PARALLEL SESSION ABSTRACTS

PL01 Plenary 1 - Screening in gynecological oncology

0830 - 0945

PL01.1 The potential and challenges of ovarian cancer screening (OCS)

<u>Ian Jacobs</u> (1), on behalf of the UKCTOCS team (1)University College London, United Kingdom

Three OCS strategies have emerged: (1) Serum based, CA125 1o test, ultrasound 2o test (sequential screening-SS); (2) Ultrasound based (US); (3) Both tests (Multimodal Screening-MS). SS has superior specificity/PPV while US may have greater sensitivity but lower PPV. MS by combining the tests can achieve the highest sensitivity but with lower specificity and PPV is only suitable for high risk populations. A pilot RCT of SS in postmenopausal women, showed a survival benefit and led to a 3-arm RCT involving 202,000 women (UKCTOCS - UK Collaborative Trial of Ovarian Cancer Screening). Analysis of >50,000 CA125 values involving 22,000 volunteers revealed static/decreasing levels in women without OC and rising levels in OC. This led to a statistical model of serial CA125 levels to calculate the 'Risk of Ovarian Cancer' (ROC) now used in UKCTOCS. The closer the CA125 profile to known cases of OC, the greater the risk of OC. UKCTOCS will establish the impact of screening with the SS and US strategies on mortality and when the full results become available (2014) clarify the place of general population screening. Initial results reveal a sensitivity of 89% for SS and 76% for US. The ROC approach has also been adapted for use in the prospective screening study of 5,000 women in the high risk population (UKFOCSS – UK Familial Ovarian Cancer Screening Study). Major efforts are in progress to improve early detection strategies using proteomic technology, with objective of finding biomarkers which give greater lead time than CA 125 or Ultrasound.

PL01.2 Should HPV screening substitute cytology?

Joakim Dillner (1)

(1)WHO HPV LabNet Global Reference Laboratory, Laboratory Medicine Skåne, Malmö, Sweden and Depts. of Laboratory Medicine, Medical Epidemiology & Biostatistics, Karolinska Institutet, Stockholm, Sweden

Objective: The presentation will review the state-of-the evidence on effectiveness, adverse effects and costs of primary HPV screening and evaluate different options for implementation of this knowledge in organised screening programs.

Methods: Systematic review of published evidence and proposed screening and management strategies. Results: Primary screening for HPV has in several randomised trials been found to have an increased sensitivity for detection of CIN2/3+ compared to cytology, including some evidence of an increased protection against cervical cancer. In most settings, HPV screening needs to be complemented with a triaging test to increase specificity (reduce the amount of referrals). Conclusion: The higher sensitivity of HPV screening offers the possibility for increased and more long-lasting cancer protection after a negative test, enabling a possible lengthening of screening intervals. The specificity is in most settings lower, resulting in an increased emphasis on organised rather than opportunistic testing. Two options will in particular be discussed: 1) HPV screening, followed by triage with cytology and repeat HPV testing of HPV+/Cyt- women.

PS01.1 Antenatal magnesium sulfate and neurologic outcome in preterm infants Lex W Dovle (1)

(1)The Royal Women's Hospital, the University of Melbourne, and Murdoch Childrens Research Institute, Melbourne, Australia

Very preterm infants have rates of neurological impairments and disabilities that are too high relative to infants born at term. As more very preterm infants now survive, they are contributing disproportionately to the burden of illness in childhood, and in later life. Neuroprotective strategies for the very preterm infant are urgently required. Basic science research suggests that magnesium sulfate before birth may be neuroprotective for the preterm fetus. Magnesium ions are essential for many key cellular processes, and overall, are associated with more than 300 enzymatic systems. Magnesium may influence mechanisms implicated in cell death or dysfunction, and magnesium also has some beneficial haemodynamic effects. Some, but not all observational studies in humans suggest a protective effect of antenatal magnesium sulfate on cerebral palsy. However magnesium sulfate could have some deleterious effects. There are five randomised trials (RCTs) of antenatal magnesium sulfate where long-term neurological effects in surviving infants have been reported, but only one RCT was designed specifically to evaluate the long-term effects of treatment. Of the five RCTs (6145 fetuses), in four studies (4446 fetuses) the primary intent was neuroprotection of the fetus. Antenatal magnesium sulfate therapy given to women at risk of preterm birth substantially reduced the risk of cerebral palsy in their child (relative risk [RR] 0.69; 95% confidence interval [CI] 0.54 to 0.87; P=0.002; five trials; 6145 infants). Moreover there was a significant reduction in the rate of substantial gross motor dysfunction (RR 0.61; 95% CI 0.44 to 0.85; P=0.003; four trials; 5980 infants). No statistically significant effect of antenatal magnesium sulfate therapy was detected on pediatric mortality, or on other neurological impairments or disabilities in the first few years of life. There were no significant effects of antenatal magnesium sulfate on combined rates of mortality with neurologic outcomes, except in the studies where the primary intent was neuroprotection where there were reductions in both death or cerebral palsy (RR 0.85; 95% CI 0.74 to 0.98; P=0.03; four trials; 4446 infants) and death or substantial gross motor dysfunction (RR 0.84; 95% CI 0.71 to 1.00; P=0.05; three trials; 4387 infants). Antenatal magnesium sulfate therapy given to women at risk of preterm birth is neuroprotective against motor disorders for the preterm fetus.

PS01.2 Antibiotics in preterm delivery: The ORACLE trial and children study <u>Sara Kenyon</u> (1)

(1)University of Birmingham, United Kingdom

The ORACLE trial evaluated the effects of prescription of erythromycin or co-amoxiclav for women with either preterm rupture of the membranes (PROM) or spontaneous preterm labour (SPL) with intact membranes and no overt infection, using a 2x2 factorial design. For women with PROM erythromycin was associated with prolongation of pregnancy and improvements in short-term maternal and neonatal morbidity; for singletons there was a reduction in the composite primary outcome (death or abnormal cerebral ultrasound or use of supplemental oxygen at 36 weeks post menstrual age). Co-amoxiclav was associated with increased risk of neonatal necrotising enterocolitis. For women with SPL there was no evidence of either benefit or harm at discharge from hospital. The ORACLE Children Study (OCS) found that, for children whose mothers had PROM, the prescription of antibiotics seemed to have little effect on the health and educational attainment of children at 7 years. For children whose mothers had SPL the prescription of erythromycin (with or without co-amoxiclav) was associated with an increase in the proportions of children with any level of functional impairment from 38 to 42%. Similarly there was an increase in the proportions of children with cerebral palsy from 1.7 to 3.3% associated with erythromycin and from 1.9 to 3.2% with co-amoxiclav. There was a suggestion that more children who developed CP had been born to mothers who had received both antibiotics.

PS01.3 Genetics in preterm delivery No abstract submitted

PS02 Parallel Session 2 - Gynecological update: Endometriosis. Fibroids. New Treatment options

1030 - 1200

PS02.1 Enzymes of E2 synthesis/metabolism - a target for treating endometriosis and myomas

<u>A Perheentupa</u> (1,2), K Huhtinen (2), P Suvitie (1), M Poutanen (2) (1)Turku University Central Hospital, Turku, Finland

(2)Institute of Biomedicine, Department of Physiology, University of Turku, Finland

Recent data have revealed that local production of estrogens within the endometriosis and myomas may be of importance in the pathogenesis of the diseases. Inhibition of locally expressed steroidogenic enzymes may, thus, offer a novel treatment approach. Accordingly, HydroxySteroid (17beta) Dehydrogenase 1 (HSD17B1) as well as P450 aromatase activities have been shown to be expressed both in myomas and endometriosis lesions. As part of our global gene expression profiling in various types of endometriosis specimens we have evaluated the expression of all 14 HSD17B enzymes in eutopic endometrium, peritoneum and various types of endometriosis specimens. Among the analyzed HSD17Bs, we identified a clear up-regulation of HSD17B2 in the secretory phase endometrium of both healthy women and endometriosis patients, while no such increase could be observed in the endometriosis lesions. This is in line with the suggested progestin resistance of endometriosis. Among the other enzymatic activities, HSD17B2 metabolizes estradiol to a less potent estrone. Thus, the lack of HSD17B2 up-regulation in endometriosis by progesterone is expected to increase the proliferative potency of estradiol. In contrast to HSD17B2, HSD17B6 expression was markedly up-regulated in various types of endometriosis tissues irrespective of menstrual cycle, and the enzyme was localized mainly in the epithelium of the disease tissue. The HSD17B6 enzyme has also shown to possess $3(\alpha \rightarrow \beta)$ hydroxysteroid epimerase and oxidative 3α -hydroxysteroid dehydrogenase activities, and its role in the regulation of intratissue sex steroid concentrations needs to be studied further.

PS02.2 Non-hormonal targets for new medical treatment of endometriosis

Thomas D'Hooghe (1)

(1)Leuven University Fertility Center, Belgium

Endometriosis, a chronic gynecologic disease frequently resulting in chronic pelvic pain, severe dysmenorrhoea, and subfertility, is defined as the presence of endometrial tissue at extrauterine locations, most commonly on the peritoneum and ovaries. Conclusive diagnosis requires laparoscopic surgery followed by histological confirmation. The treatment options -at present- are limited to hormonal therapies and/ or surgical ablation of the lesions, and are characterized by high recurrence rates, significant side-effects and limited duration of administration. The pathogenesis of endometriosis is still unclear and numerous immunological and inflammatory factors have been suggested to be involved in the development of the disease, including interleukin (IL)-1, IL-2, IL-6, IL-8, IL-12, tumour necrosis factor $_{\rm i}$ Valpha (TNF- $_{\rm f}$ N), regulated on activation, normal T-Cell expressed and secreted (RANTES) and its receptor cognate chemokine receptor 1 (CCR1), peroxisome proliferator activated receptors (PPARs), matrix metalloproteinases (MMPs) and cyclooxygenase (COX). Another crucial mechanism in endometriosis is the vascularisation of the endometriotic lesions, with a key role for vascular endothelial growth factor (VEGF). Recently, protease activated receptors (PARs), mitogen-activated protein kinases (MAPKs) and tyrosine kinases have also been associated with the pathophysiology of endometriosis. The aim of this presentation is to discuss which molecules, recently found to have connections with the pathogenesis of endometriosis, can serve as potential

targets to develop new methods for novel medical management of this disease. This review also critically addresses how new nonhormonal drugs can and have been tested in basic, preclinical and clinical research, the status of this research and the importance of efficacy/safety studies before clinical application.

PS02.3 Treatment of uterine myomas with embolisation of uterine vessels: possibilities and limitations

<u>Kirsten Hald</u> (1) (1)Oslo University Hospital, Norway

Objective: To give an overview of Uterine Artery Embolization(UAE) and its current place in the treatment of uterine myomas. Summary: UAE is performed by interventional radiologists in local anesthesia. Both uterine arteries are accessed and embolized under angiographic quidance. Since the myomas are mainly supplied by these arteries, the tumor is usually inactivated. The uterus survives because of compensatory collaterals. Relief of excessive menstrual bleeding is reported in 81-96% and reduction in bulk symptoms in 61-92% of the patients after treatment. Prospective studies report reduction in uterus volume between 23 and 53% and reduction of the dominant leiomyoma volume of 37-68% measured by ultrasonography or MRI 3-12 months after treatment. The procedure involves considerably post procedural pain and a substantial amount of narcotic painkillers are often needed the first 24 hours after treatment. Postembolization syndrome is defined by low-grade fever, pelvic pain, nausea, vomiting and malaise after treatment and occurs in approximately 40% of the patients. Five year recurrence rate is reported to be between 11- 20%. Major complications are rare, Comparison with myomectomy and hysterectomy have shown shorter hospital stay and recovery time after UAE, while symptom reductions and complication rates are variably reported. Desire to maintain childbearing potential is still a relative contraindication, since preservation of fertility cannot be assured according to the existing literature. Conclusion: UAE is a safe and effective alternative for women with symptoms caused by uterine myomas if myomectomy or hysterectomy is not the preferred option. How the treatment affects fertility is still unclear.

PS02.4 Robot-assisted laparoscopic (da Vinci) surgery in reproductive medicine *Jan Persson* (1)

(1)Skane University Hospital, Lund, Sweden

Objectives: To describe applications for robot assisted laparoscopic surgery within the field of reproductive medicine Robot assisted surgery was introduced in gynecology and gyneoncology in 2004 worldwide and in late 2005 in Europe. The system provides wristed, tremor eliminated movement downgraded instruments, a 3D stable view and a comfortable working position for the surgeon, in all enabling surgery with unsurpassed precison with the surgeons' full focus on the procedure. Most applications are within gynecological oncology but with increased experience a number of rare but complex procedures within reproductive medicine have been described, i.e early pregnancy complications, surgery for uterine malformations, surgery during pregnancy including abdominal cerclage and surgery for ovarian neoplasms, repair of post Cesarean wound dehiscence and tubal reanastomosis. The robot also facilitates surgery for uterine fibroids, in particular those with an unfavourable localization. The presentation will cover those applications with exemplified with selected video parts of the surgical procedure. Conclusion: Robot assisted laparoscopy has widened the applications for minimally invasive surgery also to rare but advanced procedure in reproductive medicine.

PS03.1 Victim - assailant relationship: Injury pattern and legal outcome

<u>Cecilie Therese Hagemann</u> (1,2), LE Stene (1), AK Myhre (3,4), K Ormstad (2,5), B Schei (1,2,3) (1)Department of Public Health and General Practice, Norwegian University of Science and Technology, Norway (2)Department of Obstetrics and Gynecology, St Olav's Hospital, Trondheim University Hospital, Norway (3)Resource Centre about violence, traumatic stress and suicide prevention, St. Olav's Hospital, Trondheim University Hospital, Norway

(4)Department of Laboratory Medicine, Children and Women's Health, Norwegian University of Science and Technology, Norway

(5)Institute of Forensic Medicine, Oslo University, Norway

Objectives: To assess injury pattern and legal outcome among police-reported rapes and attempted rapes, and evaluate whether these factors differ according to the victim's relationship to the assailant. Methods: We identified police-reported cases of rape and attempted rape on women (? 16 years) in the county Sør-Trøndelag in Norway in the period January 1, 1997 to June 20, 2003. Among 185 cases, 101 had undergone medico-legal examination at the Trondheim SAC (Sexual Assault Center). Data were collected from police files and merged with corresponding data from the SAC. Information on injury pattern and legal outcome was assessed in groups of victim- assailant relationships. Results: Among the 101, the relationship between the victim and the assailant was known in 97 cases; 7 had been assaulted by a partner (current/former), 45 by a friend (known > 24 hours), 19 by an acquaintance (known < 24 hours), and 26 by a stranger. Extragenital injuries were documented in 47 cases, and were documented significantly more often when the assailant was a partner. Charges were filed in 18 cases, and were significantly more often filed when the assailant was either a partner or a friend. Conclusions: Victims assaulted by a partner are more likely to sustain injuries. Charges were more often filed when the victim had been assaulted by a partner or a friend. Thorough documentation of injuries is important medico-legal evidence, and may be decisive for a case with a known assailant to proceed to court.

PS03.2 Post-traumatic stress disorder (PTSD) after rape

Anna Möller (1), HP Soondergaard (2), M Hartig (1), L Helström (1)

(1)Dept of Clinical Science and Education, Karolinska Institute. Dept of Womens Health, Stockholm South Hopital, Sweden

(2)Institute of Neuroscience, Karolinska Institute, Sweden

The Rape Victim Emergency Clinic at Stockholm South Hospital meet 6-700 rape victims each year. Rape is known as the strongest risks for development of Post Traumatic Stress Disorder (PTSD) characterized by reexperiencing of the trauma by flashbacks, avoidance of triggers for reexperiencing, arousal such as sleep disorders and cognitive dysfunctions. All victims seeking help at the clinic were included in the study and followed up in 6 months. Self-rating questionnaires for acute and chronic stress reaction were filled in 10-14days after the rape and after 6 months plus a standardised diagnostic interview at 6 months. Preliminary results indicate that as much as 41% of rape victims fill the criterias for PTSD according to DSMIV after six months as measured by the questionnaires (SASRQ,PDS) and structured personal interviews (SCID). More than half of the victims show moderate or severe depression (53%) (BDI). A majority of the women (80%) report a previous trauma before the rape (PDS). Our data show that PTSD is a common disorder after rape. Post traumatic stress disorder is a serious disabling condition that strikes young women in the middle of their development into adulthood. Finding methods for preventing development of the disorder is of greatest importance for the society as well as for the individuals.

PS03.3 Presentation of data and clinical results from a public sexological clinic during a three-year period

<u>Astrid Højgaard</u> (1), L Kempf (1), R Pristed (1) (1)Regional Hospital, Randers, Denmark

The aim of the paper is to describe treatment results and distribution of sexual dysfunctions presented at a new public sexological clinic during January 1, 2006 – December 31, 2008 in Denmark with an uptake population of 3 millions. The clinic is a unit of a regional gynaecological obstetrical department. Only patients without abuse of alcohol or drugs and without major psychiatric illness or borderline disturbances are admitted. Method. Data concerning age, sex, diagnosis, numbers of visits and marital status were collected from the patient files. Patient satisfaction was elucidated by an anonymous postal survey including all patients who completed treatment in 2006. Results. A total of 256 female and 238 male patients have completed treatment. The 494 patients were seen at 1296 sessions of 50 minutes. If needed PDE5 inhibitors were prescribed. The diagnoses among female patients were: Hypoactive Sexual Desire 39.4%, Vaginism 21.9%, Dyspareunia 12.1%, Anorgasmia 3.9%, Partner-performance problems 18.8%, other problems 3.9%. The distributions of dysfunctions among male patients were: Erectile dysfunction 16.8%, Premature Ejaculation 7.6%, Anejaculation / Retarded Ejaculation 3.8%, Hypoactive sexual disorder 8.8%, Hypersexuality 0.8%, Partner-performance problems 59.7%, and other problems 2.5%. The patients delay was substantial, 83 % waited > 2 years before seeking help and 40% waited > 6 years. Two thirds of patients reported to have their sexual problems solved, 78% found that their couple relationship had improved and 50% thought that their general wellbeing had improved during their therapy. Conclusion. Sexological therapy is effective with high patient satisfaction.

