in the last six months were excluded. Linear regression analyses included 951 women, and were adjusted for age, height, body mass index, menstrual status (regular/irregular), smoking and centre.

**Results:** Lung function was significantly associated with progesterone; both forced expiratory volume ( $FEV_1$ ) and forced vital capacity (FVC) increased with increasing progesterone ( $p_{FEV_1} = 0.022$ ;  $p_{FVC} = 0.025$ ) until a maximum level was reached and decreased with further increase in progesterone ( $p_{FEV_1} = 0.031$ ;  $p_{FVC} = 0.007$ ), thus showing an inversely U-shaped association. An inversely U-shaped association was indicated between  $FEV_1$  and oestradiol, but did not reach statistical significance ( $p = 0.08$  and  $p = 0.12$ ).  $FEV_1$  appeared to increase with increasing levels of DHEA ( $p = 0.047$ ), an indicated increase in FVC with increasing DHEA did not

reach statistical significance ( $p=0.13$ ). LH, FSH, LH/FSH ratio or cortisol were not associated with lung function.

**Conclusion:** Among women in reproductive age from general European populations, lung function was significantly associated with levels of progesterone and DHEA. This supports previous findings suggesting that sex hormones influence airways physiology and pathology, and should be further investigated.

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### Localization of Essure® microinserts using 3D ultrasound after hysteroscopic sterilization. A prospective single-center study.

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**Introduction:** To evaluate the ability of 3D ultrasound for the localization of Essure® micro-inserts after hysteroscopic sterilization.

**Methods:** Prospective single-center study. Between September 2006 and June 2007, all patients undergoing ambulatory hysteroscopic sterilization were assessed using 3D Transvaginal ultrasound and plain pelvic X-ray three months after surgery. 28 patients of the series were also evaluated using 3D ultrasound immediately after the procedure. Three positions of the micro-inserts crossing the utero-tubal junction were described by 3D ultrasound: ((I, II, III) ideal position. (I, II) proximal position. (II, III) distal position).

**Results:** During the study period, 54 patients were included. The mean age was 41.6 years (range, 30-48 years). Two patients had a history of unilateral salpingectomy. 100% of procedures were ambulatory. Eight procedures (14.8%) and 46 procedures (85.2%) were performed with and without general anaesthesia respectively. All procedures were uneventful.

Bilateral or unilateral (when documented contralateral salpingectomy) tubal placement of the micro-inserts was successful in 48 patients (92.6%). The mean operative time was 13 minutes (range, 6-30 minutes). In case of failure, laparoscopic tubal ligation was systematically proposed. The mean number of coils visualised by hysteroscopy was 4.6 (range, 2-10) on the right side and 3.8 on the left (range, 1-11). Transvaginal 3D ultrasound imaging successfully demonstrated adequate placement of the micro-inserts within the uterine mucosal and cornual portion to the proximal fallopian tube. On the right side, immediate 3D ultrasound showed position (I, II, III) and position (II, III) in 44 cases and 12 cases respectively. On the left side, immediate 3D ultrasound showed position (I, II, III) and position (II, III) in 17 and 11 patients respectively. 3D ultrasound performed three months after surgery showed coils

position (I, II, III) and (II, III) in 40 cases and 56 cases respectively on the right side and position (I, II, III) and (II, III) in 48 cases and 48 cases respectively on the left. Positions I (intra-uterine device) and III (distal fallopian tube or intraperitoneal position) were not found in our patients. Coils position at day 0 and day 90 was the same in all cases. Radiologic assessment using plain pelvic X-ray performed at three months after surgery confirmed the intrapelvic placement of the implants without further description. No pregnancy was reported in our series since the beginning of our experience.

**Discussion:** Transvaginal 3D ultrasound performed either immediately or 3 months after hysteroscopic sterilization could confirm adequate Essure® micro-inserts localization. Further studies are needed to assess whether immediate 3D ultrasound would definitely assess appropriate localization of the implants.

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### Case series of Peritoneal Calcification in utero

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Intra-abdominal calcifications and other echogenic masses are relatively common findings during fetal sonography. Many are associated with no additional risk for the fetus or neonate. They may arise from the liver, gallbladder, spleen, kidneys, adrenal glands, gastrointestinal tract, or peritoneal cavity. The causes to be considered depend on the location of the areas of increased echogenicity, which can be classified as intestinal, peritoneal, hepatic, retroperitoneal, and parietal. Detection of such lesions should prompt a detailed survey for additional findings and a review of the maternal history. In some cases, fetal karyotyping may be indicated.

A case series of 6 pregnant women diagnosed with having peritoneal calcification in utero were identified from routine mid-trimester scans and were followed up all through pregnancy and their babies were rescanned at 6 weeks and 6 months postnatal.

The ages of the women ranged from 22 to 37 and all these women had serial ultrasound scans since 20 week when peritoneal calcification in utero was diagnosed. The peritoneal calcifications varied from being in the upper abdomen of the fetus around liver and the spleen, in two women who were gestational diabetics, the calcification was localised around the fetal gut. All these women underwent TORCH (Toxoplasma, Rubella, Cytomegalovirus and herpes simplex) screen and CF (Cystic Fibrosis) screening and were found to be negative for both.

They underwent serial growth and liquor scans. At 24 weeks the peritoneal calcification remained unchanged in four of the six women and the fetal growth was



consistent with the weeks of gestation. In two women there was persistent IUGR (Intra Uterine Growth Restriction). All the six women had scans repeated at 28 at a tertiary referral centre to get a fetal medicine specialist opinion. A detailed scan was performed to assess bowel, spleen and kidneys as well.

