

ORAL PRESENTATIONS

Or 1

Saline infusion sonography in a general population: success rate, feasibility and complications

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Background: Saline infusion sonography (SIS) is recommended to supplement traditional transvaginal sonography in detecting focal intrauterine lesions. Patient related factors and sonographers' skills influence the performance of SIS.

Objective: To determine rates of success and complications, and evaluate patients' acceptance.

Methods: In a population-based study 686 women were intended for SIS, using a babyfeeding tube with no balloon and no tenaculum. Women were instructed in Visual Analogue Score (VAS) and filled in VAS for both SIS and their experience of gynecological examination (GE.). Women were encouraged to contact the department if side effects occurred. VASs were measured in mm, rates of success and complications were calculated.

Results: Success rate was 91%. 622 procedures were sufficient. Inconclusive SIS led to repeated procedure in 37 women. Cervical stenosis was present in 82 women. For SIS VAS median was 19 mm, mean=25 mm (range 0-99 mm). For GE. VAS median was 10 mm, mean=15 mm (range 0-99 mm). For SIS 32% had scores more than 30 mm indicating need for analgesia - for GE 15% had scores more than 30 mm. Significant predictors for high VAS at SIS were: being nulliparous, postmenopausal and scoring high on GE. VAS. Complications: 4 women had vasovagal reaction (0.6%), 3 vaginal bleeding. 2 lower abdominal pain, 1 foul-smelling discharge, cultures were negative. Total complication rate was 1.6%

Conclusion: Generally saline infusion sonography had a high success rate and low complication rates. Discomfort was reported in 32 %. Anamnestic information could help in selecting of women for analgesia before SIS.

Or 2

Chlamydia trachomatis and chlamydial heat shock protein 60 specific antibody and cell mediated responses predict tubal factor infertility

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Background: To evaluate the role of Chlamydia trachomatis -induced humoral and cell mediated immune responses in predicting tubal factor infertility (TFI).

Material and Methods: Blood samples were taken from 88 women with TFI and 163 control women. C.trachomatis and chlamydial heat shock protein 60 (CHSP60) specific IgG antibodies were analyzed by ELISA. Proliferative reactivity of peripheral blood mononuclear cells was studied in vitro against C. trachomatis elementary body (EB) antigens and recombinant CHSP60 antigens.

Results: C.trachomatis specific IgG antibodies were found more frequently (43.2% vs. 13.5%) and the antibody levels were higher in the TFI cases than in the controls (p<0.001). C.trachomatis EB induced lymphocyte responses were positive in 81.8% of the TFI cases and 58.9% of the controls (p<0.001). Similarly, CHSP60 induced lymphocyte responses were found in 45.5% of the cases and 30.7% of the controls (p<0.001). CHSP60 antibody test was the best single test predicting TFI. Compared to cases with all four markers negative, the estimated risk for TFI was 4.1 (95% CI 1.4-11.9) among those with one positive marker and 19.9 (CI 6.9-57.4) among those with three or four positive markers.

Conclusions: Our results show that TFI prediction model can be improved by combining tests for humoral and cell mediated immune response to chlamydial antigens.

Or 3

Heregulins in human endometrium; in healthy, endometriotic and cancer tissue

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Background: The heregulins (HRGs) are ligands of the Epi-dermal Growth Factor (EGF) system and present two groups, HRG1a, 1b, 2a and 2b in one group, HRG3 and 4 in the other. Besides the HRGs, the EGF-system comprise of four receptors and a third group of ligands. The EGF-system is pivotal in normal growth in all human tissues and the receptors and some of the ligands are known to show cyclical variation in healthy endometrium.

Objective and hypothesis: We describe the expressions of the heregulins under normal conditions and under benign and malignant transformation of the endometrium. We hypothesise cyclical variation in normal endometrium and changes in expression after transformation whether this is benign or malignant.

Methods: Endometrial tissue samples obtained by vacuum extraction from 14 healthy women three times during one menstrual cycle, from 23 women with proven endometriosis and 45 women with endometrioid endometrial cancer were examined by quantitative real-time PCR.

Results: Healthy endometrium shows a statistically significant variation in expressions of HRG1a, HRG1b and HRG2b. The same pattern of variation is seen with a decrease from proliferative to early secretory phase, no variation during secretory phase and an increase from late secretory to proliferative phase. There is no statistically significant difference in expression level between the healthy endometrium, endometriotic endometrium and endometrioid endometrial cancer tissue.

Conclusion: Cyclical variation in the heregulins in healthy premenopausal endometrium supports the theory of the EGF-system as an important player in the regulation of the normal growth of the human endometrium.

Or 4

Randomised trial of total versus subtotal abdominal hysterectomy with 5-year follow up

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Background: Total versus subtotal hysterectomy has been studied. Results from this trial with 1-year follow-up have already been published. Significantly less women were incontinent after total than after subtotal abdominal hysterectomy.

Objectives: To assess the effect of total versus subtotal hysterectomy on urinary incontinence, postoperative complications, constipation, descensus of the vaginal top/cervix uteri, pelvic pain, satisfaction with sexual life, vaginal bleeding (after subtotal hysterectomy) at 5-year follow up.

Hypothesis: Less women were expected to suffer from urinary incontinence, prolapse and dissatisfaction with sexual life after subtotal than after total hysterectomy.