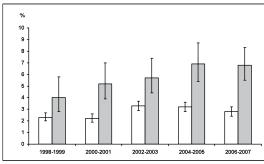


Figure 2. Rates of severe postpartum hemorrhage with 95% CI over a 10-year period;
vaginal deliveries cesarean sections.

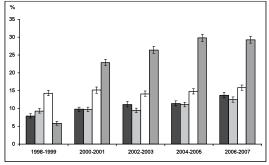


Figure 3. Rates of obstetric interventions with 95% CI over a 10-year period;

■ cesarean sections □ operative vaginal deliveries □ inductions of labour □ augmentations of labour □ augmentations

PS03.4 Botulinum toxin type A - a novel treatment for provoked vestibulodynia? Results from a randomized, placebo-controlled, double-blinded study

<u>Christina Damsted Petersen</u> (1), A Giraldi (1), L Lundvall (2), E Kristensen (1)

(1)Sexological Clinic, Psychiatric Centre, Rigshospitalet University Hospital of Copenhagen, Denmark (2)Department of Gynecology, Juliane Marie Center, Rigshospitalet University Hospital of Copenhagen, Denmark

Objective: A randomized, double blinded placebo controlled study on the effect of Botox on vestibulodynia and concomitant sexual dysfunction. Methods. Sixty-four women were randomised to receive 20 units (0.5 mL) Botox (n = 32) or 0.5 mL saline placebo (n = 32). Botox or Saline was injected in the mm. bulbospongiosus at baseline. Pain was measured monthly on a VAS likert scale for 6 months. Sexual function was measured using the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS) at baseline and at 3 and 6 months follow up. Results. Sixty women (94 %) completed the six months follow up. Both Botox and

placebo produced significantly pain reduction (p < 0.001). There was no significant difference in the median VAS score between the groups at six months follow up (p = 0.984). An improvement on the FSFI full score from baseline until 6 months was not significantly different between the groups (p = 0.635). In the placebo group a statistical significant larger reduction in sexual distress was observed from baseline until six months follow up compared to the Botox group (p = 0.044). Conclusion. Injection of 20 units of Botox in the vestibule of women diagnosed with vestibulodynia does not reduce pain or improve sexual functioning compared to placebo. Both groups experienced a reduction in pain at 6 months follow up. Women with vestibulodynia have impaired sexual function and report sexual distress, which has to be addressed when treating the pain condition.

PS03.5 Influence of female obesity on long-term live birth rates after assisted reproductive technology – a prospective multi-centre cohort study of 544 couples

<u>Anja Pinborg</u> (1), C Hougaard (2), A Nyboe Andersen (1), PK Andersen (2), J Boivin (3), L Schmidt (2) (1)Fertility Clinic. Rigshospitalet. Copenhagen University. Denmark

(2)Institute of Public Health, Copenhagen University, Denmark

(3) Fertility Studies Research Group, School of Psychology, Cardiff University, United Kingdom

Objectives To investigate impact of female bodyweight on overall birth rates after consecutive ART cycles with adjustment for important covariates. Materials & methods Data included clinical files and three questionnaires (80% response rate) with 5-years follow-up on 544 ART-couples. To explore predictors of live births over time in all IVF cycles a discrete survival model with random effect was performed. Results Following the first IVF cycle a positive correlation was observed between higher BMI and total FSH dose (P=0.001). A U-shaped relationship between BMI and the number of aspirated oocytes and developing embryos was observed with less aspirated oocytes and developed embryos in both underweight and obese women. After the first IVF cycle clinical pregnancy rate at week 7 ultrasound was 31.5% vs. 21.4% in normal weight and obese women, respectively (P=0.1). The similar figures for live birth rates were 22.0% vs. 16.9% (P=0.1). The 544 couples underwent 1334 IVF cycles. The survival model included all repetitive IVF cycles with random effect to account for the fact that each couple could have several treatment cycles. The analysis showed that the only independent predictors of live birth following IVF treatment over time were BMI (P<0.05) and female age (P<0.05). Male age was close to significant (P=0.06). Years of involuntary childlessness, infertility diagnosis, smoking and social class were not significant in univariate analyses and not entered into the final model. Conclusions Women with high BMI start treatment at a disadvantage that persists throughout treatment and leads to fewer women achieving parenting goals.

PS03.6 Perinatal outcome of singleton siblings born after assisted reproductive technology and spontaneous conception. Danish national Sibling-Cohort study

<u>Anna-Karina Aaris Henningsen</u> (1), A Pinborg (1), Ø Lidegaard (2), C Vestergaard (2), JL Forman (3), AN Andersen (1)

(1) Fertility Clinic, Rigshospitalet, Copenhagen, Denmark

(2)Dep. of Obstetrics and Gynecology, Rigshospitalet, Copenhagen, Denmark

(3)Dep. of Biostatistics, University of Copenhagen, Denmark

Objective: To compare the perinatal outcome of singleton siblings conceived differently. Methods: National population-based register study assessing the differences in perinatal outcome of 13,692 pair of siblings (n=27,384 children) conceived after in-vitro fertilization (IVF), intracytoplasmatic sperm injection (ICSI), frozen embryo replacement (FER) or spontaneous conception (SC) subcategorized into five groups according to succession; A: IVF/ICSI vs. SC (n=7758), B: IVF/ICSI vs. FER (n=716), C: FER vs. FER (n=34), D: IVF/ICSI vs. IVF/ICSI (n=2876) and E: SC vs. SC (n=16,000). Results: Mean birth weight was 65 grams [95%CI 41-89]

lower in all assisted reproductive technology (ART) children compared to their SC siblings. FER children were 167 grams [95%CI 90-244] heavier than siblings born after replacement of fresh embryos. A decline in birth weight of 62 grams from child one to child two was found if the SC birth preceded the ART birth. The same was seen if a FER child preceded a sibling born after replacement of a fresh embryo. Higher risk of low birth weight with OR 1.4 [95%CI 1.1-1.7] and preterm birth with OR 1.3 [95%CI 1.1- 1.6] was observed in IVF/ICSI vs. their SC siblings. Conclusion: When differentiating between order and mode of conception it seems that ART does play a role in mean birth weight and risk of low birth weight and preterm birth. Birth weight was higher in siblings born after FER versus replacement of fresh embryos.

PS03.7 Can the bleeding pattern during consecutive use of the LNG-IUS be predicted?

Oskari Heikinheimo (1), P Inki (2), M Kunz (3), K Gemzell-Danielsson (4)

(1)University of Helsinki, Helsinki, Finland

(2)Bayer Schering Pharma AG, Turku, Finland

(3)Bayer Schering Pharma AG, Berlin, Germany

(4)Karolinska Institutet, Stockholm, Sweden

Objective: Consecutive use of the levonorgestrel-releasing intrauterine system (LNG-IUS) is increasing. We analyzed factors which may predict the bleeding pattern during consecutive use of the device. Design and Methods: Fertile aged women (n=204) who had used their 1st LNG-IUS between 4 years and 3-9 months and who opted for a 2nd LNG-IUS were recruited. Bleeding data were reported using 90-day reference periods (RP) starting from the last 90 days of the 1st LNG-IUS use (baseline) until the end of the 1st year of the 2nd LNG-IUS (RPs 1to4). Effect of number of factors (age, parity, BMI, indication of LNG-IUS use, smoking, presence of uterine fibroids, endometrial thickness and baseline bleeding category) on the bleeding/ spotting (B/S) days was analyzed. Results: Mean (\pm SD) number of B/S days was 8.9 (\pm 9.1) at baseline. This increased slightly to 11.5 (\pm 10.2), during RP1, due to B/S associated with the insertion procedure, and fell to 6.4 (\pm 8.1) during RP4. Age, parity, BMI, indication of LNG-IUS use or smoking did not predict the bleeding pattern. Women with uterine fibroids, or those with >9 days of spotting or any bleeding at baseline had more B/S days during RPs1-4. The number of B/S days decreased from baseline to RP 4 in all groups except in women with fibroids. Conclusions: Uterine bleeding is reduced during consecutive use of the LNG-IUS. Women with uterine fibroids or any bleeding at baseline continued to have more B/S. Factors such as age, parity, BMI and smoking did not predict the bleeding pattern.

PS03.8 Influence of mode of anesthesia on outcome of fast-track hysterectomy

Ninnie Borendal Wodlin (1), L Nilsson (2), P Kjølhede (1)

(1)Clinical and Experimental Medicine, Linköping, Sweden

(2)Medical and Health Sciences, Linköping, Sweden

Objective: To determine whether the patient recovery after abdominal hysterectomy for benign conditions in a fast track setting differed between women operated under general anesthesia (GA) or in spinal anesthesia with intrathecal morphine (SA). Methods: 162 women participated in an open randomized multicenter study; 80 randomized to GA (propofol, fentanyl, rocuronium) and 82 to SA (20 mg hyperbaric bupivacaine and 0.2 mg morphine). A fast track model comprising no use of sedatives for premedication, i.v. fluid restriction, analgesics based on non-opioids, pre-emptive antiemetic therapy using acupressure wrist bands, early enteral nutrition and mobilization and standard criteria for discharge were used. End points were duration of hospital stay, use of analgesics, antiemetics and antipruritics, occurrence of vomiting, and bowel function recovery. Results: The mean duration of hospitalization did not differ between groups (GA 48 vs. SA 46 hours). The SA group used significantly less opioids day 0 (= day of surgery) and day 1. The use of rescue antiemetics and occurrence of

vomiting episodes did not differ between the groups. Significantly more women needed rescue antipruritics in the SA group on day 0 (38% vs. 2.5%). Time to first pass of gas and bowel movement were significantly faster in the SA group. Conclusion: The duration of hospital stay in fast track abdominal hysterectomy is less than 2 days. SA provides less need of opioids postoperatively and subsequently a faster recovery of bowel functions. The disadvantage of SA is pruritus. Care after spinal anesthesia with morphine in the gynecological ward is safe.

PS03.9 Climate and health. Challenges for gynaecologists

Øjvind Lidegaard (1)

(1)Rigshospitalet, Denmark

Background. Human made global warming is a reality. The climate changes that follow will have a profound impact on human health worldwide. Do gynaecologists have special challenges in adapting to these and to mitigate further changes? Methods. Literature survey Results. A key element in mitigating dramatic climate changes is a 90% reduction in our emission of greenhouse gases in Europe and a 50% reduction worldwide before year 2050. As health professionals we all have a responsibility to spread the scientific insight we have, and to explain that climate change is not one, but the most important global health threat in this century, and that only a determined collective action from the world's societies could prevent major future health disasters. As gynecologists we could emphasize the importance of global access to birth control and free access to elective abortion as two important instruments to reduce the growth rate in the global population, but also that some degree of equalizing the cleft between developed and developing countries is necessary in order to achieve a responsible concerted global action in the years to come. Conclusion. The sooner we realise these challenges and make personal changes in our lifestyle, the easier will the transition phase be, which we under all circumstances have to go through with the expenditure of fossil fuels.

PS04 Parallel Session 4 - Surgery for urinary incontinence – the Nordic approach 1330 - 1500

PS04.1 Pregnancy, delivery, and the pelvic floor - vaginal or caesarean?

Guri Rørtveit (1)

(1)University of Bergen, Norway

Pregnancy and childbirth are risk factors for urinary incontinence among young and middle-aged women. The risk of pelvic floor damage due to pregnancy and childbirth, with consequent urinary incontinence, anal incontinence or pelvic organ prolapse may be analyzed in both a short term and a long term perspective. This abstract will predominantly deal with urinary incontinence, which is the most prevalent problem of the three. In a short term perspective, there is substantial risk of urinary incontinence both during pregnancy and in the period up to one year post partum. In a previous study, as many as 58% of all pregnant women reported incontinence by week 30. A review of the combined prevalence of urinary incontinence in the post partum period shows double prevalence in the vaginal delivery group (31%) compared to the cesarean section group (15%). One could imagine that women who are incontinent in pregnancy are specifically vulnerable to the vaginal delivery with regards to persistent incontinence. However, recent research indicates that the risk of incontinence after vaginal delivery is equivalent in women who were incontinent in pregnancy compared to those who were continent, with an RR of 3.2 in the first group, and RR 2.9 in the second. In a long term perspective, it seems that incontinence in the first pregnancy is an indication of vulnerability to persistent incontinence. However, caesarean section also seems to have a long term protective effect on incontinence, at least among young and middle-aged women.

PS04.2 Retropubic, transobturator or 'mini' – which sling is best? No abstract submitted

PS04.3 Concomitant prolapse and incontinence-colporraphy plus sling or colporraphy plus wait-and-see?

Ellen Borstad (1)

(1)Oslo University Hospital, Ullevål, Norway

Urinary stress incontinence (USI) occurs in about one forth of women with POP. The studies in this field are usually small with very different design and therefore contribute little to evidence for treatment strategies. I will try to summarize the studies from the last 15 years and share with you the results and implications of our own recently published prospective multicenter study. Reviews conclude that there are not sufficient data, but that "concomitant TVT or Burch might reduce postoperative incontinence rates" (of course). From 2002 to 2007 7 centers in Norway randomized women with POP and USI to have a TVT at the moment of prolapse surgery or 3 months later, if needed. The study was powered to detect a difference of 20% in the cure of USI. We found no difference in the cure of USI as long as a TVT was performed. But 29% of women were cured from USI by only prolapse repair, indicating that unnecessary surgery would have been performed in these women if TVT had been done concomitantly. The majority of complications were caused by the TVT and less by the prolapse surgery. Women with a large prolapse especially of the anterior wall had better chance to be cured from prolapse repair alone. Both strategies have good results, but unnecessary complications and costs could be avoided by reserving the incontinence procedure to those who will need it. These results should useful in counseling of women with POP and USI prior to surgery.

PS04.4 Mixed urinary incontinence - drugs or surgery?

Søren Brostrøm (1)

(1)Herlev Hospital, Denmark

Mixed urinary incontinence is defined by the ICS and IUGA by purely symptomatic criteria, as the complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing or coughing. In large epidemiological studies as well as published clinical series of urinary incontinent women there seems to be an overrepresentation of mixed urinary incontinence. Treatment-seekers may be more likely to present mixed symptoms, as mixed urinary incontinent women generally have more severe complaints. However, it may also be that severity confounds diagnosis, as mixed symptoms (not mixed condition) is associated with severity. The occasional leakage is more easily discriminated by both patient and caregiver; if you leak all the time it may be difficult to elucidate factors associated with leaks. It may also be that one symptom drives the other, as stress urinary incontinent women adapt by frequency-urgency behaviour. This is supported by the finding of reduced urgency-frequency after surgery in patients with symptomatic mixed urinary incontinence and urodynamic stress incontinence with a stable bladder. Behaviorial therapies such as pelvic floor muscle training has been shown to be effective, but the evidence is poor. Midurethral slings are more effective than drugs, but there is a risk of de-novo urgency. The clinician should consider the benefits of preoperative urodynamic studies in such cases. Duloxetin is effective in both stress- and urge-predominant conditions, but there are some safety concerns with this drug. Antimuscarinics reduce urgency leakages, but their clinical benefit is small, sideeffects frequent and long-term persistence poor.

PS05.1 Prepregnancy counselling and pregnancy management with serious co-morbidity Catherine Nelson-Piercy (1)

(1) Guy's & St Thomas' Foundation Trust, United Kingdom

Prepregnancy counselling provides an opportunity for women with medical conditions to be fully informed about the likely effect of pregnancy upon the medical condition, and also how the medical condition may adversely effect pregnancy outcome and any risks to herself or her fetus during pregnancy. The safety of drug therapy can be discussed and if necessary plans made to stop or change medications prior to or in early pregnancy. Multidisciplinary pre-conception assessment and counselling, also allows appropriate investigation and management of the medical disorder to ensure optimal disease control, postponement of conception if appropriate and thereby maximize the chances of successful pregnancy outcome. Clinicians advising women should be aware of the few medical conditions which are absolute contraindications to pregnancy, such as pulmonary hypertension. Women with serious co-morbidity require close supervision in pregnancy by a team of midwives, specialist nurses, physicians, anaesthetists and obstetricians with expertise in the care of such women in pregnancy. It is this expertise which allows clinicians to counteract the common misconceptions that all such women require delivery by Caesarean section or preterm. Similarly important drug therapy (such as azathioprine) may be erroneously omitted or avoided if clinicians are not aware of published data supporting safety in pregnancy notwithstanding alarmist cautioning by the drug manufacture and without such drugs having a licence for use in pregnancy. These important general principles will be illustrated with reference to women with cardiac disease, renal disease and connective tissue disease.