The two women who were gestational diabetics developed macrosomia which was detected in the form of fetal growth over 95<sup>th</sup> centile, both these women went on to have insulin towards the third trimester and needed induction of labour at 38 weeks one of them ended in normal vaginal delivery and the other had to have caesarean section due to failed induction.

Of the remaining four women one developed severe preeclampsia and needed emergency caesarean section at 34 weeks gestation. The remaining three women had spontaneous vaginal delivery at term. All these babies had paediatric team in attendance either at delivery or immediately thereafter to check them over. The babies had routine scan at six weeks and six months postnatal to check the status of the peritoneal calcification.

In three babies there was no evidence of any calcification by six weeks and in three babies the calcification was persistent till six months but with less intensity. None of these babies were symptomatic in any way and all of them including the two IUGR babies were meeting the milestones and thriving well.

**Discussion:** The hyperechogenic areas in the fetal abdomen are abnormally bright areas with an echogenicity similar to that of surrounding bones. This could be found in normal and abnormal babies; hence once found a thorough check is mandatory to look for other anomalies. The most important causes may arise from the liver, gallbladder, spleen, kidneys, adrenal glands, gastrointestinal tract, or peritoneal cavity. Hence a thorough sonographic check of the fetus and the placenta is done periodically in a tertiary referral centre.

A fetal karyotyping will help to look for familial factors, and testing for possible associated cystic fibrosis, infection, or a chromosomal anomaly. The outcome depends on the possible cause rather than the extent of the hyperechogenicity. In most cases, expectant management is sufficient, but some patients require transfer to a facility where early postnatal intervention is available.

In the current era of high-quality scanning equipment combining variable-frequency transducers with improved spatial resolution, improved visualization of the intraabdominal structures may lead to documentation of previously undocumented anomalies and normal variants. Many carry little or no additional risk to the fetus or neonate.

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## Welsh Trainers and Trainees views on value of OSATS (Objective Structured Assessment of Technical Skills).

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**Background:** Postgraduate medical training in Obstetrics and Gynaecology is undergoing radical changes with its future still evolving. Surgical skills have been traditionally assessed informally within firms in individual hospitals, during appraisals and by team observation. These however lacked objectivity and overlooked finer details of skills to be assessed. Assessment of performance of doctors has become an important issue because of high-profile cases, with changing training hours and modifications in the training system<sup>1</sup>. Valid, reliable and reproducible assessment of any technical skills includes methods based on direct observation of performance. Performance assessment ranks highest in the 'Miller's Triangle' concept of levels of assessment (Knowledge, competence and performance)<sup>2</sup>. Postgraduate Medical Education and Training Board (PMETB) and Modernising Medical Careers (MMC) emphasise need for performance based assessment strategies.

OSATS is a performance based assessment tool, measuring technical ability of surgeons. It is a valid, reliable tool with 10 procedures included at present. There are two components to the form-a procedure Checklist and a Generic Technical assessment. Following the launch of OSATS (Objective Structured Assessment of Technical Skills) forms for various skills in Obstetrics and Gynaecology its uptake, trainers and trainees' views on usefulness for training has not been studied.

**Methods:** We conducted a questionnaire survey of all Consultants and Specialist Registrars in Wales in June 2007 prior to it being mandatory for assessment from August 2007. Trainer's questionnaire included questions on their educational role, familiarity with OSATS on the RCOG website, current usage, numbers of forms used. Trainers were asked to grade their view on design, layout, suitability and relevance to individual skills on a Likert's scale. Trainees' were asked to define their post and problems they encountered in having the OSATS forms completed.

**Results:** 93 questionnaires were sent to consultants (including locums) and 55 to trainees in Wales. 58 consultants replied to the questionnaire (62%). 28 trainees responded (49%) 39 trainers and 21 trainees found forms useful. Those who found it useful commented on its objectivity, being a better tool than a tick box exercise and a useful tool for the junior trainees. Problems highlighted included Consultants' time and

interest, feedback opportunity; obstetric procedures happen out of hours (feasibility issues) and reliability on trainees to collate forms.

**Conclusions:** There is a need for trainers and trainees to be updated on the use and value of OSATS. Measures

to ensure reproducibility of forms such as online serialised forms need to be highlighted to the RCOG. Number of forms for senior trainees for ARCP (Annual Review of Competency progression) needs to be clearly outlined.

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## OBSTETRICS II

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### Noninvasive, abdominal, fetal electrocardiography for evaluation of fetal heart rate variability

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**Introduction:** In fetal surveillance, fetal heart rate is still assessed by cardiotocography. Standard procedures used in the quantification of heart rate variability, such as spectral analysis, are seldom applied as cardiotocography is sound based and does not allow detecting beat-to-beat intervals with the same accuracy as the electrocardiogram. The cardiotocography technique averages heart rate values over several beats, which makes the use of standard measures of heart rate variability inappropriate. Fetal electrocardiography promises to become an important method since it permits precise determination of the full range of fetal heart rate variability.

**Methods:** In an ongoing study, we apply both methods – computerized cardiotocography and a portable abdominal, fetal electrocardiography (Monica AN24) – simultaneously and sequentially in healthy and high-risk pregnancies (e.g. gestational diabetes, intrauterine growth retardation, preeclampsia). Heart rate variability measurements in time and frequency domains as well as non-linear methods (e.g. the entirely new method “phase-rectified-signal-averaging”) are analyzed in R-R interval series derived from fetal electrocardiography recordings (20th-38th week of gestation). Resulting heart rate variability measures are compared to the standard measure, short term variation derived from computerized cardiotocography following the algorithm created by Dawes and Redman in the early 1980s.

**Results:** The study began in October 2007 with ongoing recruitment. We present first results and an overview of general advantages and disadvantages of the fetal electrocardiography versus cardiotocography.