Methods: This Danish multi-center, randomized trial included women undergoing hysterectomy for benign disease from 1996 to 2000. The sample size is 158 women with total hysterectomy and 161 women with subtotal hysterectomy. The endpoints were measured by validated questionnaires filled out by the women before and 8 weeks, ½ year, one, five and 10 years after the operation. Information about postoperative complications was collected by files filled out by the operating gynecologist. The randomisation procedure was computer-controlled and used block randomisation and stratification by center and ovarian status.

Results: As 5-year follow-up of the patients has just terminated but not yet analysed we will be able to present data regarding urinary incontinence, constipation, postoperative complications, pelvic pain, descensus of vaginal top/cervical stump, satisfaction with sexual life and vaginal bleeding 5 years after the operation of total versus subtotal abdominal hysterectomy.

Conclusions: We present data from the largest randomised trial of total versus subtotal hysterectomy with the longest follow-up.

Or 5

The effect of hysterectomy or levonorgestrel-releasing intrauterine system on serum inhibin B levels and intraovarian artery blood flow among menorrhagic patients

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Background: A third of women suffer from menorrhagia during their reproductive years. Hysterectomy and levonorgestrel-releasing intrauterine system (LNG-IUS) are its well-adopted treatment options. However, the influence of these two treatment modalities on ovarian function remains unclear.

Objective and Hypothesis: The objective of the study was to evaluate the effect of hysterectomy or LNG-IUS on ovarian function. The hypothesis was, that hysterectomy alters ovarian function more than LNG-IUS.

Methods: We conducted a randomised controlled trial on 107 women referred for menorrhagia to the University of Helsinki, Finland, between 1994 and 1997. 54 women were treated by hysterectomy and 53 by LNG-IUS. The pulsatility indexes (PI) of ovarian arteries and intraovarian arteries were measured by transvaginal ultrasound at baseline, six months and twelve months after the treatment. Serum concentrations of follicle-stimulating hormone (FSH) and inhibin B were measured at the same occasions.

Results: Serum FSH concentrations increased during the last six months only in the hysterectomy group ($p < 0,05$), but the decrease in serum inhibin B concentration was seen after six months in both groups ($p < 0,05$). PI of the intraovarian arteries decreased at six months and twelve months ($p < 0,05$) in the hysterectomy group. Such decrease was not seen among LNG-IUS users. Change in PI's between treatment modalities was also significant ($p < 0,05$). In univariate analyses treatment modality explained the change in serum FSH concentration and change in PI of intraovarian artery ($p < 0,05$). FSH increase was also explained by age ($p < 0,05$). However, treatment modality did not explain decreased serum inhibin B concentrations.

Conclusions: Hysterectomy but not LNG-IUS alters ovarian blood flow, which in turn may impair ovarian function.

Or 6

Laparoscopic surgery of early-stage endometrial cancer - 5 years of experience

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Background: The laparoscopic approach in the surgical treatment of endometrial cancer has gained wide acceptance by gynaecologic surgeons. Objective: To compare characteristics, per operative factors and postoperative outcome of patients who had undergone laparoscopic surgery versus patients undergone laparotomy.

Method: In the years 2000 to 2004 a total of 91 patients underwent laparoscopic surgery for early-stage endometrial carcinoma. Of a total 205 patients with histological endometrial adenocarcinoma and estimated low- or medium-risk, 80 were operated laparoscopically while 125 underwent laparotomy. We compared these two groups retrospec-

tively. Sampling of lymph-nodes from the pelvic area was performed in the medium-risk group unless morbidity made it unfeasible.

Results: The median age was higher in the laparotomy-group (69y. vs. 61.5y.). Weight and morbidity were also higher in the open group. Per operative blood-loss was equal. Although operating-time was longer for the laparoscopic procedure (122 min.) than for the laparotomy-procedure (84 min.), the laparoscopically operated patients were discharged from hospital after a median 3 days compared to 6 days after the open procedure. The number of lymph-nodes removed was comparable if not better in the laparoscopic group (9 vs.7). There was a distinct difference in surgery-related complications. Particularly there were only 5 cases (6%) of surgical wound complications after laparoscopy while we found 20 cases (16%) after laparotomy.

Conclusions: Laparoscopic surgery of early-stage endometrial cancer is as safe as the open procedure. Shorter hospital-stay compensates for the longer operating-time. Lower rate of complications and almost invisible scars make it an attractive procedure for both the surgeon and the patient.

Or 7

Fertility after trachelectomy for cervical cancer-the Göteborg experience

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Background: Cervical cancer is the type of gynaecological cancer that is most prevalent in women of childbearing age. In order to preserve the uterus and thereby the fertility potential of the patient trachelectomy combined with pelvic lymph node dissection has been introduced for surgical treatment of early stage cervical cancer. The aim of the present study was to follow up the completed trachelectomy cases at Sahlgrenska University Hospital.