PS05.2 Assisted reproduction in the medically complicated patient

Nick Macklon (1)

(1) Division of Origins of Health and Disease, Southampton University Hospital, United Kingdom

As we enter the second generation undergoing IVF, the patients being treated are very different to those of three decades ago. Clinics are increasingly seeing women approaching and exceeding their 40's seeking assistance to become pregnant. Not only does this affect the efficacy of fertility therapies, it also means that more of our fertility patients present with co-morbidities which can impact on IVF and vice versa. The changing demographics of our patients, in combination with the new indications for ART such as fertility preservation for cancer patients and PGD for carriers or sufferers of serious inherited disease present us with new clinical challenges. In addition, the improved prognosis associated with some serious medical conditions mean that many patients who would have never had children are approaching us after controlling their serious heart disease or diabetes or cystic fibrosis. These changes in the population being treated for subfertility, and the extending indications for IVF therapy are making new demand on the expertise of Reproductive Endocrinologists. At the interface between Reproductive Medicine and Perinatalogy a new field of Periconceptional Medicine is emerging. Increasing recognition that periconceptional events determine not only fertility, but pregnancy and long-term health outcomes for mother and child is increasing the focus of both fertility specialists and perinatologists on this crucial phase of early development. In this lecture, the approach to the assessment and management of the medically complicated IVF patient will be outlined, and placed in the wider context of the emerging field of Periconceptional Medicine.

PS05.3 IBD - Fertility, pregnancy and breastfeeding

Lisbet Ambrosius Christensen (1)

(1)Aarhus University Hospital, Denmark

Ulcerative colitis (UC) and Crohns disease (CD) often affect young women in their reproductive age. Fertility is normal in women with unoperated UC, but might be decreased in women with complicated CD and previous operations. Disease activity during pregnancy increases the risk of abortion and preterm delivery To keep the disease in remission, medical treatment is necessary in approximately fifty percent in an unselected group of patients. The treatments include 5-aminosalicylic acid (5-ASA) preparations, especially in ulcerative colitis, and has proven of no harm during pregnancy and lactation. Immunosuppressants, such as Azathioprine, are now widely used especially when repeated courses of steroids have been necessary. Published data on pregnancy outcome are still below a few hundred cases, but at present treatment during pregnancy is considered safe. Minimal amounts are excreted in the maternal milk, and lactation is advised in general. A small group of patients with very complicated disease requires continuous treatment with biologic therapy, such as Infliximab or Adalimumab as prophylactics to be kept in remission also during pregnancy. Data on fetal outcome are rapidly increasing, and the outcome seems not to differ when compared with other treatments of this selected group of patients. Infliximab treatment is usually stopped in third trimester to avoid high fetal plasma concentrations at delivery. So far no maternal milk excretion has been demonstrated.

PS06 Parallel Session 6 - Free communications Obstetrics - exprimental approaches

1330 - 1500

PS06.1 Metformin during pregnancy in PCOS: results of a RCT

<u>Eszter Vanky</u> (1), S Stridsklev (1), R Heimstad (1), P Romundstad (2), K Skogøy (3), O Kleggetveit (4), S Hjelle (5), P von Brandis (6), T Eikeland (7), K Flo (8), KF Berg (9), SM Carlsen (10)

- (1)Institute for Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and TechnologyTrondheim, Norway and Dept of Obstertics and Gynecology, St Olavs Hospital, Trondheim University Hospital
- (2)Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway
- (3)Sentral Hospital of Northern Norway, Bodø, Norway
- (4)Elvebredden Gynekologpraksis, Kristiansand, Norway
- (5)Ålesund Hospital, Ålesund, Norway
- (6) Stavanger University Hospital, Stavanger, Norway
- (7)Haugesund Hospital, Haugesund, Norway
- (8)Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway
- (9)Buskerud Hospital, Drammen, Norway
- (10)Unit of Applied Clinical Research, Institute of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim and Department of Endocrinology, St. Olav's Hospital, Trondheim University Hospital

Background: Women with polycystic ovary syndrome (PCOS) have an increased incidence of pregnancy complications. Retrospective, non-randomized and small studies report beneficial effects of metformin on pregnancy complications. The present study was designed to test the hypothesis that metformin use in pregnancy reduces preeclampsia, preterm delivery and/or gestational diabetes mellitus in PCOS. Methods: The Metformin treatment in pregnant PCOS women (PregMet) study is a prospective, randomized, double-blind, multicentre trial comparing metformin 2000 mg daily with placebo. Inclusion criteria: PCOS diagnosed according to The Rotterdam Consensus criteria, age 18 – 45 years, gestational week 5 - 12 at inclusion and singleton viable fetus. Exclusion criteria: ALAT > 90 IU/L, creatinine > 130 mol/L, alcohol abuse, previously diagnosed

diabetes mellitus or fasting s-glucose > 7.0 mmol/L at inclusion and use of glucocorticoids or drugs known to interfere with metformin. Three-hundred-forty-seven PCOS women, with altogether 363 pregnancies were informed about the study; 32 did not meet inclusion criteria, 58 declined and 16 women participated twice. Two-hundred seventy-three pregnancies were randomly assigned to metformin or placebo treatment. Primary outcomes: incidence of preeclampsia, preterm delivery and GDM or the composite of these three disorders. Secondary outcomes: weight, heart rate and blood pressure development in pregnancy, and the mode and length of delivery. Results: Data from the PregMet study on primary and secondary end points and safety data will be available for presentation in June 2010. Keywords: PCOS, pregnancy complications, metformin.

PS06.2 Metformin versus insulin in the treatment of gestational diabetes: a prospective randomised study

<u>Hilkka Ijäs</u> (1), M Vääräsmäki (1), L Morin-Papunen (1), R Keravuo (2), T Ebeling (3), T Saarela (4), T Raudaskoski (1) (1)Dept. of Obstetrics and Gynecology, Oulu University Hospital, Finland

(2)Kainuu Central Hospital, Finland

(3)Dept. of Internal Medicine, Oulu University Hospital, Finland

(4)Dept. of Pediatrics, Oulu University Hospital, Finland

Metformin is the first-line treatment option of type 2 diabetes mellitus. It would be a logical option in the treatment of gestational diabetes mellitus (GDM), but only one randomized study is available. This prospective randomized controlled study aimed to compare the efficacy of insulin and metformin treatment in GDM. Women with singleton pregnancies and GDM diagnosed by 75g oral glucose tolerance test (OGTT) in a risk-factor based screening at 12-34 gestational week were randomized either to insulin (n=50) or metformin (n=47) therapy if normoglycemia was not achieved by diet. The primary and secondary outcomes were incidence of LGA (large for gestational age) and need for supplemental insulin in the metformin group and neonatal morbidity, respectively. The study groups did not differ as regards to mean age, body mass index (BMI) or parity. Fifteen (32%) of the women randomized to metformin needed supplemental insulin. Women with supplemental insulin were more obese (BMI 36 vs. 30 kg/m2, P=0.002), had higher fasting blood glucose in OGTT (6.1 vs. 5.0 mmol/l, P=0.001) and needed medical treatment for GDM earlier (26 vs. 31 gestational weeks, P=0.002). There were no significant differences between the groups in neonatal outcomes such as birth weight, umbilical artery pH or neonatal morbidity. Incidence of LGA was 8.5% in the metformin and 10.0% in the insulin group (NS). Metformin seems to be a promising alternative to treat mild GDM. In cases with considerable overweight or severe disease determined by early need for medication and fasting hyperglycemia, supplemental insulin was often needed.

PS06.3 The influence of parental history of diabetes on offspring birth weight and glucose metabolism in adulthood

<u>M Jørgensen</u> (1), Jeannet Lauenborg (2), P Damm (1), O Pedersen (3), T Hansen (3) (1)Center for Pregnant Women with Diabetes, Departments of Obstetrics and Endocrinology, Rigshospitalet, Faculty of Health Sciences, University of Copenhagen, The Capital Region of Denmark, Denmark (2)Department of Gynecology and Obstetrics, Hvidovre Hospital, Faculty of Health Sciences, University of Copenhagen, The Capital Region of Denmark, Denmark (3)Steno Diabetes Centre, Gentofte, Denmark

Aim: To investigate the influence of parental history of type 2 diabetes (T2DM) on offspring birth weight and adult offspring glucose tolerance status, and to examine for associations of birth weight with measures of pancreatic beta-cell function and insulin sensitivity in adult non-diabetic offspring of type 2 diabetic patients. Subjects/Methods: Patients with verified T2DM diagnosed according to 1985 WHO criteria after age 40 years with a spouse without known diabetes and four or more offspring were identified at Steno Diabetes Centre

or at the University of Copenhagen, enrolling 58 families. All non-diabetic individuals underwent an oral glucose tolerance test (OGTT) and a frequently sampled intravenous glucose tolerance test. Birth weight and length were obtained from birth records. Results: Among offspring with a maternal history of T2DM (n=122) 14.8% had diabetes compared to 8.0% with a paternal history of diabetes (n=137) (p=0.087). Offspring with maternal diabetes had a mean birth weight 196 g higher than offspring with paternal type 2 diabetes, 3,651g vs. 3,456g (p = 0.011). Non-diabetic offspring with birth weights below 3,350g had significantly higher glucose levels, AUCglucOGTT 1795 vs. 1683mmol/l, p=0.022, and lower insulin sensitivity, Si 9.60 vs. 11.79, p=0.023 in adulthood compared to the offspring with birth weights above 3,800g. Conclusions: Offspring of mothers developing type 2 diabetes after pregnancy is born with a higher birth weight than those born to fathers developing type 2 diabetes. Lower birth weights associate with elevated glucose levels after an oral glucose load and decreased insulin sensitivity in adulthood.

PS06.4 Short interpregnancy interval as a risk factor of spontaneous preterm labor due to low cervical collagen

<u>Iben Sundtoft</u> (1), S Sommer (2), N Uldbjerg (1) (1)Aarhus University Hospital Skejby, Denmark (2)Horsens Regional Hospital, Denmark

OBJECTIVE: The incidence of preterm labor is increasing and continues to be a significant cause of neonatal mortality and morbidity. Various risk factors of preterm labor are known, among those a short interval between labor and a subsequent conception. The risk of spontaneous preterm labor increases with interpregnancy intervals shorter than 12 months, the strongest association with intervals shorter than 6 months. Cervix uteri consist predominantly of fibrous connective tissue, and it is from this tissue cervix derives its "strength". A prerequisite for vaginal delivery is a decrease in the cervical collagen concentration. The aim of this study is to describe the normalization of the cervical collagen after labor. METHODS: Cervical biopsies were collected 3, 6, 9, 12, and 15 months after labor from 15 women. Collagen concentrations of the biopsies were measured following a standard Hydroxyproline assay. The repeated measures of collagen concentration after labor were analyzed by a one-way analysis of variance. RESULTS: Compared with collagen 3 months after labor the collagen concentration was still increasing until 12 months after labor. Statistical significant difference were found in the collagen concentration 3, 6, 9, and 12 months after labor (50.2 (48.0;52.3), 57.9 (55.7;60.0), 61.9 (60.1;63.8) and 65.2(63.4;67.0) µg/mg dry weight; p<0.01). No statistically significant difference was found between the collagen concentration 12 and 15 months after labor. CONCLUSIONS: The human uterine cervix has not normalized until 12 months after labor. The lower collagen concentrations may explain the association between short interpregnancy interval and preterm labor.

PS06.5 Previous preeclampsia and risks of adverse outcomes in subsequent nonpreeclamptic pregnancies

<u>Anna-Karin Wikström</u> (1,2), O Stephansson (1), S Cnattingius (1) (1)Karolinska Institutet, Sweden (2)Uppsala University, Sweden

OBJECTIVE Preeclampsia, stillbirth, placental abruption, spontaneous preterm birth and giving birth to a small-for gestational age (SGA) infant are the most common adverse pregnancy outcomes. We hypothesized that these adverse outcomes have a shared pathophysiology, and that women who developed preeclampsia in first pregnancy may have increased risks of the other outcomes, also in the absence of preeclampsia in next pregnancy. METHODS We performed a population-based cohort study of women with two successive single births in Sweden between 1992 and 2006, and only included women with a non-preeclamptic second pregnancy (n=354,676). Using women with no preeclampsia in first pregnancy as reference, we estimated risks of adverse

outcomes in second pregnancy related to preterm (<37 weeks) and term (>37 weeks) preeclampsia in first pregnancy. RESULTS Women with a prior preterm preeclampsia had more than doubled risks of stillbirth, placental abruption, very (<32 weeks) and moderately (32-36 weeks) spontaneous preterm births (adjusted odd ratios: 2.08 [95% confidence interval (CI) 1.03-4.19], 2.34 [95% CI 1.32-4.15], 2.22; [95% CI 1.10-4.48] and 2.56 [95% CI 2.06-3.18], respectively) and an even higher risk of giving birth to a SGA infant. In contrast, women with term preeclampsia in their first pregnancy only had a slightly higher risk of a SGA infant in the second pregnancy. CONCLUSION Women with previous preterm preeclampsia have increased risks of adverse pregnancy outcomes in subsequent pregnancy also in the absence of preeclampsia. These findings support a shared pathophysiology for preterm preeclampsia, stillbirth, placental abruption, spontaneous preterm birth and a SGA infant.

PS06.6 Gene profiles in maternal blood during early onset preeclampsia and towards term

Berit Dahlstrøm (1), Y Esbensen (1), H Vollan (1), P Øian (2), G Bukholm (1)

(1)Fakulty Division Akershus, University of Oslo, Norway

(2)University of North Norway, Norway

Inflammatory processes are present during preeclampsia and in normal pregnancy. Maternal inflammatory reactions may change towards term. Our objective was to evaluate genome signaling in blood during preeclampsia and towards term using microarrays. RNA microarrays (Illumina) were conducted on blood from preeclamptic pregnancies delivered preterm, normal pregnancies at term and normal pregnancies in gestational week 31. Two statistical methods (Q-value cut off 1%) identified data structures in the three groups and retrieved activated genes along a time axis and a diseased-healthy axis. Signaling genes were localized within known pathways and gene sets, and genes associated with inflammation were identified. Early onset preeclampsia and term pregnancies both showed distinct expression patterns when compared to normal pregnancy in gestational week 31. In preeclampsia, 19 genes were differentially expressed, including a down regulation of cc-chemokine receptor 3 (CCR3). Among the 183 differentially expressed genes towards term, tumor necrosis factor superfamily member 15 (TNFSF15) was up regulated and interferon $f \times$ receptor 2 (IFNGR2) and cxc-chemokine receptor type 4 (CXCR4) were down regulated. Seven other of the genes changed during preeclampsia and towards term were identical. A possible type 1 immune response was identified both during preeclampsia and towards term. In preeclampsia a premature activation of leucocytes might be present.

PS06.7 Elevated inflammation marker calprotectin in diabetic pregnancies

Meryam Sugulle (1), AS Kvehaugen (1), K Brække (2), AC Staff (1,3)

(1)Department of Obstetrics and Gynaecology, Oslo University Hospital, Ulleval, Norway

(2) Department of Paediatrics, Oslo University Hospital, Ulleval, Norway

(3) Faculty of Medicine, University of Oslo, Norway

OBJECTIVE: Calprotectin, an inflammatory protein, is expressed in neutrophils, activated macrophages and endothelial cells. It has been ascribed a modulatory role in inflammatory responses. We previously found augmented calprotectin concentrations in maternal plasma in preeclampsia. Elevated calprotectin plasma concentration in type 1 diabetes mellitus (DM1) has been reported. Excessive inflammatory response is a pathophysiological feature both in preeclampsia and DM. Pregnancies complicated by DM or preeclampsia are associated with augmented risk for cardiovascular disease later in life, both in mother and offspring. We investigated whether plasma concentration of calprotectin is elevated in pregnancies complicated by DM and if calprotectin correlates with the inflammation marker hsCRP. METHODS: EDTA plasma from 130 women with DM (DM1: 53, DM2: 12, gestational DM=GDM: 65), superimposed preeclampsia (in DM, n=11) and uneventful pregnancies (controls, n=37) was analyzed for calprotectin and maternal serum for hsCRP. RESULTS: Median calprotectin concentration was elevated in diabetic pregnancies and in superimposed preeclampsia as compared

to controls (680 and 969 ig/L vs 551 ig/L, p=0.02 and 0.01). The subgroup of women with GDM had elevated median maternal plasma calprotectin as compared to controls (718 ig/L vs 551 ig/L, p=0.006). There was a significant positive correlation between calprotectin and hsCRP in DM1 pregnancies (Spearman's correlation: 0.52, p<0.001), but not for GDM and DM2 pregnancies. CONCLUSIONS: The elevated plasma concentrations of calprotectin in pregnancies complicated by diabetes mellitus may reflect an excessive inflammatory process, which may possibly contribute to the augmented risk of preeclampsia in these pregnancies.