**Conclusions:** We believe, that non-invasive, abdominal fetal electrocardiography permits a substantially more sophisticated and informative evaluation of fetal heart rate variability than the analysis of the cardiotocography data. It may offer new insights into the regulation of the fetal autonomic nervous system.

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### Serum testosterone and free testosterone index measured by liquid chromatography–tandem mass spectrometry during early pregnancy in women who develop pre-eclampsia

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The role of androgens in the pathogenesis of pre-eclampsia (PE) is unsettled. Several researcher groups have reported elevated serum testosterone (T) and androgen levels in pregnant women prior to and during pre-eclampsia, but these findings have not been verified in all studies. The problems of direct immunochemical assays for T and their poor correlation with reference mass spectrometric methods especially at low female T levels, are well documented. We therefore measured serum T and free testosterone index (T/SHBG) in a well defined group of pregnant women, including women who later developed pre-eclampsia (PE) and controls, using a novel, specific and sensitive liquid chromatography-tandem mass spectrometric testosterone assay.

Serum T, sex hormone binding globulin (SHBG) and T/SHBG were determined in PE patients (n= 92, aged 29.9 ±4.7 years) and in pregnant controls (n= 184, aged 29.7 ±4.5 years) matched for maternal age and parity. Serum samples were collected at the time of the first (9 -17 pregnancy weeks) and second (17 - 22 pregnancy weeks) screening sonographics. Hormone levels were further compared with matched controls carrying a foetus of either the same or opposite fetal sex. Serum T was analyzed by liquid chromatography-tandem mass spectrometry ( API 3000, LC-MS/MS, Applied Biosystems, CA, USA), serum SHBG with IRMA (AutoDelfia, Perkin-Elmer, Turku, Finland) and T/SHBG was calculated.

There were no differences in serum T or SHBG levels or T/SHBG between the PE patients and controls matched for fetal sex. Serum T levels in patients and control subjects in the first sample were 2.72 ±1.59 vs. 2.78 ±1.63 nmol/l (n=77, p = n.s.) and in the second

sample 2.96 +1.42 vs. 2.96 +1.86 nmol/l (n=75, p = n.s.). The corresponding values for and T/SHBG were 8.89 +5.76 vs. 8.73 +4.51 (n=77, p=n.s.) and 8.12 +4.59 vs. 7.85 +4.74, (n=75, p=n.s.), respectively. There were not any significant differences in individual changes of hormone concentrations between the first and the second sample (calculated by subtracting the first hormone result from the second one). Also fetal sex did not have any influence on T, T/SHBG or their changes when PE patients were compared with matched controls after adjustment for pregnancy week using multiple of medians of the (MoM) of hormone values.

In conclusion, the concentrations of serum T and the T/SHBG index in early pregnancy do not differ between women later developing pre-eclampsia and normal controls when T is measured with a reliable LC-MS/MS method. Thus, our data do not support the hypothesis that high T levels or hyperandrogenemism precede pre-eclampsia or would have a significant role in the early pathogenesis of pre-eclampsia. The discrepancy is possibly explained by the poor specificity of direct immunological methods.

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### Prevalence of thyroid antibodies in Gestational Diabetes Mellitus

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**Background:** Pregnancy alters the natural history of autoimmune thyroid disorders. The incidence rate of positive thyroid antibodies (T-abs +) in asymptomatic women during pregnancy has been reported to be between 6 and 19.6 %.

**Aim:** To determine the prevalence of thyroid antibodies (T-abs) in Gestational Diabetes Mellitus (GDM).

**Subjects & Method:** In 408 women, at the time of diagnose of GDM, TSH, free thyroxine, free tri-iodothyronine and anti-thyroid antibodies (T-abs) (thyroperoxidase and thyroglobulin) were measured. In these women we evaluated: previous thyroid disease, maternal age, BMI, spontaneous abortion, first degree relatives with D.M., Sullivan and OGTT values, insulin needed for diabetes control, new-born weight, gestational age at the time of GD diagnose and at delivery, evaluation of glucose tolerance after delivery. Statistical analysis involved SPSS (Statistical Analysis for Social Sciences); p<0.05 was considered to indicate statistical significance.

**Results:** From the women (408) who were enrolled in the study 21 (5.1%) had positive T-abs. Only 20 women

had thyroid disease (2%), with no direct relation with the presence of T-abs. The presence of T-abs + had a positive correlation with type 1 DM abs (r=0.202, p<0.001). There was no correlation between T-abs + and TSH, free thyroxine and free tri-iodothyronine values, as well as with the other maternal and fetal variables.

**Conclusion:** The results revealed a prevalence of autoimmune thyroid disease of 5.1% in women with GDM, identical to normal pregnant women, thus this measurement should not be systematic in women with GDM during pregnancy. However, in the sub-group of GDM with type 1 DM positive abs, the positive correlation founded, suggests a systematic screening for T-abs. These data reinforce the importance of screening of latent pluri glandular auto immune disorders during pregnancy in women prone for those.

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### Maternal and fetal thrombophilia as a risk factor of obstetric complications

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**Background:** Maternal thrombophilia plays a major role in pathogenesis of obstetric complications including preeclampsia, placental abruption, thromboembolism, fetal loss syndrome, premature birth. Recent findings suggest not only maternal, but also fetal thrombophilia being related to reproductive losses. In spite of this, the role of fetal thrombophilia has not been clarified.