Methods: Eight patients were operated between 2002-2004 with complete procedures. Two additional patients underwent trachelectomy, but with conversion to radical hysterectomy because of positive endocervical margins. The age of the eight patients were between 25 and 32 years (mean 29) and two patients were mothers (1 and 2 children, respectively). The Figo stages were 1A1 with LVSI=1, 1A2=4, 1B1=3 and histology was squamous carcinoma (n=5) and adenocarcinoma (n=3)

Results: The procedure was carried out with laparoscopic lymph node dissection, vaginal radical trachelectomy and prophylactic cervical cerclage. Blood loss was < 500 ml and postoperative symptoms are minor to moderate lymphoedema (n=2), numbness on medial aspect of thigh (n=3). None of the patients have symptoms of cervical stenosis. At follow up visits of the eight patients only one abnormal smear (HPV induced atypia, spontaneously resolved) has been noted and no recurrence has occurred. Half of the patients are on hormonal contraception since the procedure and four patients have attempted to conceive. All these four patients have become pregnant spontaneously; one patient had a legal abortion in gw. 8+4, one patient is pregnant (at present gw. 20), one patient gave birth by CS at gw. 37, and one patient gave birth by CS at gw. 38. The last patient is again pregnant in gw. 17.

Conclusions: In this case series of trachelectomy for cervical cancer the fertility post surgical treatment is high. No premature deliveries have been observed so far.

Or 8

Despite treatment of severe cervical dysplasia (carcinoma in situ) women face a long-term increased risk of invasive cancer

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Aim of study: To study the long term risk for women treated for severe dysplasia (carcinoma in situ) to develop invasive cancer.

Method: The Swedish cancer register has recorded all cases of invasive cancer and carcinoma in situ in histopathology since 1958. The register was searched for women with a diagnosis of carcinoma in situ of the cervix (CIS). This cohort contributed 2,3 million person years. These women were followed in the same register for invasive cervical cancer occurring after one year or more. Standardized Incidence Ratios (SIR) were calculated, with the cancer risk of the general Swedish female population as reference. The influence of time-period, age and birth cohort at the time of CIS-diagnosis, as well as time interval between the diagnosis of CIS and invasive cancer, was explored and controlled for in multiple logistic regression models.

Results: Having a prior CIS diagnosis increases the risk for invasive cancer compared with the general female population (SIR= 2,34 (CI =2,18-2,50)) The increased risk does not decrease substantially with time since CIS-diagnosis. There is an effect of age with an accentuated increase in risk for women older than 50. The excess risk for invasive cancer of having a CIS-diagnosis has steadily increased since 1958.

Conclusion: It can be assumed that practically all women in the register with a CIS diagnosis in histopathology have been treated and received some follow up. These women are at an increased risk for developing invasive cancer and the hitherto existing follow up programs have not had sufficient effectiveness.

Or 9

Fertility, pregnancy outcome and parenthood in women with Turner syndrome (TS) from southwest of Sweden

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Background, objectives: In TS spontaneous menarche (SM) or pregnancy (SP) occurs in 10-15% and 5 % respectively. Since 2003 oocyte donation (OD) is allowed in Sweden. Miscarriages are frequent in SP and after OD. Cardiovascular malformations are common. High risk for aortic dissection and mortality during pregnancy has been reported. The aim was to study fertility, pregnancy outcome, parenthood and the opinions concerning OD of women with TS.

Methods: A questionnaire was sent to TS women > 20 years old (n= 109) known by our Turner Centre.

Results: Seven had moved, 78/102 responded (76,5%), 24/49 after reminder. Five of 15 women with SM had pregnancies (SP n= 4, OD n=1). Ten of 78 (12.8%) reported 32 pregnancies, either SP or after

OD. After exclusion of one woman with 14 miscarriages the outcome of 18 pregnancies was miscarriages 28%, legal abortion 17% and deliveries 55%. Three women had 5 children after SP and 5 had 5 children after OD. All children were reported to be healthy. Eight women reported treatment with IVF and/or OD. During pregnancy one woman was operated due to aortic dissection (before the diagnosis of TS), one had hypertension and in one ablatio placentae was suspected. Caesarean section was performed in 6/10 pregnancies. Totally 15 women lived with 18 children, 9 adopted, 9 biological. Thirtyseven of 61 women had pregnancy desire, predominantly women < 30 years old (27/29). Of those <40 years old, 23/31 intended to apply for OD. A majority (68%) was positive to anonymous donation, equally 44% positive and negative to known donation.

Conclusions: Miscarriages were frequent. Young TS women have pregnancy desire and consider treatment with OD as an option. Due to the high risk of cardiovascular complications early diagnosis and preconceptual examination is of utmost importance. In women with a combination of premature ovarian failure, short stature, habitual abortion TS has to be excluded by karyotyping.

Or 10

Midwives conducting perineal repair: The Danish Suture Trial

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Background: Suture techniques and materials for post partum perineal repair of 2nd degree lacerations and episiotomies have been tested in several clinical trials. Danish midwives and obstetricians have developed a new, simple and time-efficient suture technique which needs systematic evaluation before implemented in clinical practise.

Objective: To compare two standardized suture techniques for perineal repair of 2nd degree perineal lacerations or episiotomies after vaginal deliveries.

Methods: A double-blind randomised clinical trial conducted at Aarhus University Hospital, Denmark. Initiated August 2004, enrolment of patients finished October 2005. Sample size: 400 (5%, power 80%, expected difference 15%).

Inclusion: Healthy primipara sustaining a 2nd degree perineal laceration or an episiotomy following vaginal birth.

Exclusion: Lacerations involving the sphincter ani, post partum haemorrhage >1000 ml, Diabetes, mental disorders. Both suture techniques were 2-layered using a polyglactin 910 multifilament suture (Vicryl Rapid or Vicryl). Treatment A was a continuous suture technique and treatment B was interrupted, inverted stitches. The suture was performed by midwives.