PS06.8 Microparticles and its relation to doppler studies in cases of preeclampsia

Mahmoud E Salem (1), S Zaki (1), SK Hussein (2), GM Helal (3)

- (1)Obstetrics & Gynecology department, Kasr Al Ainy Hospital, Cairo University, Cairo, Egypt
- (2)Clinical Pathology department, Kasr Al Ainy Hospital, Cairo University, Cairo, Egypt
- (3)Obstetrics & Gynecology department, Police Hospital, Cairo, Egypt

Endothelial cell activation is a central feature in the pathophysiologic mechanisms resulting in preclampsia. Microparticles can affect endothelial cell and smooth muscle cell responses and, hence, vasoreactivity. Hypothesis: Circulating microparticles could be considered as a surrogate marker of vulnerable plague or global vascular damage and thus, may be useful as a diagnostic tool for preeclampsia in pregnant women. Material and methods: the study group included 43 women with preeclampsia, pregnancy > 20 week gestation, and with no chronic disease and no history of recurrent pregnancy loss and 28 normotensive pregnant women as a control group. Flowcytometric assay of endothelial microparticles (EMPs) and platelet microparticles (PMPs) using CD31 and 42b respectively, was performed Results: EMPs were significantly higher in pre-eclamptic patients as compared to control group (p-value < 0.001). Platelet microparticles were not significantly different in preeclampic patients compared to control group (p-value 0.957). EMPs were significantly correlated to uterine RI (r=0.374, p-value 0.001), PI (r=0.345, p-value 0.003) and umbilical RI (r=0.424, p-value <0.001). No significant correlation was found between EMP and umbilical PI (r=0.182, p-value 0.128). EMP was significantly correlated to poor maternal outcome (p-value < 0.05) and perinatal outcome (p-value 0.004). However, no statistically significant correlation was found between PMPs and Doppler findings or maternal or fetal outcome. Conclusion: EMPs were significantly higher in preeclamptic patients with significant correlation to increased uterine RI, PI and umbilical RI.

PS06.9 Pregnancy after Roux-en-Y gastric bypass surgery

<u>Alda Birgisdottir</u> (1), BG Leifsson (2), H Hardardottir (1), RT Geirsson (1,3) (1)Dept. of Obstetrics and Gynecology, Landspitali University Hospital, Iceland (2)Dept. of Surgery, Landspitali University Hospital, Iceland (3)University of Iceland, Iceland

Introduction: Obesity is a growing problem among women of reproductive age. Surgery is best for achieving lasting weight loss and reduction of obesity-related ill health. Roux- en-Y gastric bypass surgery (RYGB) is the most common obesity operation performed in the Nordic countries. Aim: To compare pregnancy outcome between women who had RYGB and a matched control group with no previous obesity surgery. Methods: Information was obtained on all women who underwent RYGB at Landspitali University Hospital in 2001-2007 and had given birth since (n=30). As controls the next consecutive woman who gave birth after the index patient and was of the same age, BMI and parity (n=30), was selected. Results: There was no difference in pregnancy-related complications between the cases and controls. Gestational length, numbers of instrumental delivery or cesarean sections did not differ, but induction of labour was more common after RYGB (chi-squared 5.11, p<0.05). Women with gastric bypass surgery gained less weight and birthweight (t = 2.44, p<0.03) and birth length (t = 2.81, p<0.01) were significantly lower. All neonates were born in good

condition. Conclusion: There is a scarcity of data on the influence of this operation on subsequent pregnancy. Although the newborns are lighter and shorter, also compared to the national mean, gastric bypass surgery of the Roux-en-Y type does not have a major impact on short-term pregnancy outcome.

PL02 Plenary 2 - Which country is right? Let us hear your voice!
An interactive session

1530 - 1700

PL02.1 Contraceptive counselling in Sweden – do we have the optimal concept?

Lene Marions (1)

(1) Karolinska University Hospital/Institutet, Sweden

Unwanted pregnancy is a problem of major concern worldwide and, especially in young women, often results in induced abortion. Teenage abortion rate is higher in Sweden than in the other Nordic countries however we also have the lowest birth rate in this age group. Prevention of unwanted pregnancy is an important task for family planning providers.

Contraceptive counselling in Sweden is mostly performed by midwives that after special training have a right to prescribe hormonal contraception. It is estimated that 85-90% of all contraceptive methods are prescribed by midwives.

The role of gynaecologists in family planning activities are mainly focused on pregnancy termination and contraceptive counselling for women carrying certain risk factors. Midwives are competent and are performing an excellent job within the area of family planning however it is important also for physicians to take more active part in this important field.

PL02.2 Prenatal diagnosis, what should be allowed?

Riitta Salonen (1)

(1) Väestöliitto, Department of Medical Genetics, Helsinki, Finland

In Finland prenatal diagnostics of chromosome abnormalities was started for the whole country in 1977, using maternal age 40 years as the cut point for amniocentesis. Eventually the age limit lowered. Mostly 37 years was used, until serum markers in the beginning of 1990's, and ultrasound with nuchal translucency measurements took over. The Finnish public health care has provided prenatal screening equally to all, in principle. However, in practice the ways of doing it has varied a lot, because the individual local authorities have been able to decide, which methods to use. After a few working groups an order was issued 2006 about preferable methods. For the screening of chromosome abnormalities these were, 1) first trimester combined test, ie. biochemical serum markers with nuchal translucency measurement, or if this was missed, 2) second trimester triple serum test. It was later altered to double test, because of the lack of a suitable commercial test. In addition there is a possibility for and early ultrasound scan without screening for fetal chromosomes, and a second trimester ultrasound scan for screening structural abnormalities. This is what has been offered, and the mothers or couples have been able to choose, what they want, after adequate counseling in the mother health care centers. The debates about the matter have not been very strong in Finland, even if groups against abortion have raised the question about prenatal screening every now and then.

PL03.1 Exercise in pregnancy

Bente Klarlund Pedersen(1)

(1) Centre of Inflammation and Metabolism (CIM), Rigshospitalet and University of Copenhagen, Denmark

The Centers for Disease Control and Prevention has designated physical inactivity as an actual cause of chronic disease. In Denmark, physical inactivity is considered the number two actual cause of death and physically inactive people have a life span, which is 5 years shorter than physically active.

In line with an increasing focus on physical activity as a preventive action against Type 2 Diabetes and other lifestyle related chronic disorders, national guidelines in many countries now recommend a substantial level of physical activity during pregnancy. However, it has been questioned whether leisure time physical activity (LTPA) during pregnancy is beneficial or deleterious to pregnancy outcome, and whether a sedentary lifestyle during pregnancy has a negative impact on pregnancy. The prevailing literature clearly indicates that LTPA before and/or during pregnancy have a protective effect on the development of gestational diabetes mellitus and pre-eclampsia. Furthermore, LTPA does not seem to have a negative impact on the rate of preterm delivery or on birth weight, whereas it is controversial whether a high amount of intense exercise during early pregnancy increases the risk of miscarriage.

In the light of the available findings, it seems justified to encourage healthy pregnant women who are already physically active at the onset of pregnancy to maintain their activities but to reduce their intensity and to encourage pregnant women who are not already physically active to initiate physical activity.

PL03.2 Bariatric surgery: indications and reproductive outcomes

Roland Devlieger (1), Poppe A (1), Vansant G (2), Guelinckx I (2)

- (1)Departments of 10bstetrics and Gynaecology, University Hospital Leuven, Belgium
- (2) Nutrition-Public Health Medicine, Catholic University Leuven, Belgium

BACKGROUND: After many cycles of weight loss and gain, more and more morbidly obese patients undergo bariatric surgery, like gastric banding or gastric bypass, as the ultimate treatment for their obesity-problem. Since women of reproductive age are candidates for bariatric surgery, concerns arise regarding the potential impact on future pregnancy.

METHODS: English-language articles were identified in a PUBMED search from 1982 to January 2008 using pregnancy and bariatric surgery or gastric bypass or gastric banding as keywords.

RESULTS: The few reported case-control and cohort studies show improved fertility and a reduced risk in obstetrical complications, including gestational diabetes, macrosomia and hypertensive disorders of pregnancy, in women after operatively induced weight loss when compared to morbidly obesity women. The incidence of intrauterine growth restriction (IUGR) appears to be increased, however. No conclusions can be drawn concerning the risk for preterm labour and miscarriage, although these risks are probably increased compared to BMI matched controls. Operative complications are not uncommon with bariatric surgery and several cases have pointed to the increased risk for intestinal hernias and nutritional deficiencies in subsequent pregnancy. Deficiencies in iron, vitamin A, vitamin B12, vitamin K, folate, and calcium can result in both maternal complications, such as severe anemia, and fetal complications, such as congenital abnormalities and failure to thrive.

CONCLUSIONS: Close supervision before, during, and after pregnancy following bariatric surgery and nutrient supplementation adapted to the patient's individual requirements can help to prevent nutrition-related complications and improve maternal and fetal health, in this high risk obstetric population.

PS07.1 New national outcome data on pregnancies in women with type 1 diabetes No abstract submitted

PS07.2 Aggressive antihypertensive treatment of pregnant women with pregestational diabetes

No abstract submitted

PS07.3 Short-term risk of gestational diabetes-focus on the large-for-gestational-age infants and offspring body composition

Patrick Catalano (1)

(1)Department of Reproductive Biology, Case Western Reserve University, MetroHealth Medical center, Cleveland, Ohio United States of America

We have known for a quite a long time that good glucose control can decrease the risk of many problems in the mother and fetus of the woman with Gestational Diabetes Mellitus (GDM). This presentation will focus on fetal growth and in particular the body composition of the fetus of the GDM mother. At birth the human has the most amount of adipose tissue as compared with other mammals, approximately 10-14%. Based on works by Sparks and others, the fat free mass or lean body mass more closely reflects genetic factors relating to fetal growth. For example, males at the time of birth weigh more than females because of an increase in lean body mass and not fat mass. In contrast the fat mass of the neonate is more closely related to the maternal in utero environment. We have reported that the fetus of the GDM mother weighs more at birth because of an increase in fat mass and not lean body mass. This holds true even in the fetus of the GDM mother's when the birth weight is in the average for gestational age weight group, adjusted for gender and gestational age. The increase in fat mass is most strongly correlated with maternal pregravid insulin resistance. Because the International Association of Diabetes in Pregnancy Study groups (IADPSG) recommendations for the diagnosis of GDM may significantly increase the number of women we classify as having GDM, we have examined the growth of infants of obese women with normal glucose tolerance using current GDM criteria. Maternal overweight/obesity is a significant risk factor for glucose intolerance and fetal macrosomia. Similar to what we reported in the infant of the GDM mother, the infant of the overweight/obese woman (BMI >25) weighs more at birth in comparison to a lean/ average weight woman (BMI <25) not because of an increase in lean body mass but an increase in fat mass. Furthermore at birth these neonates have evidence of increased insulin resistance which is correlated with their fat mass. Based on these data we hypothesize that the infants of the GDM and obese women are at increased risk of childhood obesity and related metabolic dysfunction, thereby creating a viscous cycle into the next generation. Supported by NIH HD-22965

PS07.4 GDM and implication for long term offspring health

Tine D Clausen (1)

(1)Center for Pregnant Women with Diabetes, Department of Obstetrics, Rigshospitalet, Copenhagen, Denmark

The epidemic of obesity and type 2 diabetes has major impact on public health and underlines the urgency for identification of risk groups to target preventive strategies. Studies of developmental origins of health and disease have highlighted the possible role of intrauterine exposure to hyperglycemia as in maternal diabetes in the pathogenesis of overweight, type 2 diabetes and cardiovascular disease; and diabetes in pregnancy may also affect cognitive function in the offspring. Our knowledge is primarily based on studies from the Pima Indians from Arizona, US. In this population diabetes in pregnancy as well as 2-hour blood glucose during an oral glucose tolerance test in pregnancy were strong predictors of overweight and type 2 diabetes

in the adult offspring. Solid data also exist from the Northwestern group in Chicago. Here the offspring of an ethnically mixed group of diabetic women have been followed to the age of 16 years. The main findings were in accordance with the findings in the Pima Indians. This presentation will focus on data from our recent follow-study of 18-27 year old Caucasians exposed to various degrees of maternal glucose intolerance during pregnancy. Our focus was on associations between maternal glucose metabolism during pregnancy and offspring outcome. The studied outcomes were the risk of prediabetes and type 2 diabetes, the risk of overweight and the metabolic syndrome as well as the cognitive function. We found that offspring of women with diet-treated GDM had an eight-fold higher risk of type 2 diabetes/prediabetes, two-fold higher risk of overweight and four-fold higher risk of the metabolic syndrome than offspring from the background population. Furthermore associations between the level of maternal glycemia during pregnancy and these outcomes were found. Data on cognitive function will also be presented.

PS08 Parallel session 8 - Minimally invasive surgery in gynecology

1030 - 1200

PS08.1 New trends in laparoscopic surgery

<u>Anton Langebrekke</u> (1) (1)Oslo Univ. Hospital

During the last 20 years there has been a tremendous development in laparoscopic surgery. Laparoscopy has in many places replaced the place of laparotomy. In this way the surgical trauma has been reduced. Lately multiple attempts to further reduce the trauma and visible scars have been proposed. Recently even natural orifice transluminal endoscopic surgery (NOTES) has been proposed as a less invasive alternative to conventional laparoscopy. Single Port Access (SPA) is an even more recent advance, considered a derivate of NOTES, and represents a step toward even less invasive surgery than standard laparoscopic surgery. The paper will discuss the new methods and its indications in gynecological surgery and personal experiences will be demonstrated by video.

PS08.2 Laparoscopic endometriosis surgery

Marjaleena Setälä (1)

(1)Turku University Hospital, Finland

Endometriosis surgery has changed almost entirely during last two decades, with the advances in minimally invasive surgery. Advantages of laparoscopic approach are clear in terms of recovery time and postoperative discomfort, and therefore laparoscopic approach has replaced laparotomy. Laparoscopic approach is especially beneficial in the treatment of endometriosis, as magnification provided by laparoscope enhances the ability to find, diagnose, and treat all types of endometriotic lesions. At present, laparoscopic excision of all forms of endometriosis can be considered the gold standard of endometriosis surgery. Complete laparoscopic excision of all visible endometriotic lesions has been shown to result in a significant reduction of pain symptoms, and improvement of quality of life. There is some evidence that complete excision also improves fecundity, but the evidence supporting the efficacy of surgery as a fertility-enhancing procedure is still limited. Laparoscopic excision of superficial peritoneal lesions can be considered as general gynaecological laparoscopic surgery, but gynaecological surgery is facing a new challenge from patients with the severe disease. Especially deeply infiltrating lesions are frequently found in bowel and bladder, locations, which gynaecologists are not familiar to operate with. In order to completely excise all endometriosis from these locations, gynaecologists have to practise new operating skills, and also more often co-operate with surgeons. This kind of surgery carries a risk of severe complications, and it should only be performed after thorough planning, consultation with the patient, and consideration of the benefits and possible adverse effects, in hospitals specialized in the surgical treatment of severe endometriosis.

PS08.3 Optimal fibroid surgery

Olav Istre (1)

(1)Department of Gynecology and Obstetrics, Brigham and Women Hospital, Harvard Medical School, Boston, United States of America

Study's objective: The past decade has witnessed highly sophisticated diagnostic and therapeutic technology for fibroids. Nonsurgical treatments interfering with the blood supply to the uterus or the fibroids: uterine artery embolization, laparoscopic uterine artery occlusion/compression, Surgical treatment includes. Hysteroscopic, Laparoscopic, Robotic and Single Port access surgery. Results: The acute degenerative procedure can be painful and infection can occur. Delivering fibroids or sections of fibroids may be a natural process after uterine artery embolization. Possible risk of infectious symptoms like heavy discharge, fever, consequently close follow-up is essential. The spontaneous expulsion of fibroids occurs over several months resulted in a significant reduction in menstrual loss and dysmenorrhea. A long -term side-effect could be premature ovarian failure secondary to interference with the ovarian blood supply. In cases with submucosal fibroids hysteroscopic resection is the method of choice. Robotic and Single port surgery is more time consuming and have a higher cost. Comparable studies will be presented. Conclusions: Fibroids present with different symptoms in different patients; i.e. infertility, bleeding problems, pressure and pain, single or multiple, different ages, which should be treated differently. In bleeding problems, an important issue is the location of the fibroid. In cases with intramural, subserosal and even multiple fibroids, uterine artery therapy with embolization or laparoscopy seem to achieve good results on both bleeding problems and pressure symptoms. In infertility patients, the single fibroid should be removed, while when multiple fibroids are present medical or circulation therapy may be the only option for uterus saving therapy.

PS08.4 Laparoscopic surgery in gynecological oncology

Ole Mogensen (1)

(1)Odense University Hospital

Objective. To evaluate the scientific evidence from randomized controlled trials (RCT) of laparoscopic surgery versus conventional laparotomy in endometrial, ovarian, and cervical cancer. Methods. A search (Title and Abstract) in the PubMed and the Cochrane Library using the keywords: "laparoscopy and endometrial/ ovarian/cervical cancer". No limit for period or language. Results. 720 papers (endometrial: 164, ovarian: 378, cervical: 178) were identified. No RCTs comparing conventional laparotomy with laparoscopy in ovarian and cervical cancer were identified. In endometrial cancer 8 RCTs (period: 2001- 2009) could be identified. The laparoscopic approach to endometrial cancer is associated with longer operating time, lower intraoperative blood loss and fewer postoperative complications. The number of removed pelvic and para-aortic lymph nodes and the intraoperative complications seem unaffected by the method of surgery. Regarding the quality of life (QoL) the advantages using laparoscopy seem modest. Survival was addressed in only 3 studies (359 patients) of which none were powered to identify differences in survival between laparotomy and laparoscopy. However, no differences in overall survival, disease free survival and cancerrelated survival could be demonstrated. Conclusion. Laparoscopic surgery for endometrial, ovarian, and cervical cancer seems widely used. However, laparoscopy in ovarian and cervical cancer is not based on evidence from RCTs and no information concerning survival is available. Endometrial cancer patients seem to benefit from a laparoscopic approach with fewer complications and a lower intraoperative blood loss. However, survival is not sufficiently investigated. Additional information is needed before laparoscopy in endometrial cancer should be considered a standard procedure.