**Aims:** To examine whether fetal thrombophilia is involved in pathogenesis of obstetric complications.

**Methods:** We examined newborns from 89 women with thrombophilia using genetic tests for mutations FV Leiden, MTHFR C667T, prothrombin G20210A and antiphospholipid antibodies (APA) determination. 100% of women had personal history of thromboembolism and specific obstetric complications: 53,9% - fetal loss syndrome, 24,7% - severe preeclampsia, 19,1% - pulmonary embolism, 2,25% - stroke. All women were verified to have thrombophilia: APA, mutations of MTHFR C667T, FV Leiden, Pt G20210A, multigenetic thrombophilia was found in 26%, 34%, 4%, 3% and 31% respectively.

**Results:** Thrombophilia was determined in 84% newborn from women with hereditary and acquired thrombophilia: 26% - APA circulation, 29% - mutation of MTHFR C667T, 5% - FV Leiden, 4% - Pt G20210A, 20% - multigenetic thrombophilia.

**Nonclusions:** High incidence of fetal thrombophilia in newborns from women with hereditary and acquired thrombophilia allows us to suggest a critical role of fetal thrombophilia in reproductive losses. In addition to

prothrombotic effects thrombophilia might induce obstetric complications by nonthrombotic mechanisms affecting early stages of implantation and placentation. Combination of maternal and fetal thrombophilia is a most unfavorable condition associated with the highest risk of obstetric complications.

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### **Effectiveness of anticoagulant therapy for prevention of recurrent pregnancy complications in women with thrombophilia**

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**Aims:** To determine the role of thrombophilia in pathogenesis of obstetric complications and to evaluate the effectiveness of prophylactic treatment for their prevention.

**Methods:** During the period from 2000 to 2007 we examined 150 women with infertility and IVF failure, 105 women with history of placental abruption, 750 women with history of preeclampsia for genetic thrombophilia and antiphospholipid antibodies (APA). 150, 700 and 75 women respectively were followed prospectively and received treatment in the preconception period and during pregnancy. The preconception treatment included LMWH, aspirin (75 mg/day) in case of APA-circulation, antioxidants, vitamins of B group, folic acid (up to 4 mg/day in women with hyperhomocysteinemia). The basic therapy during pregnancy was LMWH guided by D-dimer.

**Results:** In women with IVF-failure multigenic thrombophilia was detected in 92% including homozygous forms in 18%, APA in 23%, endogenous hypofibrinolysis in 69, hyperhomocysteinemia in 63%. Of note, in 88% women the reason for infertility was not known. Preconception treatment allowed to increase a success rate of IVF up to 65% ( $\delta < 0,001$ ). Thrombophilia was detected in 90% women with history of placental abruption, genetic thrombophilia + APA in 20%, endogenous hypofibrinolysis was the most important cause of genetic thrombophilia. Preconception treatment allowed avoiding recurrence in 100% cases. Thrombophilia was detected in 100% women with 2 and more recurrent preeclampsia (n=355) (genetic thrombophilia + APA were detected in 70%), in 80% with history of one episode of preeclampsia. In the prospective group nobody had moderate or severe form of preeclampsia, mild preeclampsia was observed in 16%.

**Conclusions:** Thrombophilia might be the main pathogenetic mechanism of recurrent pregnancy complications. Due to thrombophilia involvement in

trophoblast invasion and placentation, early treatment is essential. Preconception treatment with LMWH allowed preventing recurrent pregnancy complications in most cases.

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### **What are the active ingredients of effective obstetric emergencies training?**

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The Confidential Enquiries into Maternal and Child Health have repeatedly identified substandard care in a significant proportion of maternal, fetal and neonatal deaths in the UK, and they have repeatedly recommended training for rare emergencies. The NHS Litigation Authority (NHSLA) have also mandated annual training in the management of obstetric emergencies for all clinical staff involved in the care of obstetric patients through their Clinical Negligence Scheme for Trusts. However, evidence for the effectiveness of training is limited. The Simulation and Fire-Drill Evaluation (SaFE) study has shown that training improves knowledge; improves individual management of emergencies like shoulder dystocia and eclampsia and was associated with improved neonatal outcome in the units where it started. We have also shown that training using a high-fidelity mannequin improves the management of shoulder dystocia.

There are other examples of training not improving outcome at all, but there is accruing evidence that some programmes may lead to improved clinical outcomes.

It is difficult to know why some training programmes appear to be effective and some not. We suggest that for obstetric emergencies training to be effective it should include the following: a) institution level incentive to train, b) relevant and situated training, c) team working, d) realistic training tools, e) 100% penetration, and f) self-directed infrastructure changes.

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### **Conservative Management Of Placenta Accreta : Arterial Ligation Or Uterine Artery Embolisation?**

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**Introduction :** Placenta accreta is an abnormal adherence of the placenta to the uterine wall and may complicate the third stage of labour by severe uterine haemorrhage. Hysterectomy has long been the primary treatment. Recently, conservative treatment has been proposed to be an alternative to decrease morbidity. The aim of this study was to compare morbidity of different conservative treatment of placenta accreta.

**Materials and methods :** A retrospective study of medical charts to identify all patients with placenta accreta was conducted at two tertiary maternity wards of Marseille, France. The study included all patients diagnosed during the period from January 1993 to August 2007. Information on subsequent gynaecological events was obtained from records of follow-up consultations.

**Results :** During this 14-year period, 73 cases of placenta accreta were recorded among 59 900 deliveries. Incidence of placenta accreta was about 1/821. Ten patients had standard management with a primary hysterectomy. A subgroup of 63 patients was treated conservatively. Twenty-five patients received additional treatment by arterial ligation and 14 by embolisation. A portion and the entire placenta was left in situ in 20 cases of 25 arterial ligation and in all cases of embolisation. Conservative treatment failed in 11 cases and led to hysterectomy. The procedure was arterial ligation in 6 cases and embolisation in 3 cases. This three cases were directly related to complications of the embolisation procedure. There was one maternal death after arterial ligation. There was no statistically significant difference in term of morbidity between the two groups. The rates of transfusion were comparable but the quantity of blood and plasma transfused was superior in case of arterial ligation. The rate of septicemia was superior in case of embolisation but it was not significant.