Primary outcomes: Perineal pain and wound healing assessed day 1-2 and 10 postpartum. Secondary outcomes: patientsatisfaction with wound healing, need for secondary repair, superficial pain during intercourse. Data management: Double entry of all data and intention-to-treat analysis.

Results: The follow up rate was 97%. Baseline data were evenly distributed between the two treatment groups. Major difference in pain and healing was observed between spontaneous lacerations and episiotomies. Follow up 6 months post partum will be finished by April 2006.

Conclusion: Primary results will be presented on the NFOG Congress in Göteborg, May 2006.

Or 11

Evidence regarding alcohol during pregnancy - two ways of reading the literature

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Background: In 2005, the Departments of Health in Norway and Britain appointed expert committees to evaluate the literature regarding alcohol in pregnancy.

Objective and hypotheses: To compare the methodology applied by the two countries and the conclusions reached. It was hypothesised that the underlying scientific theory would differ in the two countries.

Methods: Review of the two reports from the expert committees.

Results: The Norwegian report is largely based on an American, a Dutch, and a Swedish report. The report operates with levels of the strength of scientific proof, the lowest level (apart from "not studied") being "not documented", defined as "studied but the studies are not sufficiently strong; an effect cannot be ruled out". It is recommended that pregnant women abstain from alcohol. In Britain, a systematic search of studies on low and moderate alcohol intake was performed, including binge drinking. All studies were critically judged, methodological strengths and weaknesses described and scored. It is suggested that a few drinks a week is acceptable during pregnancy.

Conclusion: The underlying literature is essentially the same, but the conclusions are based on two very different arguments: 1) Essentially, intake of small amounts of alcohol has not been associated with adverse effects. Hence, it is likely that a pregnant woman can drink small amounts of alcohol without harming her fetus (British argument); 2) It has not been proven that intake of small amounts of alcohol in pregnancy is not harmful, hence pregnant women should abstain from alcohol (Norwegian argument). However, the hypothesis that small amounts of alcohol (or any other exposure) is harmless can never be proven, but if the hypothesis despite continuous efforts cannot be falsified, then it is likely to be true. If one is not prepared to accept this basic fact of science, any future research in this or any other field is pointless.

Or 12

Comparison of biochemical and ultrasound screening in first trimester for Down syndrome in Northern Finland

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Background: With current trends toward smaller families and delays in childbearing, prenatal diagnosis has an important role in the management of most pregnancies. We wished to compare the efficacy of both separate and combined maternal serum test and fetal nuchal translucency measurement in the first trimester screening for Down syndrome in Northern Finland.

Methods: The following first trimester screening tests for fetal Down's syndrome were evaluated: measurement of nuchal translucency (NT) alone; serum screening (PAPP-A and free β -hCG)

alone; combined screening (NT plus PAPP-A and free β -hCG). The adjusted estimated risk for trisomies was calculated using Wallac Life Cycle program.

Results: The participants comprised 9739 volunteer pregnant women in northern Finland during the 10th-13th weeks of pregnancy in 2002-2004. The mean age of giving birth and the number of older women (>35 year) conforms exactly to the average Finnish pregnancy statistics. All 9739 subjects participated in NT screening, 7534 women participated in serum screening, and 4765 of those women participated in combined screening. In the NT alone screening group there were altogether 40 cases of trisomy 21 and using risk figure program 26 cases (60%) were detected. In the serum screening alone group there were altogether 31 cases of trisomy 21 and 21 cases were detected, 68%. In the combined screening group there were altogether 23 cases of trisomy 21 and 20 cases were detected, 87%.

Conclusions: This prospective study suggests that combined screening is the method of choice for Down's syndrome screening.

Or 13

Extension of and epidural for vaginal delivery to anaesthesia for surgery does not cause time delay

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Background: We have previously shown that the use of indwelling epidural catheter for epidural anaesthesia in emergency caesarean section (Cs) resulted in a prolongation of the time to start of surgery and delivery.

Objective: In this prospective study we wanted to test if the use of fast acting local anaesthetic drug for rapid epidural top-up dosing could eliminate the delay in start of surgery in caesarean sections with an immediate threat to life of women or child (Grade 1 Cs).

Hypothesis: The use of epidural top ups should not cause any time delay as compared to general anaesthesia in Grade 1 Cs.

Methods: During a one year period all parturients with an indwelling epidural catheter presenting for a Grade 1 Cs were included in the study. The anaesthetic team was instructed to use the epidural catheter for a top-up dose of 2- chloroprocaine 30 mg/ml whenever possible. The interval from decision of surgery until start of surgery (DSI) and delivery (DDI) were noted, as well as any complications or side-effects.

Results: 49 patients were included in the study. Epidural top-ups were attempted in 33 (67%) of the cases and 25 (75%) of these were successful. The mean DSI with epidural top-up was 9.1 ± 4.7 min, similar to 8.0 ± 3.4 in patients receiving general anaesthesia (ns). The DDI was significantly longer in the patients receiving epidural anaesthesia 14 ± 5.8 min compared to 11 ± 4.2 in the patients receiving general anaesthesia ($P < 0.05$). The one-minute Apgar scores were significantly better after epidural anaesthesia, whereas the 5 min scores were similar in the two groups.