PS09.1 Assisted reproduction is a stronger predictor of placenta previa than a previous cesarean section - A Danish national cohort study

Lone Nikoline Nørgaard (1), A Pinborg (2), Ø Lidegaard (3), T Bergholt (4)

- (1)Department of Obstetrics and Gynaecology; Copenhagen University Hospital, Hillerød, Denmark
- (2) Fertility Clinic, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
- (3) Gynaecological Clinic, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
- (4)Department of Obstetrics and Gynaecology; Copenhagen University Hospital, Hillerød, Denmark

Objective To assess the proportion of assisted reproduction technology (IVF/ICSI) conceptions in deliveries with placenta previa (PP) and to evaluate risk factors associated to PP. Method National cohort study based on the Danish National IVF- and Patient Register. All singleton deliveries with PP in Denmark from 2001 to 2006 were included. Each case was matched (using date and year of delivery) with five controls without PP. Logistic regression analysis was performed to explore predictors of PP including assisted reproduction, previous cesarean section, smoking, parity, maternal age and gender of the child. Results 10324 singleton deliveries were identified; 1721 cases with PP and 8603 controls. 129 (7.5%) of cases versus 188 (2.2%) of controls were conceived by assisted reproduction (OR 3.6 95%CI 2.9-4.6). Logistic regression analysis showed assisted reproduction to be the strongest independent predictor of PP (OR 3.1 95%CI 2.4-4.0) while other significant factors were previous cesarean section (OR 1.4 95%CI 1.2-1.7), smoking (OR 1.2 95%CI 1.1-1.4), male offspring (OR 1.1 95%CI 1.00-1.3) and maternal age (OR 1.08 95%CI 1.06-1.09 per year). Conclusion Pregnancies conceived by assisted reproduction have a significantly higher risk of PP compared to pregnancies conceived spontaneously and assisted reproduction seems to be a stronger predictor of PP than a previous cesarean section. Since an increasing number of pregnancies are achieved by assisted reproduction and PP is a significant risk factor of severe complications to the mother and child, more studies are needed to assess, if this is caused by elements of the reproductive technology itself.

PS09.2 Strong association between maternal HPA 1a alloimmunization and reduced birth weight

Heidi Tiller (1), MK Killie (1), A Husebekk (1,2), B Skogen (1,2), H Ni (3,4) J Kjeldsen-Kragh (5,6), P Øian (7,8)

- (1)Immunology and Transfusion Medicine, University Hospital of North Norway, Tromsø, Norway
- (2)Division of Immunology, Institute of Medical Biology, University of Tromsø, Tromsø, Norway
- (3)Division of Transfusion Medicine, St. Michael's Hospital, Toronto, Canada
- (4)Canadian Blood Services and Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada
- (5)Immunology and Transfusion Medicine, Oslo University Hospital, Ullevål, Oslo, Norway
- (6) Faculty Division Ullevål University Hospital, University of Oslo, Oslo, Norway
- (7)Department of Obstetrics and Gynaecology, University Hospital of North Norway, Tromsø, Norway
- (8) Department of Obstetrics and Gynaecology, Institute of Clinical Medicine, University of Tromsø Tromsø, Norway

Objectives HPA1 alloimmunization is the major cause of fetal and neonatal alloimmune thrombocytopenia (FNAIT). The α IIb β 3 integrin complex is a platelet specific receptor with the HPA1 antigen epitope located on the β 3 subunit. β 3 subunit is also found on vascular endothelial cells and invasive trophoblasts as part of the α V β 3 integrin complex. It is therefore conceivable that anti-HPA1a antibodies could have a direct effect on the placenta. The aim of this project was to study whether maternal anti-HPA1a antibodies during pregnancy affects birth weight.

Methods We studied birth outcome from 165 HPA1a negative pregnancies in Norway. The effect of anti-HPA1a antibody level on birth weight was evaluated using a linear mixed model. Anti-HPA1a antibody level, maternal age, parity, pre-eclampsia, diabetes mellitus, smoking habits during pregnancy (obtained for 60% of population) gestational age at time of delivery and fetal gender were included as independent variables. Results The level of anti-HPA1a antibodies was significantly and inversely associated with birth weight after correcting for confounding variables (p<0.001). The mean birth weight when the mother had a high level of anti-HPA1a antibodies (>36 IU/ml) during pregnancy was 363 grams lower compared with an anti-HPA1a antibody negative pregnancy when using estimated marginal means.

Conclusions A linear relationship between maternal anti-HPA1a antibody levels and reduced birth weight was demonstrated for the first time. Reduced placenta function should be considered a possible complication of fetal and neonatal alloimmune thrombocytopenia.

PS09.3 Childhood abuse, fear of delivery and c-section as preferred mode of delivery

Berit Schei (1,2), M Lukasse (1-3)

- (1)Department of Public Health, NTNU, Norway
- (2)St.Olavs hospital, Norway
- (3)University of Tromsø, Norway

Maternal request for cesarean section (CS) is a controversial issue. Aim of this study was to assess the relative impact of childhood abuse on fear of delivery and reported CS as preferred mode of delivery taking into account the experience of previous delivery. Material and Method Data were drawn from the Norwegian Mother and Child Cohort Study (1) and linked to the Medical Birth Registry of Norway. Potential risk factors for fear of delivery and reporting CS as preferred mode of delivery were assessed in a longitudinal design, following 4889 women with information from two pregnancies and deliveries. Information on child abuse, and mode of and subjective experience of first delivery were examined in relation to fear of delivery and CS as preferred mode of delivery in the subsequent pregnancy. Results Of the 4889 women, 21 % reported any childhood abuse. For women reporting any childhood abuse the crude OR for fear of delivery in subsequent pregnancy was 1.62 (95 % CI: 1.4 -2. 0). However, having experienced first delivery worse than expected was a stronger predictor; OR 4.8 (3.9 - 5.9). Adjusting for this factor the association was no longer statistical significant. The same pattern was shown also for reporting CS as preferred mode of delivery during subsequent delivery. Conclusion Childhood abuse is associated to fear of delivery and CS as preferred mode of delivery during pregnancy. However, to experience previous delivery as worse than expected was a stronger predictor.

PS09.4 CTG and ST analysis of the fetal electrocardiogram – reduction of metabolic acidosis rate during 5 years of regular use

<u>Jørg Kessler</u> (1), G Midbøe (1), F Macsali (1), S Albrechtsen (1) (1)Haukeland University Hospital Bergen, Norway

Objective: To assess the clinical performance of intrapartum monitoring with STAN. Hypotheses: Intrapartum surveillance with STAN should gradually reduce the frequency of operative deliveries and cord artery metabolic acidosis at birth. Methods: Retrospective study for the period 01.01.2004-31.12.2008, with data retrieved from maternal and neonatal medical records, and from The Medical Birth Registry of Norway. Inclusion criteria: Singleton pregnancies, gestational age \geq 36 weeks, STAN monitoring. Exclusion criteria: twin pregnancies. Results: During the study period 5997 (25%) of 23219 deliveries were selected to monitoring with STAN. Fetal blood sampling was performed in 145 (2.4%) deliveries. A total of 2206 (37%) had an operative delivery. The frequency of emergency caesarean section decreased from 19% in 2004 to

14% in 2008. When STAN clinical guidelines indicated hypoxia (1182 cases, 20%), the time to delivery was median 24 minutes for caesarean section and 14 minutes for operative vaginal deliveries. 490 newborns (8%) were transferred to the neonatal intensive care unit. Acid base data from the umbilical artery was available in 5123 (85%) cases. There was a total of 35 (0.6 %) cases of metabolic acidosis at birth, defined as pH<7.05 and base deficit >12 mmol/l. The frequency of metabolic acidosis decreased from 1% in 2004 to 0.3 % in 2008. There were 6 cases of perinatal death (diaphragmatic hernia, N=1; sepsis, N=2; shoulder dystocia, N=1; unknown, N=2). Conclusion: Intervention according to the time frame given in STAN clinical guidelines resulted in a decreasing frequency of metabolic acidosis at birth.

PS09.5 Association between adverse neonatal outcome and lactate concentration in amniotic fluid

<u>Eva Wiberg-Itzel</u> (1), H Åkerud (2), U-B Wennerholm (3), E Andolf (1), L Hellström-Westas (2), B Winbladh (1) (1)Karolinska Institute. Sweden

(2)Uppsala University, Sweden

(3)Institute of Clinical Sciences, Sweden

Objectives To estimate whether high concentration of lactate in amniotic fluid (AF) at delivery, together with other well-known risk factors during ongoing labor, has an association with adverse neonatal outcome. Method: A population-based cohort study where 825 women with low-risk, term ($_1$ Ý 37 weeks of gestation) singleton pregnancies in cephalic presentation were included. Composite adverse neonatal outcomes (umbilical cord artery pH<7.10, metabolic acidosis, Apgar score <7 at 5 minutes, meconium aspiration, resuscitation, hypoxic ischemic encephalopathy, and admission to neonatal intensive care unit), were evaluated in relation to lactate concentration in AF and labor outcome. Logistic regression was used to estimate obstetrical risk factors during labor, the last lactate value in AF before delivery and adverse neonatal outcome. RESULTS: An increased risk of adverse neonatal outcome was shown in deliveries with a pathological cardiotocography (CTG) recording (especially bradycardia) before delivery and a lactate value in AF >10.1 mmol/l. Adjusted for other risk factors during labor, the odds of having a poor fetal outcome was raised 4 times if the lactate value in AF was >10.1 mmol/l and 16 times if also fetal bradycardia was present. CONCLUSION: An association was shown between adverse neonatal outcome at delivery, abnormal CTG and a high concentration of lactate in AF. CTG recording together with lactate concentration in AF could be a useful risk assessment of neonatal outcome at delivery.

PS09.6 May ultrasound be used during labour?

Erik Andreas Torkildsen (1), KÅ Salvesen (2), TM Eggebø (1)

(1)Department of Obstetrics and Gynaecology, Stavanger University Hospital, Stavanger, Norway. (2)National Center for Fetal Medicine, St Olav University Hospital of Trondheim and Department of Laboratory Medicine, Women's and Child Health, Norwegian University of Science and Technology, Trondheim, Norway

INTRODUCTION: Progress of labour has traditionally been evaluated with digital examinations, a subjective method with high interobserver variability. Transperineal ultrasound can be an accurate and reproducible method in predicting operative delivery. However, there are limitations like shadowing behind the symphysis pubis. We propose a new ultrasound method; the fetal head-perineum distance. OBJECTIVES: To investigate transverse transperineal ultrasound as predictive factors for labour outcome, and to compare different ultrasound methods. MATERIAL AND METHODS: Prospective observational study with 110 primiparous women with single pregnancy and cephalic presentation at term. In prolonged first stage labour, the shortest distance from the outer bony limit of the fetal skull to the skin surface of the perineum is measured in a transverse view. This method will be compared with sagittal imaging methods in 2D and 3D. Vaginal delivery

is the primary outcome. RESULTS: Preliminary results from the first 21 examinations will be presented. The cesarean section rate among women with a long distance from fetal head to perineum (>40 mm) was 80% compared to 27% with a shorter distance. Sensitivity in predicting cesarean section was 0.73, specificity 0.80, positive predictive value 0.8 and negative predictive value 0.73. ROC-curve analyses discriminated between a vaginal delivery/cesarean section with 77% under the curve using the transverse scan and 73% using the sagittal scan. Digital examinations could not predict labour outcome. CONCLUSION: Ultrasound predicts labour outcome better than digital examinations. Sagittal and transverse methods seem to be equally good, but the latter tends to be easier to perform.

PS09.7 A prospective multi-centre randomised comparison on induction of labour with double-balloon installation device versus prostaglandin 2 minprostin

<u>Ellen Leth Løkkegaard</u> (1), M Lundstrøm (2), M Mandrup (3), H Pedersen, IJ Christensen, H Nyholm (4) (1)Hillerød Hospital; Glostrup Hospital, Denmark

(2)Hvidovre Hospital, Denmark

(3)Glostrup Hospital, Denmark

(4)Herlev Hospital, Denmark

Background The use of prostaglandin E2 for induction of labour in women with unfavourable cervices is well-established. There are, however, potential side effects, an alternative approach is mechanical ripening with balloon installation. Objective To compare the efficacy of double-balloon catheter versus vaginal PGE2 (minprostin 3 mg) on induction of labour, duration of birth and fetal outcome. Material The study was a multicenter randomised study conducted at 6 labour yards in Denmark including 825 pregnancies with intact fetal membranes, vertex position and unripe cervix (Bishop score < 6) with usual indications for induction of labour, i.e. prolonged pregnancy, pre-eclampsia/hypertension, placental insufficiency, diabetes mellitus and twins. By 'telephonic automatic voice response system randomisation' participant were randomised to either the double Balloon Catheter (Atad) with 80 ml NaCl installed in the evening or 3 mg Minprostin (prostaglandin 2) in the morning. Results In total 412 were randomised to the balloon group of whom 264 actually had the ballon installed, and 413 were allocated to the minprostin group of which 305 received the prostaglandin. There were equal gestation length, bishop score and indications in the two groups. The rate having successful induction of labour among women actually receiving the treatment were equal, 89%. There was a more section caesarean in the ballon group 30% versus 25% in the minprostin group (p=0.05). There were significant more births at night in the minprostin group and more referrals to neonatal care. Conclusion It appears to be different mechanisms for induction of labour by prostaglandins and mechanical ripening.

PS09.8 Severe bleeding in cesarean section – a registry-based study – Norway 1999-2008 Finn Eqil Skjeldestad (1), P Øian (1)

(1)Department of Obstetrics and Gynecology, Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway

Background: The indications and the many medial conditions differ that much in elective and acute CS that separate analyses are necessary for understanding the risks of severe blood loss. Objectives: to examine prevalence and risk factors for severe blood loss over a 10-year time-period in elective and acute CS. Methods: The Medical Birth Registry, Norway (data source) defines severe blood loss > 1500 ml within 24 hours post partum, or the need for blood transfusion. Eligible for analysis were 80 657 births who had singleton or twin pregnancy and valid data for elective (n=32 716) or acute (n=47 941) CS over the study period. Severe blood loss was analyzed in logistic regression (SPSS) with blood loss < 500 ml as reference. Results: The prevalence of severe bleeding was 1.9% and 3.2% among mothers having elective and

acute CS (p<0.001). Shared risk factors were twin pregnancy, transverse lie, placenta previa, and general anesthesia/epidural versus spinal. Hellp syndrome and high birth weight (> 4500 g) were found for elective CS, whereas conception after assisted reproductive methods, hemoglobulin < 9.0 g/l at end of pregnancy, induction followed by arrest during 2nd phase of delivery (interaction), and abruptio placenta predicted severe blood loss during acute CS. Failed forceps or failed vacuum extraction were not a risk factor for severe bleeding during acute CS. Conclusions: Common maternal and pregnancy related conditions are risk factors for severe bleeding in both elective and acute CS, whereas more delivery related conditions add risks in acute CS.

PS09.9 The relation between caesarean section rate and neonatal outcome in breech presentation at term

Julie Elisabeth Hartnack Tharin (1), S Rasmussen (2), L Krebs (3,4)

- (1) Gynacology and obstetrics, Holbæk Hospital, Holbæk, Denmark
- (2) National Board of Health, Copenhagen, Denmark
- (3) Gynacology and obstetrics, Holbæk Hospital, Holbæk, Denmark
- (4)University of Copenhagen, Copenhagen, Denmark

In October 2000 a randomized controlled study confirmed that planned vaginal delivery of breech at term was associated with increased perinatal mortality and morbidity. Publication of the results was followed by increased rate of caesarean section in many countries. The aim of the present study was to analyze the consequences in the Danish population. Method: The study was based on information from The Danish National Birth Registry (1997-2008) on all singleton infants, in breech presentation at term, alive at onset of labor (n=23,789). Results: The rate of caesarean section increased from 80% to 95% and remained stable thereafter. The incidence of low Apgar score (below 7 at five minutes) declined from 1.0% to 0.6% (Relative Risk (RR)=0.83; 95% confidence limits (CL): 0.73; 0.95) and admission to NICU (more than 3 days) from 4.2% to 3.2% (RR=0.92 CL: [0.87; 0.97]). There was an insignificant reduction in perinatal mortality (intrapartum or early neonatal) from 0.51% to 0.38%. Planned vaginal delivery was associated with an increased risk of low Apgar score (RR= 2.09 CL:[1.88;2.33]) and admission to NICU (RR=1.86 CL[1.7;2.04]) compared to elective caesarean section, throughout the period. RR was not related to lower incidence of vaginal delivery. Conclusions: Reduction of the rate of vaginal delivery from 20% to 5% was correlated to a lower rate of perinatal morbidity. Risk of complications in planned vaginal delivery was unchanged. Thus, even in a strictly selected population, planned vaginal delivery of term breech was associated with increased risk of perinatal morbidity.