**Discussion :** The incidence of placenta accreta has dramatically increased in recent years, due to the increasing caesarean rates in most countries. Our study is the largest to date and reports the results of conservative management of placenta accreta. This procedure permit the decrease of the maternal morbidity compared with the radical treatment. Because there was no statistically significant difference in term of morbidity between arterial ligation and embolisation, the choice was made individual. Furthermore, conservative treatment was successful in the majority of cases.

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### **Temporary occlusion of the internal iliac arteries for intraoperative bleeding control during cesarean-hysterectomy for placenta percreta**

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**Introduction:** Uterine bleeding due to placenta accreta is one of the main causes of maternal hemorrhage and death. Placenta percreta is the most severe form of abnormal placental adherence and it is characterized by deep myometrial invasion, with no cleavage plan for detachment. It can also invade adjacent organs, specially urinary bladder. Several methods for bleeding control during cesarean delivery have been described and temporary ballon occlusion of the iliac arteries (TBOIA) seems to have some advantages over other techniques.

**Methods:** Two cases reported in which TBOIA was used for bleeding control for cesarean delivery near term. After peridural anaesthesia, both femoral arteries were catheterized and ballon catheters were placed in the internal iliac arteries. A corporal uterine incision was made and fetal extraction was accomplished, with the placenta left in situ. After that, both ballons were inflated and total hysterectomy was performed, with deflation of the ballons after uterine extraction.

**Results:** Case 1- 20 year-old, two previous cesarean sections, ultrasonographic diagnosis made at 33 weeks, cesarean at 35 weeks, newborn weighed 2500 grams, total blood loss 1200 ml, surgical time 4 hours 50 minutes. Case 2- 39 years-old, three previous cesarean sections, diagnosis made at 23 weeks, cesarean at 36 weeks, newborn weighed 2525 grams, total blood loss 1100 ml, surgical time 5 hours. None of the patients needed blood transfusions.

**Discussion:** Precise diagnosis and elective delivery with an experienced team are essential features for reduction of maternal mortality and morbidity associated with placenta accreta. TBOIA is a therapeutic option associated with better maternal outcomes and a low rate of complications.

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### **Regional and international prenatal telemedicine network for computerized antepartum cardiotocography.**

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**Objective:** To review the activity of TOCOMAT, a system for antepartum cardiotocographic (CTG) telemonitoring.

**Materials and Methods:** Nine peripheral units recorded the traces, sent them via modem to the University

operation centre, where the computerised analysis was performed, and received the medical report within few minutes, via fax or e-mail. Traces were classified as "reassuring", "non reassuring" or "pathological". The parameters of computerized analysis were grouped together for each week of gestation. The perinatal outcome was also evaluated.

**Results:** In five years, 5830 traces were analyzed, 4372 (75%) from 1344 high risk patients and 1458 (25%) from 529 patients at apparent low risk. The system allowed the identification of high risk patients (32.8% with non-

reassuring traces and 7.1% with pathologic traces) and low risk patients (16.3% with non-reassuring traces and 4.3% with pathologic traces) that required further evaluation. The neonatal outcome was overall good. At each week of pregnancy, the mean values of computerized parameters resulted into the normal ranges.

**Conclusion:** The TOCOMAT system allowed a decentralization of prenatal surveillance and improved the patients' quality of life and the level of prenatal care.

**Key words:** telemedicine; telehealth; distance learning.

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## OBSTETRICS III

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### In Utero Progression of Ventriculomegaly: Bilateral vs. Unilateral

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**Introduction:** Mild ventriculomegaly occurs bilaterally at an incidence of 0.15% - 0.7% of fetuses, and unilaterally in 0.07% of fetuses. Up to 40% of these cases resolve, however, the natural history of bilateral ventriculomegaly is unclear, in terms of whether it differs from unilateral ventriculomegaly. Our objective was to compare the progression of bilateral and unilateral ventriculomegaly.

**Methods:** The ultrasound obstetric database of our hospital was searched for all cases of isolated ventriculomegaly from 2000 and 2007. Cases with CNS and other structural abnormalities were excluded. Cases with only one ultrasonographic examination were excluded.

**Results:** 51 cases of isolated bilateral ventriculomegaly and 38 cases of unilateral ventriculomegaly were identified. 1 fetus with bilateral ventriculomegaly had severe ventriculomegaly >15mm. 37% of cases of bilateral ventriculomegaly resolved in comparison to 53% of cases of unilateral ventriculomegaly ( $p = \text{NS}$ ). The left ventricular size was  $11.5 \pm 1.3\text{mm}$  if ventriculomegaly was bilateral, and  $11.2 \pm 1.3\text{mm}$  if it was unilateral. Right ventricular size was  $11.4 \pm 1.3\text{mm}$  if ventriculomegaly was bilateral, and  $10.9 \pm 0.9\text{mm}$  if it was unilateral ( $p = \text{NS}$ ). The left ventricle regressed at  $-0.06\text{mm/week}$  if the ventriculomegaly was bilateral, and progressed at  $0.07\text{mm/week}$  if it was unilateral. The right ventricle regressed at  $-0.07\text{mm/week}$  if the ventriculomegaly was bilateral, and at a rate of  $-0.47\text{mm/week}$  if it was unilateral ( $p < 0.05$ ). There was no significant association of either maternal age, or fetal gestation at presentation with the incidence of bilateral versus unilateral ventriculomegaly.