Conclusion: Extension of an ongoing epidural block can be achieved in at least half of the cases with need of immediate Caesarean section, and did not delay DSI significantly compared with general anaesthesia. DDI was significantly prolonged, however, Apgar scores after one minute were higher when epidural anaesthesia was used.

Or 14

Fetal MRI of ultrasound detected anomalies in early second trimester

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Background: Correct antenatal information about diagnosis and prognosis of fetal anomalies is of utmost importance for management of the pregnancy and planning of the delivery. The aim of this study was to assess the value of fetal MRI as a complement to routine ultrasound in the second trimester.

Material and methods: All women with fetal anomalies detected on routine ultrasound in 2004 and 2005 were offered participation in the study. Fifty-six fetuses with gestational age 15-22 weeks were included. MRI was performed within 1 to 3 days after the ultrasound in 38 cases, 4-7 days in 13 cases and 8-14 days in 3 cases. T-2 weighted images were acquired in the three main planes with a Single-Shot Turbo Sin Echo sequence. No pre-medication was administered. The images were evaluated with full knowledge about the ultrasound findings.

Results: In 17 of the 56 cases (30%) MRI showed additional information. This was obtained in 6/7 cases with CNS anomalies, 5/8 cases with oligohydramnios and in all 3 cases of diaphragmatic hernia. In 32 cases (62 %) MRI confirmed the ultrasound findings but did not find any additional information. MRI could not confirm the main ultrasound finding in 5 cases (8%).

Conclusion: Fetal MRI, as a complement to routine ultrasound, seems to be a powerful tool in investigation of CNS anomalies, diaphragmatic hernia and cases with oligohydramnios. Due to limited resources and logistic reasons fetal MRI can not be established in all hospital and therefore regional/centralised services are needed.

Or 15

Adverse pregnancy outcome in women treated with cervical conization

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Background: The number of cervical conization in women who have not finished their reproductive period has increased as a consequence of delayed childbirth.

Objective: To assess to which extent adverse pregnancy outcome is more frequent in women treated with cervical conization.

Hypotheses: The loss of substance in cervix uteri by cervical conization represents a risk for preterm delivery.

Methods: A cohort study based on 15108 women identified treated with cervical conization in the Cancer Registry of Norway and their births as registered in the Medical Birth Registry of Norway for the period 1967-2003 compared with the Norwegian birth population (2.2 mill deliveries)

Results: In women treated with cervical conization before delivery the proportion of women delivered before 37 weeks of gestation was 18.1% (95% CI 17.45 - 18.71). During the study period there was a decrease in the proportion delivered before 37 weeks of gestation. In women who had a cervical conization the relative risk of delivery before 33 weeks of gestation was 3.6 (95% CI 3.4 - 3.8) and 2.7 (95% CI 2.6 - 2.8) before 37 weeks.

Conclusions: Women with a cervical conization had an increased risk of a preterm delivery, especially before 33 weeks of gestation the risk was increased. Even though there has been a slight decrease in the study period, probably due to change in treatment methods, it still remains a serious clinical problem.

Or 16

Contingent first trimester screening for Down syndrome: A re-analysis of the Copenhagen First Trimester Study

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Background, Objective: Modelling by Monte Carlo simulation has shown that contingent first trimester screening for Down syndrome (DS), where the doubletest (PAPP-A, β -hCG and maternal age) is used to decide whether nuchal translucency (NT) screening is warranted, is a cost-effective organisation of first trimester screening for Down syndrome. This conclusion needs confirmation in a prospective setting.

Methods: Prospectively collected data from 6441 singleton pregnancies with 11 DS pregnancies obtained from the Copenhagen First Trimester Screening Study was used to analyse the performance of contingent testing.

Results: Contingent testing, where women with a DS risk $\geq 1:65$ are offered chorionic villous sampling (CVS) or amniocentesis (AC) directly, and women with a risk between 1:1000 and 1:65 are offered NT screening followed by CVS/AC if the combined (NT+double test) risk is $\geq 1:250$ in week 12, whereas women with a risk $< 1:1000$ are not offered further procedures, was associated with a screen positive rate of 2.2%, a detection rate of 91% and a NT frequency of 25.6%. The cost of the contingent screening program was estimated to be 33% lower than the cost of normal combined first trimester screening, but it still contains the costs of gestational dating by ultrasound.

Conclusions: Contingent screening is a cost-effective alternative to combined first trimester screening for Down syndrome in the setting of a prospective screening program. Contingent screening could be used when access to NT-screening is limited.

Or 17

Benefits and risks of Antiandrogenic progestins in HRT Selective progestins from androgenic to antiandrogenic drospirenone