PS10 Parallel session 10 - Reproductive update: Developing trends in fertility treatment 1330 - 1500

PS10.1 Sperm Banking in the 21st Century

Peter Bower (1)

(1)European Sperm Bank ApS, Denmark

Abstract: Sperm banking has advanced and matured over the past Century. Sperm donors are today tested and screened for many diseases. Sperm is quarantined and the follow-up on successful or unsuccessful use of a donor's sperm are important factors in operating a sperm bank. Legislative requirements, namely the EU Tissue Directive and individual country requirements, give rise to quite complicated market segmentation. Furthermore, patients are becoming autonomous in choosing a sperm donor. This gives the patient an excellent opportunity to participate. Single women seeking donor insemination is a growing group utilizing these possibilities.

PS10.2 Does smoking, alcohol, coffee consumption and obesity affect fecundity and fertility? Ulrik Schiøler Kesmodel (1)

(1) Aarhus University Hospital, Skejby, Denmark

It has consistently been shown that female cigarette smoking reduces fecundity in the natural cycle. Male smoking status is not consistently associated with fecundity. It is unclear whether smoking increases the risk of early spontaneous abortion. While smoking does not seem to affect fertilization rates in assisted reproduction, it consistently reduces both clinical pregnancy rates and live birth rates. Despite strong evidence from experimental studies that alcohol reduces fecundity and fertility, there is no consistent evidence in humans. Most population based studies show reduced fecundity at daily intake levels but generally not at lower weekly intake levels for women; and most pregnancy based samples show either no detrimental effects or even a slightly beneficial effect of a low weekly alcohol intake, mainly of wine. Male alcohol intake is not consistently associated with fecundity. A daily intake of alcohol may also increase the risk of early spontaneous abortion. There is a surprising lack of studies in humans on the effects of female and male alcohol intake in ART. Intake of ?500 mg of caffeine/day (?4-5 cups of coffee) has been associated with reduced fecundity and increased risk of early spontaneous abortion. Male coffee consumption has not been consistently associated with reduced fecundity. Again, there is a lack of studies in humans on the effects of female and male caffeine consumption on results of ART. Obesity is inconsistently associated with ART outcomes. Possibly, obesity is mainly a problem in young women, women with insulin resistance and other subgroups.

PS10.3 Management of lifestyle habits and infertility management

Robert Norman (1)

(1)The Robinson Institute, The University of Adelaide, Australia

As IVF practices become more regulated and successful, the control of extraneous factors in outcomes of infertility become even more important. We now accept, that while we can control everything within the environment of a reproductive medicine unit using quality management and protocols, we are unable to effectively control many of the variables of patients including their genetic and lifestyle habits. The concept of preconception care is one that is gaining increasing ground and needs to be seriously looked at by practitioners of infertility treatment. There is abundant evidence that disorders of weight, smoking, excessive drug use and alternative therapies may adversely impact on outcomes of infertility treatment. It is proposed that all clinics should have a pre-conception clinic in which adequate history and examination occurs and patients are given advice about some of the complicating factors that may delay their becoming pregnant. This can be managed by a doctor or by a clinic nurse who has been appropriately trained in motivational interviewing. A reproductive life plan should be set up and reproductive pathways established for identified disorders such as obesity, smoking, addictive drug use etc. Several studies in assisted reproductive technology suggest that an approach such as this is not only valuable but also increases pregnancy rates substantially. All doctors and their clinics should become experts in identifying and managing lifestyle habits which are adverse to pregnancy outcomes.

1330 - 1500

PS11.1 Incidence, risk factors, and severity of anal incontinence after obstetric anal sphincter rupture

<u>Katariina Laine</u> (1,2), FE Skjeldestad (3), B Sanda (1), H Horne (1), A Spydslaug (1), AC Staff (1,2) (1)Oslo University Hospital, Ulleval, Norway

(2)University of Oslo, Norway

(3)University of Tromsø, Norway

OBJCECTIVES: To study incidence, risk factors and severity of anal incontinence (AI) after obstetric anal sphincter rupture (OASR). STUDY DESIGN: Study of all OASRs diagnosed during vaginal deliveries in 2003-05 at one Norwegian university hospital. Patients were examined 6-12 months after delivery. Severity of AI was assessed with St. Mark's incontinence score. Endoanal ultrasound was performed to document defects in anal sphincter muscles. Analyses were done in SPSS with logistic regression, RESULTS: Among 14 959 vaginal deliveries, 591 OASR (3.9%) were diagnosed, 3/4 during spontaneous and 1/4 during instrumental deliveries. 455 of 591 (77%), notably more 4th than 3rd degree OASR patients, met for scheduled follow-up (mean 10 months postpartum). All was reported in 38% of the patients, more often in 4th than 3rd degree OASR, with inability to control gas as the most prevalent symptom. Ultrasound detectable defects in the anal sphincter muscles were found in 33%. Al was more frequent in patients with than without ultrasound identified defects. Among maternal and obstetric risk factors, fourth degree sphincter tear was the only significant risk factor for severe AI (logistic regression). CONCLUSIONS: Severe perineal tear is associated with increased risk of anal incontinence and persisting defect in anal sphincter muscles one year after delivery additionally increases the risk. Antenatal maternal and obstetrical variables could not predict risk of anal incontinence. Al has a negative impact on quality of life. Intensified prophylactic efforts are essential to avoid OASR and may lead to improved maternal post partum health.

PS11.2 Early faecal incontinence after fist delivery and its relation to ultrasound defects Abelone Sakse (1), NJ Secher (1), M Starck (2)

(1)Hvidovre Hospital, Denmark

(2)Pelvic Floor Center, Department of Surgery, Malmö Universitets sygehus, Malmö, Sweden

Objective: To find the prevalence of early faecal incontinence in primiparous and relate this to ultrasound defects. Methods: 157 primiparous women had an endo-anal ultrasound examination in relation to delivery. We used a 3D B-K Medical pro focus machine with a 2050 transducer, to identify defects in the external or internal anal sphincter after delivery. The defects detected were both clinically undetected and defects identified after primary suture of anal sphincter rupture. The defects were identified as +/- defect. A validated questionnaire on symptoms following anal sphincter rupture was send to the women 3 months pp. In the case of AI, this was registred as: flatus, liquid stool or solid stool incontinence. Results: 94% (147/157) response rate. 64% (100/157) had no AI pp, in this group 18% (18/100) had ultrasound defects. 29% (45/157) had flatus incontinence, in this group 16% (7/45) had ultrasound defects. 6% (10/157) had liquid stool incontinence in this group 30% (3/10) had ultrasound defects and 1% (2/157) had solid stool incontinence, 50% (1/2) had ultrasound defects. In 98% of the women suffering from flatus incontinence the symptoms ceased (1-12 weeks pp), in 80% of the women suffering from liquid stool incontinence the symptoms ceased 4 weeks pp. Conclusion: 8% had liquid or solid stool incontinence. 30% of the liquid stool incontinence had defects detected on ultrasound.

PS11.3 Enterogenital fistulas: a 15 years material from Norway

<u>Jone Trovik</u> (1,2), K Torvid (1,2) (1)Haukeland University Hospital, Norway (2)University of Bergen, Norway

Background: Fistulas involving the intestines lead to severe bother due to fecal incontinence. Our department has focused on this condition. We herby report our experience. Material and methods: 118 women have been investigated for enterogenital fistulas at Dpt. of Obstetrics and Gynaecology, Haukeland University Hospital during 1995-2009. Results have been prospectively registered to evaluate outcome. Results: In 100 women (85%) fistula was verified; rectovaginal 66/100, rectoperineal 16/100, isolated vaginoperineal 9/100 other 9/100. Aetiology: Obstetric injury was most common: 31, thereafter inflammatory bowel disease (IBD) 22, surgery 17 and infection 11. 26 women had been treated for cancer, thereof 13 with radiation. Treatment: 5 fistulas had healed before consultation. 7 women did not want any specific fistula treatment. Transvaginal fistula repair were performed in 57/88, while 7 high fistulas were treated by Japarotomy. Diverting enterostomy (+/-surgery/medication) was performed for 57 women, 8 received only medical treatment. Outcome: Of the 88 women offered treatment 78 have been evaluated (3 lost follow-up, 7 ongoing treatment). In 59/78 (76%) the fistula has closed, in 19 (24%) persisting, 47/53 (89%) of evaluated vaginal repairs have successfully healed, only 3/6 (50%) closed with medical treatment alone, 4/14 (27%) by enterostomy alone. All 30 obstetrical fistulas healed, 13/15 (87%) of surgical fistulas, 6/9 (67%) with infectious aetiology, but only 11/19 (58%) of inflammatory and 2/13 (15%) of radiation fistulas. Conclusion: Vaginal fistuloplasty, +/-enterostomy, can successfully heal obstetrical and surgical enterogenital fistulas. IBDfistulas are more difficult to treat in spite of multidisciplinary approach. Radiation-fistulas have least success.

PS11.4 Endometriosis in Denmark 1980-2007. A national register survey

<u>Øjvind Lidegaard</u> (1), MVH Hansen (1) (1)Rigshospitalet, Denmark

Background. Endometriosis affects an increasing number of women in their reproductive years – a circumstance that justifies a descriptive analysis of the incidence and trends in incidence through recent decades. Objective. To quantify the incidence of endometriosis in Danish women in different age groups through the period 1980 to 2007 and the number hospital contacts among these women. Design. Consecutive historical cross section analyses. Materials and method. Discharge diagnoses from all Danish public and private hospitals were retrieved from the National Registry of Patients for the period 1980-2007. Results. Through the period 1980-2007 we observed an overall increase in number of new patients with endometriosis of 74% ranging from 21% to 135% in different age groups. The number of patient contacts increased on average 3.7 times, with a range of two to 10 fold in different age groups. The number of contacts per woman with endometriosis increased in women 30-34 years 7.3 fold and in women 45-49 years 2.9 fold. The peak incidence according to age decreased from 40-44 years in 1985-89 to 30-34 years during the period 2005-2007. Conclusion. Annual number of new women with endometriosis, number of endometriosis contacts per year and cumulated number of contacts per patient all increased substantially through the 28-year long study period. Some of this increase is probably due to changes in registration practice, but the main part is likely to be explained by an increased awareness, a lower threshold of admission to hospital, and better treatment options.

PS11.5 Complications after surgery on endometriosis. - a comparative study

Torbjørg Standal Skåravik (1), S Skrede (1), MH Moen (1)

(1)Norwegian University of Science and Technology, Department of Laboratory Medicine, Children's and Women's Health, Trondheim, Norway

Objective: To study the rate of complications in surgery for endometriosis compared to similar surgical intervention on other benign indication. Design: Retrospective case review. Setting: University hospital, Trondheim, Norway. Population or Sample: 200 endometriosis patient and 400 control cases operated at St. Olavs Hospital in Trondheim between 2000 and 2008. Methods: Women identified with the ICD-10 diagnosis endometriosis were found in database at the Gynecological department and matched with similar operative procedures. Demographic data, data concerning surgery and surgical complications were registered. Main Outcome Measures: Rate of per- and postoperative complications. Results: Repeated surgery, adhesiolysis, a longer operation time and bleeding were significantly more common in endometriosis surgery. However, there was no significant difference in rate of severe and total complications between the endometriosis and the control group (8.0 % versus 6.3 % and 28.0 % versus 25.8 %). Conclusions: The study indicates that there is no greater risk of complications in operations performed for endometriosis than for similar operations for other benign diseases.

PS11.6 Dargent's operation: the radical vaginal trachelectomy. Danish experience

<u>Danny Svane</u> (1), H Rung-Hansen (1), J Seidelin (1), C Ottosen (1) (1)Department of Gynecology, Rigshospitalet, Copenhagen, Denmark

OBJECTIVE: To present the first eight years experience from a national center for radical vaginal trachelectomy.

METHODS: Retrospective review of our first 85 patients treated by laparoscopic pelvic lymphadenectomy followed by a vaginal radical trachelectomy from January 2002 to March 2010. Data were collected from the national Danish cancer database "DGCD"

RESULTS: No recurrences were observed in 85 women with early-stage cervical cancer operated with the intent of fertility preservation with radical vaginal trachelectomy. Median follow-up time 84 months. Median age was 29 years (range, 21-41 years), and the median BMI was 25 kg/m2 (range, 21-42 kg/m2). Four patients (5%) underwent hysterectomy due to extensive endocervical disease. The median OR time was 194 min (range, 140-270 min). Median pelvic lymph node count was 24 (range, 14-34). Median hospital stay was 3 days (range, 1-6 days). FIGO stage for the group ranged 1A1 (with lymph vascular space involvement) to IIA.

One patient received neoadjuvant chemotherapy followed by vaginal trachelectomy. One patient required a second intervention for a perioperative complication. 3 patients (4%) underwent adjuvant chemoradiation because of advanced pathological findings on final pathology.

19 patients delivered by cesarean section after 35 weeks of pregnancy (26 - 39 weeks) and 3 patients are currently pregnant.

CONCLUSIONS: Radical vaginal trachelectomy preserved overall fertility in early cervical cancer and appears to be a safe alternative to radical hysterectomy in our experience. We recommend continued referral of patients with early stage cervical cancer, and desired preserved fertility, to a national center for radical vaginal trachelectomy.

KEYWORDS: Cervical cancer and trachelectomy

PS11.7 Growth-differentiation factor-15: a novel biomarker in ovarian cancer

Anne Cathrine Staff (1,2), A J Bock (1,3), C Becker (1), T Kempf (4), K C Wollert (4), B Davidson (2,3)

- (1)Oslo University Hospital, Dept of Gyn and Obst, Ulleval, Norway
- (2)University of Olso, Faculty of Medicine, Norway
- (3)Oslo University Hospital, Dept of Pathology, Radiumhospitalet, Norway
- (4) Hannover Medical School, Dept of Cardiology and Angiology, Germany

OBJECTIVES: Growth-differentiation factor-15 (GDF-15) is a member of the transforming growth factor (TGF)-â superfamily, also named macrophage-inhibitory cytokine-1 (MIC-1), originally identified in macrophage activation. GDF-15 regulates a wide variety of physiologic processes involved in tissue differentiation and maintenance. GDF-15 over-expression has been found in prostate, thyroid, pancreatic, and colonic cancers as well as in malignant melanomas. The aim of the study was to investigate whether plasma concentration of GDF-15 is elevated in patients with ovarian carcinoma, and to explore ovarian tumor protein expression of GDF-15. METHODS: GDF-15 concentration in EDTA plasma samples of women with invasive ovarian cancer (n=125), borderline ovarian tumor (BOT, n=43) or benign ovarian tumor (n=144), as well as from healthy premenopausal (n=20) and postmenopausal (n=20) women were analyzed with immunoradiometric assav. as were effusion samples (n=44) from advanced ovarian carcinoma. Tumor sections from women with ovarian carcinoma (n=20), BOT (n=9) or serous cystadenomas (n=7) were immunostained for GDF-15 expression. RESULTS: Median plasma GDF-15 concentration was elevated in ovarian cancer (1242 ng/L) as compared to pre- and postmenopausal controls (591 and 684 ng/L, both P<0.001) or women with benign ovarian tumors or BOT. Preoperative GDF-15 plasma concentration in ovarian cancer correlated with survival time and was an independent predictor of survival, after correction for FIGO stage and age. GDF-15 protein was expressed in the cytoplasm of serous tumor cells. Effusion GDF-15 concentrations correlated with plasma concentrations (with a mean ratio of 3:1). CONCLUSIONS: GDF-15 emerges as a potential biomarker for survival and follow-up in ovarian cancer.

PS11.8 Ovarian cancer risk and postmenopausal estradiol-progestin therapy use

<u>Virpi Koskela-Niska</u> (1), H Lyytinen (1), A Riska (1), E Pukkal (2), O Ylikorkala (1) (1)Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Helsinki, Finland (2)Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland

Purpose of the study: We compared associations between various estradiol-progestin therapy (EPT) formulations, modes and routes of administration of EPT and the ovarian cancer risk in postmenopausal women. Methods: All Finnish women over 50 years using EPT for at least 6 months during 1994-2006 were identified from the reimbursement register. The incidence of ovarian cancer in EPT users was compared to that in the comparable background population by means of observed to expected ratio (standardized incidence ratio, SIR). Results: The ever-use of EPT was associated with a 10% increase in ovarian cancer risk. The excess elevated to 21% for EPT use of 5 years or longer, but the prolongation of the use for 10 years or longer was not accompanied with a rise in further risk. Medroxyprogesterone acetate and norethisterone acetate as parts of EPT were associated with similar risk elevations (SIR 1.26; 95% confidence interval 0.94-1.64 and 1.42; 1.11-1.77, respectively). The risk did not differ between modes (sequential or continuous) or routes (oral or transdermal) of administration. The use of EPT for 5 years or longer led to an increase in serous cancer (SIR 1.56; 1.33-1.80) and mixed cancer (SIR 1.54; 1.22-1.91). The risk for mucinous cancer was decreased (SIR 0.47; 0.22-0.86). Conclusion: The use of estradiol-progestin therapy for 5 years or longer is accompanied with a modest rise in risk of non-mucinous ovarian cancer which does not depend on the type of progestin, mode or route of EPT administration.