**Conclusion:** Our results indicate that cases of bilateral ventriculomegaly are less likely to resolve compared with unilateral ventriculomegaly. The rate of regression of right sided ventriculomegaly in particular was significantly increased if the condition was unilateral. This may imply different etiologies for cases of unilateral and bilateral ventriculomegaly and warrants further investigation.

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### Fetal Ovarian Cysts: Prenatal Diagnosis And Pos-Natal Follow-Up. An Eleven Years Review

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**Introduction:** Ovarian cysts are the most frequent, prenatally diagnosed intra-abdominal cysts.

In this review the authors evaluate the outcome of fetal ovarian cysts in relation to their sonographic parameters (appearance and size) and prenatal and postnatal course, especially with regard to the need for surgical intervention.

**Methods:** Retrospective analysis of all cases of fetal ovarian cyst observed in our institution since 1<sup>st</sup> January 1996 until 31<sup>st</sup> December 2006. The pre- and postnatal data of 16 newborn that were suspected prenatally to have an ovarian cyst were analyzed. The postnatal outcome was known for 15 of the children.

**Results:** The diagnosis was made in all cases in the third trimester (median, 32; range, 26–37 weeks' gesta-

tion), 4 simple cysts and 12 complex cysts. In 9 of the 16 (56,25%) cases, spontaneous resolution of the cyst occurred either prenatally (n = 4) or postnatally (n = 5). The cystic structure in the cases with spontaneous resolution was analysed, there were 4 simple cysts and 5 complex cysts, and the cysts with prenatal resolution were smaller than those with postnatal resolution (Median: 38mm ± 5,62 VS 43mm ± 10,13). Postnatal surgery was performed in 5 of the 16 (31,25%) children, all of them had postnatally complex cysts, and the median size was 70mm ± 15,27. One case was associated to Jeune syndrome (asphyxiating thoracic dystrophy) and infant death occurred at 3,5 month of life, and one other case was lost for follow-up.

**Discussion:** Size and cysts characteristics are prognostic factors, with all simple cysts and all cysts <50mm having spontaneous resolution. Complications occurred in complex cysts, either prenatally or postnatally, and lead to lost of the ovary.

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### **Apoptosis and proliferation disturbances in placentas in pregnancies complicated by preeclampsia or severe pregnancy induced hypertension.**

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**Introduction:** Intrauterine growth restriction complicates 30% of pregnancies with preeclampsia. This is result of placental insufficiency considered to be an effect of failed trophoblast invasion in first trimester of pregnancy or exaggerated cytotoxic activity of maternal immunologic cells. In vitro studies proved that blood of preeclamptic women increase trophoblast apoptosis.

**Study design:** The purpose of the study was estimation of apoptosis and proliferation in placentas in pregnancies complicated by preeclampsia or severe pregnancy induced hypertension.

**Materials and methods:** The studied group consisted of 38 patients with the preeclampsia (blood pressure over 140/90 mm Hg and proteinuria over 0,3g/l) or severe pregnancy induced hypertension (blood pressure over 160/110 mm Hg, poorly controlled with antihypertensive drugs), that deliver between 24-40 weeks of pregnancy in the Obstetric and Gynecologic Department of The Institute of Mother and Child in Warsaw between 2004-2005 years. The control group included 35 pregnant women paired with the parity and age of pregnancy with the studied group, without hypertension and other cause of placental dysfunction.

Placental samples were transported to the Cytometric Lab after delivery immediately. After preparation tissue

samples were examined by flow cytometer Coulter Epics XL (Beckman Coulter, USA), we estimated percent of cells in pre-G1 DNA fraction (apoptotic cells) and the percent of PCNA positive cells as a marker of proliferating cells. In the immunohistochemical part of the study we estimate degree of staining with the TUNEL method as an indicator of apoptotic cells, and degree of expression of Ki 67 as an marker of proliferating cells in four compartment of the placenta: villous trophoblast, extravillous trophoblast, decidua, chorion. For the comparison of our results we used Mann-Whitney test.

**Results:** We found increased number of apoptotic cells in placentas from the studied group 10,3±8,9% vs 4,2±3,8% from the control group (p=0,003), while there was no significant difference between the number of PCNA positive (proliferating) cells in the placenta in the studied group in comparison with control group respectively: 19,5±12,7% vs 20,1±11,2%. Comparison of the degree of apoptosis in four studied compartments of placenta (studied with the TUNEL method) proved statistically significant increase in the degree of apoptosis only in the villous trophoblast. Medium degree of reaction (5-25% stained cells in the field) was found in 61,9% cases in studied group and 25,7% in the control group (p=0,002). There was no significant difference in any of the four compartments in aspect of proliferation measured as expression of Ki 67 (nuclear antigen of proliferating cells) between both groups.

**Conclusion:** Placentas from women with preeclampsia were characterized by increased number of apoptotic cells, especially in the villous trophoblast. Excessive process of apoptosis was not balanced with an increase in the number of proliferating cells. This can result in advancing placental insufficiency predominantly in the aspect of materno-fetal exchange.

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### **A randomised, open-label study of intravaginal misoprostol (APL-202) in comparison with dinoprostone for cervical ripening and induction of labour in multiparous women.**

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**Introduction:** The objective of this open-label study was to compare the efficacy and safety of APL-202 (Isprelor<sup>®</sup>, a specifically-developed 25 µg vaginal tablet formulation of misoprostol) with dinoprostone (3 mg tablet) for cervical ripening and labour induction.

**Methods:** Multiparous women with a singleton pregnancy,  $\geq 37$  weeks pregnant and an unfavourable cervix (Bishop Score  $< 9$ ) were randomised to intravaginal APL-202 25 µg followed by APL-202 25 µg at 4 h and 8 h or intravaginal dinoprostone 3 mg followed by dinoprostone 3 mg at 6 h. The primary endpoint was the number of vaginal deliveries achieved within 24 h of induction. Secondary endpoints included vaginal deliveries within 12 h of the start of induction, number of caesarean section deliveries, occurrence of uterine tachysystole and hyperstimulation with fetal heart rate changes, maternal and fetal safety outcomes.