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The use of androgens in the postmenopause has been suggested for those women with loss in sexual desire but only a few studies have supported this approach in ovariectomized women while estrogen seem to be sufficient to restore libido and sexual activity in postmenopausal women with intact ovaries and uterus. In parallel the development of antiandrogenic progestins has been questioned as its consequences on the libido raising the question of the benefit in selecting antiandrogenic progestins for combined Hormonal Replacement Therapy (HRT). The progestins used for HRT have varying pharmacologic properties depending on the molecules from which they derive. Very small structural changes in these molecules may induce considerable difference in their effects and the development of new generations of progestins to improve their selectivity profiles has been a great challenge. The first progestins were derived from nortestosterone and although low doses were sufficient to induce protection of the endometrium, their androgenic profile led to some negative effects such as acne, oily skin and decrease in the lipoprotein HDL. Under physiological conditions, progesterone is a natural antiandrogen and some progestins derived from 17hydroxy-progesterone or from 19nor-progesterone exert an antiandrogenic activity. These include cyproterone acetate (CPA), the most potent antiandrogenic progestin and by decreasing order of antiandrogenic potency, dienogest, drospirenone (DRSP), norgestrel acetate and trimegestone. Drospirenone differs from classic progestins as it derives from spiroactone. Its major effect is anti-mineralocorticoid. This property leads to decreased salt and water retention and lowering of blood pressure in users of combinations containing DRSP. In addition, DRSP has no androgenic effect but a partial antiandrogenic effect; its potency is about 30% of that of CPA the most potent antiandrogenic progestin. This property shared by a few of the new progestins may counteract the negative action of postmenopausal androgens on hair growth, lipid changes, insulin and possibly body composition. DRSP, which has pharmacodynamic properties very similar to progesterone has been developed as an oral contraceptive: Yasmin® and also as an HRT preparation in combination with oral estradiol (Angeliq® Estradiol 1mg and DRSP 1 or 2mg/tablet). Studies conducted in postmenopausal women have shown symptom control, improvement in quality of life scores with the combined treatment superior to estradiol given alone and good bleeding patterns. No decrease in libido was reported in studies using any of the antiandrogenic progestins when associated with estradiol replacement. Natural progesterone and some of its derivatives such as the 19-norprogesterone molecules or the new molecules DRSP and dienogest do not exert any androgenic effect and have no negative effect on the lipids. These anti-androgenic agents may benefit women who require hormone replacement therapy but have pre-existing androgen-related conditions, such as acne and facial hair, or metabolic risk factors. In studies of combined HRT, certain antiandrogenic progestins did not appear to inhibit the beneficial metabolic effects of estrogen or to have a negative effect on libido or mood. The risk of antiandrogenic progestins such as CPA on the risk of thromboembolism has been questioned when used with ethinyl-es-

tradiol in oral contraceptives. However when used with estradiol no negative effect on clotting factors were observed with CPA or other new antiandrogenic progestins. Although it is likely that the new progestins with antiandrogenic properties may be neutral on the coronary disease risk, this has not as yet been documented by large randomized controlled trials.

Or 18

Significant birth cohort effect on age at natural menopause: a study of 24.000 Danish nurses

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Background: Menopause signifies the permanent cessation of menstruation. Female reproductive aging is of interest due to fertility aspects as well as implications to female health. Early menopause increases the risk of osteoporosis and cardiovascular disease but lowers the risk of breast cancer. The age at natural menopause is influenced by life style and genetic factors but maybe also by endocrine disruptors in the environment.

Objective: To determine the age at natural menopause in different birth cohorts of Danish women in order to explore potential time trends.

Methods: The Danish Nurses Cohort was established in 1993 and re-investigated in 1999, where all Danish female nurses aged 45 years or above received an extensive postal questionnaire including information on reproductive history, life style factors and use of hormones. A total of 24.155 women returned the 1999 questionnaire (response rate 76%). Menopausal status (premenopause, natural, hormonal or surgical menopause) and age at menopause was determined based on cessation of menstrual bleedings, use of hormones, hysterectomy and oophorectomy. Kaplan-Meier survival curves were performed to evaluate the influence of birth year on the age of menopause. Cox proportional hazard models were used to adjust for covariates.

Results: Univariate analyses revealed a significant birth cohort effect on age at natural menopause ($p < 0.0001$). The median age at natural menopause was 50 years in women born before 1930, 51 years in women born 1930-39 and 53 years in women born in 1940-49. The impact of birth year remained significant after adjustment for life style and reproductive factors, which suggests that environmental factors may also play a role.

Conclusion: We find a significant trend of increasing age at menopause by increasing year of birth.

Or 19

Hormone therapy and risk of Ischemic Heart Disease. A Danish National cohort study

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Background: The randomised Women Health Initiative (WHI) Study tested two Hormone Therapies (HT) among women aged 50-79 years old. The aim of the present analyses was to assess the association between hormone therapy (HT) and risk of ischemic heart disease (IHD) in a national cohort study, with focus on the influence of age, duration, regimen, type of progestagen and route of administration.

Methods: We followed 693,710 Danish women aged 51-69 from 1995-2001 free from previous IHD or cancer. Based on central prescription registry daily updated information on HT was available. From the National Registry of Patients 12,997 incident IHD cases (ICD I20-25) were identified. National registers provided information on potential confounders. By Poisson regression analyses rate ratios (RR) with the various HT exposures were estimated.

Results: We found significant interaction ($P=0,0009$) between age and use of HT, implying RR of 1.34(1.21-1.50) for women aged 51-54 on HT compared to never users, corresponding RR for 55-59, 60-64, 65-69 years old were 1.07(0.98-1.16), 1.13(1.04-1.23) and 1.04(0.96-1.14) in multiple analyses. For younger healthy women there was a relation between duration and risk of IHD that could not be demonstrated for older age groups. The risk of IHD seemed higher with continuous combined therapy than cyclic combined therapy, whereas no association with type of progestagen was found. There was little difference between various routes of administration, however a tendency of lower risk with transdermal than oral HT was found.