PS11.9 Endometrial cancer and postmenopausal hormone therapy: a case-control study on the risk associated with various forms of therapy

<u>Susanna Jaakkola</u> (1), H Lyytinen (1), O Ylikorkala (1), E Pukkala (2) (1)Helsinki University Central Hospital, Finland (2)Finnish Cancer Registry, Finland

OBJECTIVE: To evaluate the risks of different modes of HT regimens on endometrial cancer in postmenopausal Finnish women. METHODS: Women with endometrial cancer diagnosed during 1995-2007 at the age of 50 to 80 years were identified from the Finnish Cancer Registry (N=7261). For each case, three age-matched controls were retrieved from Finnish Population Register. The uses of HT by the cases and controls since 1994 were traced from the national Medical Reimbursement Register. The odd ratios (ORs) and 95% confidence intervals (CIs) for different HT regimens were calculated with conditional logistic regression analysis, adjusted for parity, age at first birth, and health care district. RESULTS: The OR for use of sequential estradiol-progestin therapy (EPT) for < 5 years was 0.67 (95% CI 0.52-0.86), for continuous EPT 0.45 (0.27-0.73), and for continuous estradiol plus levonorgestrel releasing intrauterine device system (LNG-IUS) 0.39 (0.17-0.88). This protection persisted for the use of continuous EPT and estradiol plus LNG-IUS up to 10 years. The use of long-cycle EPT showed tendency of elevated risk (1.40; 0.82-2.38) when exposure was < 5 years; the risk for estimated use of >5 years was significantly elevated (1.63; 1.12-2.38). For those still using HT at the ages 62+ years (estimated exposure >10 years), the risk for endometrial cancer was elevated for both users of long-cycle EPT (2.95; 2.40-3.62) and sequential EPT (1.38; 1.15-1.66). For tibolone users endometrial cancer risk was close to 1.0 irrespective to duration of use, CONCLUSION: Use of LNG-IUS or continuous EPT may protect from endometrial cancer.

PS12 Parallel session 12 - Free communications Obstetrics - pregnancy 1330 - 1500

PS12.1 Early fetal growth and first-trimester serum markers of chromosomal abnormalities in relation to low birth weight

Ida Kirkegaard (1,2), TB Henriksen (2), N Uldbjerg (1,3)

(1)Dept. Obstetrics and Gynecology, Aarhus University Hospital, Skejby, Denmark
(2)Perinatal Epidemiology Research Unit, Aarhus University Hospital, Skejby, Denmark
(3)Division of Maternal-Fetal Medicine, Wayne State University, Hutzel Women's Hospital, Detroit, MI, United States of America

Objective: To examine the combination of measures of early fetal growth and first-trimester serum markers of chromosomal abnormalities in relation to the risk of delivering a small-for-gestational age (SGA) infant. Material and methods: 9450 singleton pregnant women, who attended the prenatal screening program at Aarhus University Hospital, were included. Pregnancy-associated plasma protein-A (PAPP-A) and free beta-human chorionic gonadotropin (beta-hCG) was measured in the first trimester. Early fetal growth rate was expressed as (GA20 – GA12)/Calendardays, where GA12 reflects the gestational age in days calculated from CRL at 12 weeks scan, GA20 reflects the gestational age in days calculated from BPD at 20 weeks scan and Calendardays is the number of days between the two scans. The risk of SGA, defined as birth weight below the 5th centile for gestational age, was evaluated according to various cut-offs and combinations of early fetal growth rate and the serum markers. Results: Pregnancies with the combination of PAPP-A below 0.4 MoM and early fetal growth rate below the 10th centile had an OR of 5.8 (95% CI, 2.7 – 12.7) for SGA. Furthermore, PAPP-A and free beta-hCG below 0.3, 0.4 and 0.5 MoM, and early fetal growth rate below the 2.5th centile were statistically independently associated with SGA (OR's from 3.0 to 1.8). Conclusion: The combination of slow early fetal growth and low PAPP-A resulted in an almost 6-fold increased risk of delivery of an SGA infant. The findings might improve the possibilities of early identification of fetuses at increased risk of being SGA.

PS12.2 Selective serotonin reuptake inhibitors first trimester and congenital malformations

Lars H Pedersen (1,2), TB Henriksen (3,4), M Vestergaard (5), J Olsen (1,6), BH Bech (1)

- (1)Dept. Epidemiology, School of Public Health, Aarhus University, Aarhus, Denmark
- (2)Dept. Obstetrics & Gynecology, Aarhus University Hospital, Aarhus, Denmark
- (3)Perinatal Epidemiolgy Research Unit, Aarhus University Hospital, Aarhus, Denmark
- (4) Dept. Pediatrics, Aarhus University Hospital, Aarhus, Denmark
- (5)Dept. General Practice, School of Public Health, Aarhus University, Aarhus, Denmark
- (6)UCLA School of Public Health, Dept. Epidemiology, Los Angeles, United States of America

Background: The teratogenicity of selective serotonin reuptake inhibitors (SSRI) is unsettled despite increasing use during pregnancy. Objective: To asses the association between SSRI and major malformations. Design, setting, and participants: Population-based cohort study of 493,113 children born in Denmark between 1996 and 2003. We obtained information on mothers and newborns from nationwide registers on medical redemptions, delivery and hospital diagnosis. Follow-up data was available through December 2005. Major malformations were categorized according to Eurocat with additional diagnostic grouping of heart defects. Results: Redemptions of SSRI were not associated with major malformations overall but were associated with septal heart defects (odds ratio (OR) 1.99 (95% confidence interval (CI): 1.13-3.53)). For individual SSRI, the OR for septal hearth defects was 3.25 (95% CI: 1.21-8.75) for sertraline, 2.52 (95% CI: 1.04-6.10) for citalopram, and 1.34 (95% CI: 0.33-5.41) for fluoxetine. Redemptions of more than one type of SSRI were associated with septal hearth defects (OR 4.70 (95% CI: 1.74-12.7)). The absolute risks were low for all associations. Conclusion: The study suggests an increased risk of septal heart defects among children exposed to sertraline, citalopram or more than one type of SSRI in first trimester.

PS12.3 Fetal echocardiography in Iceland 2003-2007; indications and outcomes

<u>Sigurveig Þórisdóttir</u> (1), H Harðardóttir (1,2), H Hjartadóttir (2), G Óskarsson (1,3), H Helgason (3) G Sigfússon (1,3)

- (1)University of Iceland, Faculty of medicine, Reykjavik, Iceland
- (2)Department of Obstetrics and Gynecology, Landspitali, University Hospital, Reykjavik, Icelandy
- (3) Department of Paediatrics, Landspitali, University Hospital, Reykjavik, Iceland

Objective: The aim of the study was to evaluate the indications and outcomes of fetal echocardiography (FE) and determine which indication has the highest detection rate for congenital heart disease (CHD). Methods: The referral indications and results of FE performed in Iceland during 2003-2007 were reviewed. Information regarding gestational age at diagnosis, nuchal translucency, pregnancy outcome, autopsy results and postnatal diagnosis were obtained from medical records. Results: During the five year period 1187 FE were performed. Structural heart defect was diagnosed in 73 fetuses. The most common referral indication was family history of CHD (631/1187;53.2%) which led to diagnosis of 18 heart defects prenatally (18/631;2.9%). The second most common referral indication was increased nuchal translucency (159/1187;13,4%) and abnormal cardiac findings were present in 16 cases(16/159;10.1%). A total of 30 women were referred for FE because of abnormal four chamber view (AFCV) which resulted in the diagnosis of 22 (22/30;73.3%) major heart defects, either incompatible with life or requiring immediate intervention after birth. Other indications led mostly to the diagnoses of minor defects. Conclusions: AFCV is the most important predictor for diagnosis of structural heart defects. 2,5% were referred for FE due to AFCV which led to diagnosis of 30% of all heart defects, all of which were major.

PS12.4 The clinical impact of fetal magnetic resonance imaging on management of CNS anomalies in the second trimester of pregnancy

<u>Hashem Amini</u> (1), O Axelsson (1), M Raiend (1), J Wikstrom (1) (1)Uppsala University, Sweden

Objectives: To evaluate the additional information of second trimester magnetic resonance imaging (MRI) compared to ultrasound in fetuses with identified or suspected CNS anomalies and to study the clinical impact of the MRI information on pregnancy management. Methods: Thirty-one pregnant women were prospectively included during 2004-2009. The fetal MRI examination was planned to be performed within three days after the ultrasound. The last ultrasound was compared to fetal MRI in relation to the final diagnosis, fetal autopsy if performed or postnatal diagnosis. Results: The mean gestational age at the last ultrasound before fetal MRI was 18+1 weeks (range 15+4–20+2). The mean interval between ultrasound and fetal MRI was 1.6 days (range 0 –7). In 18 fetuses (58 %) fetal MRI verified the ultrasound diagnosis but provided no additional information, while in 9 (29 %) fetal MRI gave additional information without changing the management. In 4 (13 %), fetal MRI provided additional information that changed the management of the pregnancy. Three of these women were obese/morbidly obese, and in one of these cases oligohydramnios was present. Conclusions: Fetal MRI provided additional diagnostic information compared to the ultrasound examination in 42% of the cases, and resulted in altered management in 13 % of the cases. Fetal MRI in the second trimester might be a clinically valuable adjunct to ultrasound for the evaluation of CNS anomalies, especially when ultrasound is inconclusive due to maternal obesity or oligohydramnios.

PS12.5 Complications during pregnancy and labour for women with epilepsy. A population based cohort study

<u>Ingrid Borthen</u> (1), MG Eide (2), AK Daltveit (3), NE Gilhus (1) (1)Dept of Clinical Medicine, Section for Neurology, University of Bergen, Bergen, Norway (2)Dept. of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway (3)Dept of Public Health and Primary Health Care, Section for epidemiology and Medical Statistics, University of Bergen, Norway

The purpose of this study was to investigate whether women with epilepsy have an increased risk of complications in pregnancy and delivery and to explore the impact of antiepileptic drug (AED) use. Material and methods: Population based cohort study with data from Medical Birth Registry of Norway 1999-2005 including all births delivered in Norway. All singleton births and the first child in multiple pregnancies were included, leaving 365 107 pregnancies for analyses. Main outcome was preeclampsia, gestational hypertension, bleeding in pregnancy, induction, caesarean section (CS) and postpartum haemorrhage. Crude and adjusted odds ratios (OR) with 95% confidence limits (CI) were calculated by multiple logistic regression in SPSS 15.0 for Windows. Results: We compared 2,805 pregnancies with a history of epilepsy with those who did not, n=362 302. Women with epilepsy had an increased risk of mild preeclampsia [OR 1.4(1.1-1.7)], induction [1.3(1.1-1.4)], CS [1.4(1.3-1.6)] and postpartum haemorrhage [1.2(1.1-1.4)]. Of women with epilepsy, 33.6 %(n=942)were using AED. Compared to women without epilepsy, women with epilepsy using AED had an increased risk of mild preeclampsia [1.7(1.2-2.3)], gestational hypertension [1.5(1.0-2.2]), induction [1.6(1.4-1.9)], CS [1.6(1.4-1.9)] and postpartum haemorrhage [1.5(1.3-1.8)]. Only a slightly increased risk of CS was observed for women with epilepsy without AED use. Conclutions: Women with epilepsy have a low complication rate. Still, women with epilepsy and in particular AED users have an increased risk of preeclampsia, gestational hypertension, CS and postpartum haemorrhage.

PS12.6 Maternal infection during pregnancy – is it a risk factor for spontaneous preterm delivery in a low-risk population?

Nils-Halvdan Morken (1), N Gunnes (2), P Magnus (2), B Jacobsson (3)

- (1) Haukeland University Hospital, Department of Obstetrics and Gynecology, Bergen, Norway
- (2)Norwegian Institute of Public Health, Norway
- (3)Sahlgrenska University Hospital, Sweden

Objectives. To assess if general maternal infections during pregnancy were associated with an increased risk of spontaneous preterm delivery and to utilise more proper methodology than previously used. Methods. A cohort study was designed using data from the Norwegian Mother and Child Cohort study. Data were collected prospectively and obtained from three questionnaires. Two questionnaires were answered during pregnancy in the second and third trimester and one questionnaire was answered six months after delivery. Record linkage with the Medical Birth Registry of Norway was performed. Spontaneous preterm delivery was defined as a delivery with a spontaneous onset at gestational age 22 weeks + 0 days to 36 weeks + 6 days. Hazard ratios were obtained using Cox regression with gestational age at birth as the time variable and adjusting for maternal age, parity and smoking at the beginning of the pregnancy. Data were analysed in a two-step manner to avoid introducing selection bias. Results. The spontaneous preterm delivery proportion was low in this cohort, 2.6% and 2.8% in the two steps, respectively. Ear-nose-throat infection was associated with an increased risk of spontaneous preterm delivery (HR: 1.2, 95% CI: 1.0-1.4) in the first, but not in the second step of the analysis. None of the other maternal infections; lung infections, urinary tract infections, vaginitis, febrile episodes or influenza-like infections were associated with an increased risk of spontaneous preterm delivery. Conclusions. The lack of association questions older studies on the issue and may indicate differences between high-risk and low-risk populations.

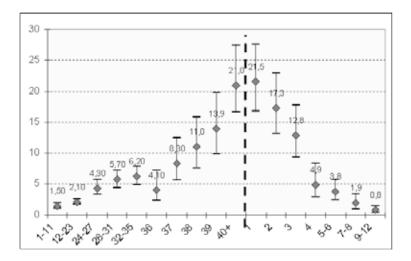
PS12.7 Venous thromboembolism in pregnant and puerperal women in Denmark 1995-2005

Rie Adser Virkus (1), ECL Løkkegaard (1), T Bergholt (1), U Mogensen (2), J Langhoff-Roos (3), Ø Lidegaard (3)

- (1)Hillerød Hospital, Hillerød, Denmark
- (2)Copenhagen University, Copenhagen, Denmark
- (3) Rigshospitalet, Copenhagen, Denmark

Objective: Venous thromboembolism (VTE) is still among the leading causes of maternal death in the western world. The aim of this study was to estimate the relative risk of VTE at different gestational ages in pregnant women compared to non-pregnant, fertile women. Method: Danish Women 15 to 49 years old through the period January 1995 through December 2005, free of previous VTE and current use of oral contraceptives. All first ever VTE in pregnant and non-pregnant women were identified in the National Registry of Patients. All non-pregnant women who did not use oral contraceptives constituted the control cohort. Poisson regression analysis was performed controlling for age, calendar year and educational status. Results: In total 819,751 pregnant women were identified of whom 727 had a diagnosis of VTE. The incidence rate of VTE increased with gestational age. Compared with non-pregnant woman the incidence rate ratios for VTE were 1.5 (1.1-1.9, p=0.0031) in week 1-11, increasing to 21.0 (16.7-27.4, p<0.0001) at week 40, 21.5 (16.8-27.6, p<0.0001) in the first week after delivery and thereafter declining. After 6 weeks the rate ratios were not significantly increased (figure). Age, calendar year and educational status did not influence the incidence rate of VTE in pregnant or puerperal women. Conclusion: The risk of VTE increases almost exponentially through pregnancy. The risk decreased gradually through the puerperal period. Key words: Venous thromboembolism, deep venous thrombosis, pregnancy, puerperium.

women versus non pregnant women not on hormonal contraception



^{*)} Adjusted for age, calendar year and education

PS12.8 Self-reported smoking habits and serum cotinine levels in women with placental abruption

<u>Minna Tikkanen</u> (1), H-M Surcel (2), A Bloigu (2), M Nuutila (1), O Ylikorkala (1), V Hiilesmaa (1), J Paavonen (1) (1)Helsinki University Hospital, Department of Obstetrics and Gynecology, Finland (2)National Public Health Institute, Finland

Objective: Smoking is one of the most important risk factors for placental abruption with strong dosedependency. Pregnant smokers often may underreport their tobacco use. We examined the accuracy between self-reported smoking habits and early pregnancy serum cotinine levels in women with or without placental abruption. Design: Retrospective case-control study. Setting: University Hospital. Population: A total of 184 women with placental abruption and 377 control women. Methods: Serum samples collected for routine screening during the first trimester (mean 10.4 gestational weeks) were analysed for serum cotinine levels. Cotinine concentration over 15 ng/ml was considered as the cutoff indicating active smoking. Smoking habits of the women and their partners were recorded at the same visit. Main outcome measure: Placental abruption. Results: Of the case women with subsequent placental abruption 26.1% and of the control women 14.1% reported smoking (p<0.001). Based on serum cotinine levels, 29.3% of the case women and 17.8% of the control women were considered smokers. Self-reported number of cigarettes smoked daily correlated well with the cotinine levels (r=0.67, p<0.001). Serum cotinine level among smokers was higher in the abruption group than in the control group (median 229.5 ng/ml [interquartile range {IQR} 169.8-418.1] versus 153.5 ng/ml [56.6-2241.4], p=0.002). Conclusion: Pregnant women with subsequent placental abruption are heavier smokers than pregnant control women. Self-reported smoking habits correlate well with serum cotinine levels. Therefore, self-reported smoking can be considered as a reliable risk marker for placental abruption.