**Results:** 268 patients were enrolled at 17 UK centres. The rates of vaginal delivery within 24 h were similar with APL-202 and dinoprostone (63% [85/136] vs 69% [89/129]). The incidence of vaginal deliveries within 12 h of induction was higher with dinoprostone than APL-202 (33% vs 20%;  $p=0.018$ ). There were no statistically significant differences between treatment groups for other secondary efficacy outcomes including caesarean section deliveries. APL-202 was as well tolerated as dinoprostone, although the incidence of maternal nausea was higher with dinoprostone vs APL-202 (13% vs 5%;  $p=0.031$ ). The incidence of maternal and of neonatal adverse events (AEs) and their classification by severity were similar with APL-202 and dinoprostone (women experiencing  $\geq 1$  AE: 81.6% vs 79.8% or a serious AE: 18.4% vs 17.8%; neonates experiencing  $\geq 1$  AE: 59.6% vs 51.2%, or a serious AE: 14.0% vs 18.6%). In the APL-202- and dinoprostone-treatment groups, the levels of uterine tachysystole (0% vs 1%) and of hyperstimulation (4% vs 2%) were similar.

**Conclusions:** APL-202 is efficacious in cervical ripening and labour induction, and has a similar maternal and fetal safety profile to dinoprostone.

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### Analysis of 62 Cases of Stillbirth: Which Classification Shall We Use?

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**Introduction:** Despite improvements in antenatal care, stillbirth remains one of the largest contributors to perinatal mortality. Although several conditions have been linked to stillbirth, many fetal deaths remain unexplained. These concerns have led to the development of several classification systems of stillbirth. The authors sought

to identify risk factors, value of diagnostic exams and causes of death of stillborn infants using two different classifications.

**Methods:** A retrospective analysis of the 62 stillbirths occurring for the last 5 years in our institution was performed. Stillbirth was defined as fetal death occurring from 22 weeks onwards (WHO). An adapted *Wigglesworth* classification and *ReCoDe* (relevant condition at death) classification were used.

**Results:** There were 77% preterm stillborn infants and 18% were twins. Most prevalent risk factors were smoking (19%), hypertensive diseases (13%), thrombophilia- diagnosed after stillbirth in 11%, prepregnancy obesity (10%) and previous stillbirth (5%). The exams that yielded the most information were placental investigation and autopsy, which were abnormal in 97% and 95% of cases. According to *Wigglesworth* classification most stillbirths were related to asphyxia before onset of labour (34%) and to causes not included in other groups (34%), while 16% remain unexplained. When *ReCoDe* classification was used, there were 35% of fetal causes, 22% of placental causes and 11% of unexplained deaths.

**Discussion:** The causes of stillbirth are many and varied, which turns it into an event of difficult prevention. Thanks to a thorough and protocolled evaluation in the workup of fetal death, assessment of most of the causes is possible, even if a few remain unclear. *ReCoDe* classification seems to be the most suitable stillbirth classification, as it does not consider neonatal deaths and leaves fewer stillbirths in the unexplained category.

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### Review of Management of patients with Obstetric Cholestasis

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**Introduction:** Obstetric Cholestasis is being suspected in increasing numbers and the management practices vary within units in the UK. Though RCOG has produced a guideline recently, the current management practices have not been uniform.

**Materials & Methods:** Retrospectively 58 case notes of women, between January 2005 to December 2005, with suspected cholestasis were reviewed with an aim to determine if relevant investigations were performed; and to review current treatment regimen, as well as to determine outcome of patients suspected with Obstetric Cholestasis

**Results:** 35/58 women were between the age 21-30 years, and 17 between 31-40 years. 12/58 were primiparous and the common gestational age at presentation was between 28-36 weeks although obstetric cholestasis was



suspected and investigated in 12 women before 28 weeks gestation. 53 women had pruritus, 5 had rash and 1 had reported with right upper quadrant pain. Bile acids were elevated in only 8 women, while liver functions (LFT) were altered in 11 women. Women were monitored on alternate days with CTG and checking LFT's and Bile acids. Only 5 women were treated with UDCA and as per the records nobody received Vitamin K orally. Four women were induced before 38 weeks and rest at term and 43 of them had intrapartum monitoring. There were 58 live births including one set of Twins and one unexplained intrauterine death at 33 weeks gestation. Post partum LFTs were checked in 10 patients and LFT's returned to normal before 11 days.

**Discussion:** Obstetric cholestasis is a multifactorial disorder associated with intense pruritus and elevated Liver function tests having an adverse outcome in pregnancy. Though easily suspected based on symptoms, a definitive diagnostic biochemical marker has been elusive. Our audit showed that systematic investigations as outlined by RCOG guidelines were not performed. Since the adverse outcome in pregnancy cannot be foreseen or predicted it seems prudent to monitor the women twice weekly for reassurance and check LFT's weekly to detect unsuspected deterioration. Though there is no evidence to deliver the women preterm, not allowing them to go past their dates has become an accepted practice.

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### Prediction of neonatal state by computer analysis of CTG and st signals, using the Omniview-Sisporto® system.

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**Introduction:** To evaluate the validity of computer analysis of cardiogram (CTG) and ST signals provided by Omniview-SisPorto® 3.5 in predicting newborn umbilical artery acidosis.