Conclusion: We found a highest risk of IHD among younger women using HT, possibly influenced by higher risk of IHD with early menopause. We found no indication that progestagens used in Scandinavia have different risk profile than those used in the WHI, but risk may vary with regimen.

Or 20

Mucosal vaccination of the female genital tract-a possibility for future development of STD vaccines

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Background: Sexually transmitted diseases are a major global health problem and interest has focused on development of vaccines against such infections.

Methods: The induction of B-cell immune responses in the genital tract was studied after mucosal vaccination in healthy women. Study subjects were immunised vaginally and orally with the registered mucosal vaccine Dukoral® which contain the highly immunogenic cholera toxin B-subunit (CTB). Specific IgA and IgG antibody responses in genital secretions were evaluated with ELISA.

Results: Three vaginal doses of Dukoral® induced prominent CTB-specific IgA antibody responses in 6 of 7 women whereas only 3 of 7

orally vaccinated women demonstrated genital tract antibody responses. Two vaginal doses of Dukoral® were more efficient than a single dose in generating specific antitoxin responses in cervical secretions. A third dose did not further increase the responses. Twelve months after vaccination, increased antibody levels could still be detected in half of the women who had initially responded to the vaccine. It is well known that sex steroids influence the immune system in the female genital tract. However, exogenously administered steroid hormones did not seem to have any impact on the production of specific antibodies in the genital tract. A majority of women exhibited, regardless of contraceptive method, strong CTB-specific IgA and IgG antibody responses in genital secretions after vaccination.

Conclusion: The study demonstrated that vaginal vaccination effectively induced long-term durable IgA and IgG antibodies in cervical secretions. Our observations may be of relevance for future development of vaccines against sexually transmitted infections including HIV.

Or 21

Real-life Evaluation of the Cost-Benefit of HPV Triaging of ASCUS and CIN I by Randomized Health Care Policy

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Objective: To evaluate whether the predicted cost-benefits of HPV triaging of women with ASCUS/CIN1 can be materialized in a real-life setting.

Methods: All the 15 hospitals in the greater Stockholm area were randomized to either continue with established policy (colposcopy/biopsy of all ASCUS/CIN1) or to implement new policy with HPV-triaging by HPV-testing and colposcopy only of HPV-positive women.

Results and Conclusions: As of 2nd of September 2005, 2487 women had been diagnosed with ASCUS or CIN1; 65% of women with ASCUS and 76% of women with CIN1 were HPV-positive. There was a strong correlation between age and HPV positivity. 84% of women below 32 were HPV positive, whereas 48% of women above 40. All of the women with CIN3 and cancer identified at HPV triaging hospitals were HPV positive. However there were significantly fewer women diagnosed with CIN2+ in the triaging arm than within the control arm. The lower yield of CIN2+ diagnoses was restricted to women with ASCUS below 32. Similar amounts of CIN2+ diagnoses were found by the 2 policies for women with CIN1 at all ages and for women with ASCUS above 32. The HPV triaging policy was found to be more cost-effective, particularly in older age groups. We conclude that HPV triaging below the age of 32 results in limited cost savings and can possibly be unsafe. HPV triaging in older age groups appears to be cost-effective and safe. The exact age at which to recommend for or against HPV triaging may depend on local circumstances.

Or 22

Hormone therapy increases the risk of breast cancer, but not the risk of dying from the disease. The Danish Sex Hormone Register Study (DaHoRS)

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Objectives: To assess the risk of BC in women on different HT regimens, to explore the risk in past users of hormones, and to detect mortality after the BC diagnosis.

Material and methods: All Danish women, 51-69 years old were followed from 1995 through 2002. From the National Register of Medicinal Product Statistics (NRM) a daily update on HT during the eight-year study period was established and linked to the National Register of Patients (NRP) for BC diagnoses.

Results: In total, 785,397 women free of previous malignant diseases were followed for an average of 5.4 years (4.2 million women-years), during which 12,831 incident cases of first ever breast cancer were detected, 2,347 (18.3%) of which died after their diagnosis. Compared to women never on HT, women on current HT aged 51-54, 55-59, 60-64 and 65-69 had a rate ratio of BC of 1.02 (0.93-1.13), 1.47 (1.36-1.59), 1.85 (1.71-2.00) and 1.91 (1.75-2.09), respectively. The risk increased with duration of use, steeper the older the women were. Estrogen-only therapy implied no significantly increased risk of BC in women below 60 years. Long term continuous combined therapy conferred a higher risk of BC than long term cyclic combined therapy. The risk in current users increased significantly and consistently with increasing estrogen as well as progestagen dose. An increased risk of BC in recent users of hormones was after 3-6 months not elevated significantly above the risk of never users of hormones. The case-fatality rate in women who got breast cancer while on HT was 0.50 (0.45-0.57) as compared with women never exposed for HT. The rate ratio of lethal BC in women ever on hormones was 0.81 (0.71-0.92) as compared with women never on HT.

Conclusion: The risk of breast cancer in women on HT is higher on combination therapy than on estrogen only therapy. The risk in past users approaches the risk in never users within half a year after cessation. The risk of lethal BC is not increased in ever users of hormones.

Or 23

Adult granulosa cell tumour of the ovary. A population-based study of 163 women

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Objective: The aim of the study was to evaluate the malignant potential and prognosis of granulosa cell tumour (GCT). GCT is a rare malignancy with hormonal activity, and hence, diagnosis and consensus about operative treatment is difficult to achieve.