PS12.9 Incidence and risk factors of fetal death in Norway

<u>Linda Björk Helgadóttir</u> (1,2,3), FE Skjeldestad (1), AF Jacobsen (2), PM Sandset (1,3) E-M Jacobsen (1,3) (1)Oslo University Hospital, Dep. of Hematology, Oslo, Norway (2)Oslo University Hospital, Dep. of Obstetrics, Oslo, Norway (3)University of Oslo, Norway

Objectives: To investigate incidence and risk factors for intrauterine fetal death (IUFD) and to compare registry- and hospital-based control data. Methods: Retrospective study of 377 women diagnosed with IUFD, January 1990- December 2003, at two large delivery wards in Oslo, Norway. Two control groups: one including 1,229 women with live births at one of the hospitals in the study period (hospital-based control group), the other all 87,692 women giving birth at both hospitals in the same period (registry-based control group). Information from cases and the hospital-based control group was collected from medical records. Data on the registry-based control group was provided by the Medical Birth Registry of Norway. Risk factors were analysed using chi-square tests and multiple logistic regression. Results: The incidence of IUFD was 4.1/1000 deliveries (95% CI 3.9 – 4.3). We identified following risk factors: twin pregnancy, hypertension, diabetes mellitus, abruptio placenta, and placenta previa. When using the registry-based control group: age, preeclampsia, gestational diabetes, and single marital status were also significant risk factors, while comparison with the hospital-based control-group revealed associations between IUFD and smoking, small for gestational age, conization of the cervix, and thyroid disease. Conclusions: When using different control-groups the relevance of some risk factors varied. The overall of risk was identical but the magnitude of risk related to hypertension and gestational diabetes seemed to be overestimated when using the registry-based control group, possibly caused by under-reporting in the registry. The odd's ratios also varied when additional risk factors were assessed using the hospital-based control-group.

PL04 Plenary 4 - The gap between expectations and outcomes

1530 - 1700

PL04.1 Expectations and Outcomes

No abstract submitted

PL04.2 Is there a conflict between consumer expectations on mode of delivery and attitudes among obstetricians and midwives?

<u>Ingela Wiklund</u> (1) (1)BB Stockholm, Sweden

For some pregnant women, the process of giving birth appears to be uncontrollable and intimidating. The wish to avoid a vaginal delivery has resulted in an increasing amount of women approaching obstetricians asking for an elective caesarean section (CS) in the last years. During many years midwives and obstetricians had difficulties responding to these demands. Lately attitudes among healthcare personnel have been changing. In a recent study from a Swedish hospital it was found that the dominant indication for an elective CS was defined as maternal request without any co-existing medical indication (Stjernholm et al. 2010). In another Swedish study researchers reported that older and more experienced specialists had a more positive attitude towards providing CS on maternal request than their younger colleagues. The main difference between female and male physicians was that males were more positive towards providing CS on maternal request than their female colleagues (Gunnervik et al. 2008). A significant proportion of obstetricians in the USA (46 percent) would favour a CS for themselves, or for their partners, in an uncomplicated pregnancy (Gabbe et al. 2001) whilst only 1.1 percent of the Danish obstetricians would agree to this (Bergholt et al. 2004). In Norway female doctors and midwives have been found to

have a higher CS rate than other professionals with a similar length of education (Lehmann et al. 2007). Twenty-seven percent among the specialists had at least one child born with CS compared to 12 percent in the general public (Finsen et al. 2008). In contrast, Finnish midwives and obstetricians have a lower CS rate than others with similar length of education (Hemminki et al 2009). Is the management of CS on maternal request a question based on sensibility rather than sense? Will the rate of CS in the population fall as long as many obstetricians and midwives have their own children delivered by CS? Is there really a conflict between consumer expectations and attitudes among obstetricians and midwives?

PL05 Plenary 5 - New technologies and new horizionz

0900 - 1000

PL05.1 Perinatal medicine in the future: Possibilities and illusions

Magnus Westgren (1)

(1)Karolinska University Hospital, Stockholm, Sweden

Where were we 50 years ago and where will we be 50 years from now? The present presentation will try to put perinatal medicine within a historical context, and from this background try to discuss several issues relevant for the future. A broad spectrum of possibilities and limitations will be covered such as demographic changes, organisation, and prevention, technical and other scientific interventions.

It is not any easy task to predict the future. Hopefully you will find the presentation exciting and provocative. Do we really need obstetricians in the future?

PL05.2 What does reproductive biology have to offer for the future?

Claus Yding Andersen (1)

(1)Laboratory of Reproductive Biology, Section 5712, University Hospital of Copenhagen, University of Copenhagen, Denmark

Ovarian failure can occur naturally prior to the normal time of menopause or may be due to iatrogenic agents. Whereas causes of premature ovarian failure without exogenous interference may or may not be known, it is well known that treatment of many diseases, especially cancer diseases, involve gonadotoxic regimes. The ovaries are very sensitive to chemotherapy, in particular alkylating agents but also to radiation, which both are classified as high risk for gonadal dysfunction. However, each individual woman often considers functional ovarian tissue involving both fertility and menstrual cycles very important and although normal ovarian activity is classified as a quality-of-life-aspect many women and girls wants to preserve their ovarian tissue before occurrence of POF if possible. Methods to cryopreserve ovarian activity have now been developed. Freezing of ovarian tissue involves removal of one ovary or parts of one ovary prior. When the woman have been cured of her disease and is considered fit or wants to have the tissue replaced, the thawed ovarian tissue with a viable pool of follicles can be transplanted to women who entered menopause. The surviving pool of primordial follicles will be reactivated; start to grow and the patients will regain fertility and will experience cyclic variation in sex hormone levels. In Denmark more than 425 women have now had their ovarian tissue cryopreserved and 16 women have had frozen/thawed tissue replaced. All the women have regained ovarian function and the tissue appears to be surprisingly robust and provides the women with several years of ovarian function and fertility. The recent results will be reviewed and the use of ovarian tissue cryopreservation for number of other gynecological conditions will be discussed together with other new methods within area of reproductive biology.

PS13.1 Psychological factors associated with perception of pain in women with vulvodynia *Michal Granot (1)*

(1)University of Haifa, Israel

Provoked vestibulodynia (PVD) represents a complex phenomenon which is associated with enhanced pain perception. In addition to the physiological pathology in the vulvar tissue the altered systemic pain perception can be attributed to emotional and personality factors and that vulvodynia incorporate biomedical, psychological, and psychosexual factors. Accumulative evidence obtained by self report questionnaires and experimental pain studies suggests that the following factors play a role in the clinical presentation of dyspareunia: anxiety, fear of pain, low self-esteem, hypervigilance, somatization, harm avoidance, pain catastrophizing and depression. Recent study points that insecure attachment styles combined with greater somatization level are associated with greater pain sensitivity among PVD women. The existence of several sub-types of groups within the PVD patients suggesting that this disorder represents various manifestations of personality and pain-related characteristics. This presentation will focus on the psychological and cognitive aspects of vulvodynia. The associations between dysfunctional pain modulation and personality variables in women suffering from PVD and the role of experimental pain via quantitative sensory testing will be discussed. Current data regarding the relationships between psychosexual components and pain mechanisms as well as the direct and indirect role of psychological factors on pain perception among PVD patients will be presented.

PS13.2 Physical evidence of pain sensitisation in women with vulvodynia

Nina Bohm-Starke (1)

(1)Karolinska Institutet Danderyd Hospital, Sweden

Provoked vestibulodynia (PVD) is the most common form of vulvodynia and the aetiology is considered multifactorial. Effort has been made to find characteristic patho-physiological changes in women with PVD in an attempt to explain, diagnose and treat the condition. It has been proposed that PVD may represent a chronic local inflammatory condition. Similar infiltration of mucosal T-cell lymphocytes is seen in patients and healthy women. Other inflammatory markers have also been investigated without any convincing significance. The only histo-pathological finding specific for PVD is a mucosal nerve fibre proliferation. Hyper tonicity of the pelvic floor muscles is often present which is important to restore during treatment. Hypersensitivity and allodynia is present in the mucosa and QST has given evidence for peripheral sensitization for noxious stimulation. The altered peripheral pain perception is considered to be part of a neurogenic inflammation which might be initiated when primary afferents are triggered by injury or trauma, resulting in lower pain thresholds. Research has also shown evidence of an alteration of central pain perception. Many patients suffer from other bodily pain and experimental testing has shown enhanced general pain sensitivity, indicative of central sensitization Several physical evidences of pain sensitization in women with vulvodynia have been reported, but no obvious causes for these observed changes have so far been identified. Research is needed to study whether the altered pain modulation is caused by peripheral or systemic pathology. If the pathophysiology of the condition is better understood, more effective treatments can be obtained.

PS13.3 Sexual impairment in women with vestibulodynia

Christina D Petersen (1)

(1)Department of Gynecology and Obstetrics, Hillerød University Hospital, Hillerød, Denmark

Vulvodyni is defined by the ISSVD as 'vulvar discomfort, characterized by stinging, burning, irritation or rawness' in the absence of relevant visible findings or a specific, clinically identifiable, neurological disorder.

The etiology is still not exactly known, however many clinicians often encounter patients with vulvodynia and concomitant sexual difficulties. The question whether the pain condition results from sexual dysfunction or if sexual dysfunction is a natural consequence of a chronic pain condition, such as vulvodynia, is still being scientifically investigated. The purpose of the presentation is to share knowledge on the sexual aspects of vulvodynia, discuss vulvodynia as a psychosexual somatoform disorder contrary to being an organic disorder and how to treat vulvodynia. Several controlled studies have demonstrated that women with vulvodynia exhibit a significant deterioration in their sexual functioning, high levels of dissatisfaction with their sexual life, and low levels of desire, arousal, and orgasmic frequency. Maintaining or establishing a partnership can be difficult for women with vulvodynia. Dyadic adjustment appears to influence the pain intensity of vulvodynia: this pattern has also been shown in patients with other chronic pain conditions. For two decades studies have used the Female Sexual Function Index (FSFI) to evaluate the sexual functioning of women with vulvodynia and the Female Sexual Distress Scale (FSDS) to evaluate the level of sexual distress in women with vulvodynia. Results from several studies all demonstrate that women with vulvodynia are significantly affected on all domains of their sexuality and report significantly higher levels of sexual distress compared to controls. In a Danish case control study more than 90 % of all women with vulvodynia suffered from sexual dysfunction and reported high levels of sexual distress. These results among many others imply that clinicians need to address the sexual functioning and level of sexual distress in women diagnosed with vulvodynia, and to consider psychosexual treatment as part of a multidisciplinary treatment program to reduce pain in the vulva.

PS14 Parallel Session 14 - NFOG session: Environment and reproductive health 1045 - 1215

PS14.1 Semen quality of Nordic men and testicular dysgenesis syndrome: Implications for fertility rates

<u>Niels Erik Skakkebæk</u> (1) (1)Rigshospitalet, Denmark

We and others have provided evidence that testicular cancer is linked to decreased fertility and poor spermatogenesis, cryptorchidism and hypospadias through perinatal testicular dysgenesis causing impaired development of Sertoli- and Leydig cells. Therefore, we have proposed that these conditions may all be symptoms of a testicular dysgenesis syndrome (TDS). Remnants of testicular dysgenesis may be seen in testicular biopsies of infertile men with TDS as microliths and clusters of insufficiently developed seminiferous tubules often containing Sertoli cells only. Few genetic abnormalities can cause TDS, including point mutations, e.g. SRY mutations, and abnormalities in sex chromosomes, e.g. 45,X /46,XY karyotype. Most cases of TDS are, however, not linked to any known genetic abnormality. Furthermore, the sharp increase in testicular cancer seen over the past 50 years suggests that environmental factors play a role as cause of TDS. Severeral recent studies have shown that at least 20% and possibly as many as 40% of young men have subnormal semen quality. In general, semen quality of Danish and Norwegian men is poorer that that of Finnish men. To test the idea that exposures to endocrine disrupting chemicals (EDCs) may contribute to the problem, we have made synchronous studies of populations in Denmark and Finland, two countries with high and low incidences of TDS, respectively. Interestingly, we found that the concentration of persistent chemicals, including dioxins, PCBs and some pesticides was significantly higher in Denmark than in Finland(5). Further studies are planned to evaluate possible links between EDCs and TDS. Another remaining research challenge is to delineate the role of TDS as a cause of male infertility and hypospadias, two conditions, which obviously also can have many other causes. However, most cases of testicular cancer and cryptorchidism seem to be related to perinatal dysgenesis of the gonad. A consequence of the TDS hypothesis is that the full extent of the damage of environmental exposures of today may not be seen until current newborns reach adulthood.

PS14.2 Environmental endocrine disruption of the ovary

<u>Paul Fowler</u> (1), R Lea (2), K Sinclair (2), P Pocar (3), B Fischer (4), S Rhind (5), P O'Shaughnessy (6), C Cotinot (7)

- (1)University of Aberdeen, United Kingdom
- (2)University of Nottingham, United Kingdom
- (3)University of Milan, Italy
- (4)Martin Luther University Halle, Germany
- (5) Macaulay Land Use Research Institute, Aberdeen, United Kingdom
- (6)University of Glasgow, United Kingdom
- (7)INRA. Jouv en Josas. France

There is growing evidence that various female reproductive syndromes may be due to environmental chemicals, as is Testis Dysgenesis Syndrome. The detrimental effects of exposure to environmental chemicals include developmental abnormalities, adult dysfunction and cancers in the ovary, urogenital tract, genitalia, mammary gland and hypothalamus/pituitary. Some symptoms, especially premature menarche and premature ovarian ageing, are of considerable concern. This is especially true in countries where women delay childbirth until they reach ages where fecundity would de-facto be reduced even without exposure to environmental chemicals. It is now many years since ovarian formation was thought to be simply due to the absence of SRY and testosterone. We now know that the process leading to a functional ovary in the adult includes complex endocrine signalling. Therefore, the fetal ovary is susceptible to endocrine disruption during development and its controlled development in-utero is critical for the reproductive health of the adult female. Indeed, in women, and model experimental species such as the sheep, the fetal ovary contains the machinery for oestradiol production and reception prior and during to primordial follicle formation. Both real life and experimental exposures have highlighted key mechanisms that are sensitive to environmental chemicals. These include: i) establishment of somatic cell numbers, ii) primordial follicle formation, ii) follicle activation and iv) maintenance of follicle health. All these processes play an important role in the establishment of fecundity in the female and their disturbance by endocrine disruptors is of serious concern. [Supported by EC 7th Framework Programme (FP7/2007-2013) project 212885]

PS14.3 Environmental exposure and reproductive health in circumpolar areas

Jon Øyvind Odland (1)

(1)University of Tromsø, Norway

Globally, a number of persistent toxic substances (PTS), are recognised as being responsible for adverse health effects in children. The growing foetus and newborn child are especially sensitive to the toxic effects of persistent organic pollutants and heavy metals. The levels of these contaminants in maternal blood during pregnancy gives an indication of the potential risk to the developing foetus. Considerable efforts have been made over the last thirty years to characterise PTS concentrations in the environment. The Arctic Monitoring and Assessment Programme (AMAP) has initiated collaborative research programmes in a range of developed and developing countries in the Southern and Northern Hemisphere. The focus of the presentation will be on the concentrations of metals and organics found in maternal blood in these regions and the implications of environmental exposures to the emerging chemicals of concern. Good effect studies are now emerging from the compatible child cohorts initiated and ongoing in several countries. The most important reproductive health effects shown so far are impacts on sperm quality, time-to-pregnancy, birth weight, gestational age, and neurological effects in early childhood. The presentation will report from studies performed in all Arctic countries, as well as in Vietnam, South Africa, Australia and Russia. The precautious principle must be introduced and adapted in all scientific and public health policies while the results are assessed.

PS15.4 Vascular dilatory function and cardiovascular risk factors in women with previous pre-eclampsia

Lampinen Katja, (Finland)

Women with a history of pre-eclampsia have an increased risk of cardiovascular disease in later life. The mechanisms which mediate this heightened risk are poorly understood; it was long believed that pre-eclampsia was a separate disease without any connection to other pathologies. The present study was undertaken to investigate the cardiovascular risk milieu, vascular dilatory function and cardiovascular risk factors, in women with pre-eclampsia, 5–6 years after index pregnancy. The aim was to understand better the cardiovascular risks associated with pre-eclampsia and add tools to the evaluation of cardiovascular risk in women.

The study involved 30 women with previous severe pre-eclampsia and 21 controls. The 2-day study protocol included venous occlusion plethysmography and pulse wave analysis for assessment of vascular dilatory function and central pulse wave reflection, respectively, office and ambulatory blood pressure measurements, assessment of insulin sensitivity, using a minimal model technique, and tests regarding renal function, lipid metabolism, sympathetic activity and inflammation.

Vasodilatory function was impaired in women with a history of pre-eclampsia; this was seen in both endothelium-dependent and endothelium-independent vasodilatation. Proteinuria during pre-eclampsia did not predict changes in vasodilatation, and renal function was similar in the two groups. Insulin sensitivity was related to vasodilatation and features of metabolic syndrome, but only in the patient group, despite similar insulin sensitivity in the control group. Arterial pressure was higher in the patient group than in the controls and correlated with endothelin-1 levels in the patient group, whilst the overall difference between the groups was diminished in 24—hour arterial pressure measurements. Additionally, women with previous pre-eclampsia were characterized by increased sympathetic activity.

Impaired vasodilatory function at the vascular smooth muscle level seems to characterize clinically healthy women with a history of pre-eclampsia. These vascular changes and the features of metabolic syndrome may be related to the increased risk of cardiovascular disease. Furthermore, increased blood pressure in combination with enhanced sympathetic activity may be additive as regards this risk. These women should be informed about their potential cardiovascular risk profile and the possibilities to minimize it via their own actions. Medical cardiovascular risk assessment in women should include obstetric history.