**Methods:** A prospective analysis of recordings obtained in 148 labouring women, acquired with STAN S21 or S31 monitors until 5 minutes before a vaginal delivery or 30 minutes before caesarean birth. Setting: A tertiary care University hospital. Tracings were analysed online by the Omniview-SisPorto® 3.5 program. The last hour of analysis was reviewed and "pathological" alerts provided by the system based on CTG and ST analysis were compared with the occurrence of umbilical artery acidosis (pH < 7.05). Overall accuracy was calculated with 95% confidence intervals (95% CI).

**Results:** The overall accuracy for prediction of neonatal acidosis (pH less than 7.05) by the Omniview-SisPorto® system was: sensitivity of 0.571 (0.275, 0.811), specificity of 0.972 (0.957, 0.984), positive predictive value of 0.500 (0.240, 0.709), negative predictive value of 0.979 (0.964, 0.991), positive likelihood ratio of 20.143 (6.368, 49.178) and negative likelihood ratio of 0.441 (0.192, 0.758) by CTG. When clinical pathological alerts included criteria of CTG isolated or CTG conjoint with ST events (these include all possibilities of pathological alerts of the system), the program reached the following results: sensitivity of 1.000 (0.679, 1.000), specificity of 0.943 (0.927, 0.943), positive predictive value of 0.467 (0.317, 0.467), negative predictive value of 1.000 (0.983, 1.000), positive likelihood ratio of 17.625 (9.342, 17.625) and negative likelihood ratio of 0.000 (0.000, 0.346).

**Discussion:** A high sensitivity and specificity were obtained in prediction of newborn umbilical artery acidosis by combined automated analysis of CTG and ST signals using the Omniview-SisPorto® system.

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### Pubovisceral muscle trauma after instrumental delivery – 4D ultrasound in the evaluation of levator ani muscle.

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**Objective:** Three-and four-dimensional (3D/4D) pelvic floor ultrasound allow dynamic assessment of the pubovisceral muscle complex. Our aim was to estimate the incidence of trauma to the inferomedial aspects of the musculus levator ani after instrumental delivery.

**Methods:** In a prospective observational study, 76 primigravidas after instrumental vaginal delivery (forceps) underwent 3D/4D translabial ultrasound. The control group consisted of 57 nulliparous women. We examined: a) the puborectalis angle (PR): we defined this angle as the angle between the vertical line segment connecting the region of the urethra and rectum and a line that traverses the medial corner of pubovisceral muscle on the left (PRsin) and right (PRdx), b) the area of the urogenital hiatus (AUH), c) the angle gamma (ã): the angle between the axis of the symphysis and the line segment connecting the region of the internal urethral orifice and the lower margin of the symphysis), d) avulsion injury. Dimensions of the levator hiatus were determined in volumes obtained at rest and on Valsalva maneuver, angles was measured at rest and on straining.

**Results:** In the control group: a) at rest the meanwere as follows: PRdx 21.03 (SD 8.1), PRsin 22.07 (SD 8.69), AUH 13.3cm<sup>2</sup> (SD 23.63), ã 53.48° (SD 13.74), b) on straining the mean PRdx 20.67 (SD 8,38), PRsin 20.92

(SD 8,51), AUH 14.8cm<sup>2</sup> (SD 28,72),  $\bar{\alpha}$  75.8° (SD 20.09). In the forceps group: a) at rest mean: PRdx 27.62 (SD 7,81), PRsin 30.85 (SD 10.04), AUH 15.5cm<sup>2</sup> (SD 20.50),  $\bar{\alpha}$  74.89° (SD 16.33), b) on straining the mean PRdx 34.73 (SD 10.02), PRsin 37.34 (SD 12.81), AUH 17.9cm<sup>2</sup> (SD 31.45),  $\bar{\alpha}$  112.2° (SD 34.30). The values of all parameters at rest and at straining reached lower values in the control group than in the forceps group and the difference was statistically significant ( $p < 0.001$ ). Of the 76 women, levator avulsion was diagnosed in 63.6% patients. Avulsion was bilateral in 48.3% and unilateral in 51.7% cases. In the women with avulsion, the values of the parameters reached higher values than in those without avulsion. The differences were statistically significant.

**Conclusion:** Instrumental delivery can cause morphological alteration visible on 3D/4D ultrasound. Avulsion of the levator ani muscle from the pelvic wall occurred in approximately 63,6% of all women delivered instrumentally. Avulsion is associated with statistically significant changes in the morphological parameters of the urogenital hiatus. The PR angle could represent a new parameter related to avulsion. This study was supported by IGA MH-CR no.NR 8353-3

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## How can we recognize the first stage of fetal vascular redistribution in hypoxia?

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**Background:** The object of this study was to investigate the fetal renal and middle cerebral arterial blood flows in normal and hyperechogenic kidneys during the fetal period.

**Materials and methods:** Study group consisted of 82 pregnancies with intrauterine growth retardation. Group included pregnant women from the third trimester. Hyperechogenic medullae were detected in 17 out of 82 pregnancies with intrauterine growth retardation.

**Results:** Fetal renal hyperechogenicity appears to be an indicator of fetal arterial circulatory depression, correlated with pathological changes in the resistance index for the fetal renal arteries. The fetal renal arterial blood flow resistance index was significantly lower in hyperechogenic cases, while in the middle cerebral artery flow was in the normal range. This may also be an indication of subsequent intrauterine and neonatal complications, such as cesarean section because of fetal distress (47%), treatment in a neonatal intensive care unit (71%) or increased perinatal mortality (12%).

**Conclusions:** Detailed ultrasound of renal parenchyma and Doppler examination of renal and middle cerebral arteries appear to be a useful method in the prenatal diagnosis of reduced renal perfusion and of intrauterine hypoxia so as to detect possible pathological fetal conditions in utero.

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