Methods: Retrospective, follow-up study including 163 women diagnosed with GCT. The histopathological sections and medical

records were reviewed centrally. Follow-up on data was performed by contacting the patient's general practitioner and the hospital where the patient was admitted. The cause of death was confirmed by death certificate and autopsy report.

Results: The diagnosis of GCT was confirmed in 163 women. The age-standardized incidence of GCT was 1,0 per year pr 100.000 women. FIGO stage I was found in 153 women. The follow-up time of the 163 women was median 12 years (2 month-26 years) and for the 99 surviving women median 15 years (2-35 years). Relapse occurred in 24% (36/153) of women in stage I and 100 % of the other stages. Survival in stage I was 95, 87 and 72 % after 5, 10 and 20 years, respectively. Age at diagnosis was significant associated with longer interval without relapse ($p < 0.002$) and better survival ($p < 0.03$).

Conclusion: The survival rate in GCT is similar to malignant ovarian epithelial tumour. Less extensive operation increases the risk of relapse and death with advancing age. Total abdominal hysterectomy and bilateral salpingo-oophorectomy is the recommended treatment.

Or 24

The association between specific symptoms and pelvic organ prolapse

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Aims of the study: To study the association between prolapse related symptoms and pelvic organ prolapse in specific compartments.

Methods: The study design was a cross sectional study based on a population sample. Four hundred twelve women who had completed a short-form validated questionnaire regarding symptoms of POP combined with questions about age, parity, previous operations for pelvic organ disorders were recruited for clinical examination. Our classification based on the answers to the questionnaire placed 206 in the test positive category while 206 were classified as test negative with regard to symptomatic prolapse. Five validated questions were analyzed regarding urge incontinence, stress urinary incontinence, feeling of a vaginal bulge, vaginal discomfort, manual reduction to complete bladder emptying and if heavy lift aggravated their symptoms. From an additional questionnaire we analyzed questions about bowel functions. These women were invited to an examination by two gynaecologists blinded to the questionnaire responses. The pelvic floor anatomy was defined according to POPQ.

Results: Two-hundred eighty-two women, aged 29-79 years, accepted the invitation, 160 test positive and 120 test negative. The distribution of POP stage >1 (n=141) were as follows: anterior wall 25,5 %, posterior wall 44,7 %, anterior and posterior wall 24,1 %, superior vagina 0,7 % and other combinations 5%. Stress urinary incontinence and urge urinary incontinence were positively correlated with isolated anterior wall prolapse but also with isolated posterior wall prolapse and POP in any compartment > stage 1. Feeling of a vaginal bulge was strongly associated with POP in all compartments.

Conclusion: Urinary incontinence showed association with POP in both anterior and posterior compartment. Vaginal bulge was strongly associated with POP in all compartments. No correlation was found between POP and bowel symptoms.

Or 25

Vanishing twins - a predictor of intrauterine growth retardation in IVF/ICSI singletons

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Background: We have recently shown that the increased risk of preterm delivery and low birth weight in singletons after IVF/ICSI can be attributed to the vanishing twin phenomenon that occurs in 10% of IVF/ICSI singletons.

Objective & hypotheses: To assess the effect of a vanishing twin on the risk of IUGR in the surviving IVF/ICSI singleton and to evaluate the influence of gestational age at onset of spontaneous reduction on IUGR.

Methods: 642 singletons after vanish of a twin gestation (survivor cohort) and 5237 primary singletons were identified. The survivor cohort was subdivided according to gestational age at vanish in 424 early (<8 weeks), 187 intermediate (8-22 weeks) and 31 late (>22 weeks) survivors.

Results: The rate of small for gestational age (SGA) infants was significantly higher in the survivor (5.3%) than in the singleton cohort (3.6%; $P < 0.05$). The rate of SGA babies in the survivor cohort was [12.5%; 7.7%; 3.8%] among late, intermediate and early survivors ($P < 0.02$). In logistic regression analysis with maternal age, parity and child gender, vanish of a co-twin was the only significant predictor of IUGR (OR 2.1 95% CI 1.0-4.3) For term babies (born after 37 weeks) the proportion of low birth weight <2500g (LBW) infants was 3.8% in the survivor vs. 2.3% in the singleton cohort ($P < 0.03$). Further the rate of LBW infants was [18.2%, 6.3%, 2.4%] for late, intermediate and early vanish ($P < 0.01$) and a significant inverse correlation was shown ($r = -0.12$; $P < 0.01$) between gestational age at vanish and LBW in term infants.

Conclusions: IVF/ICSI singletons from vanishing twin gestations have a higher rate of IUGR than primary singletons and the rate of IUGR is inversely related to gestational age at onset of vanish. Thus vanishing twins could have long-term consequences for IVF/ICSI singletons.

Or 26

Neuroendocrine response to intimate partner violence during pregnancy: relation to pregnancy duration and fetal growth

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Background, objective: Intimate partner violence during pregnancy is associated with adverse child outcome like preterm or LBW. The aim was to analyse the neuroendocrine release of cortisol in response to perceived stress among pregnant women exposed to intimate

partner violence in pregnancy as part of the mechanism through which violence may affect the duration of the pregnancy and the intrauterine growth of the child.

Methods: One hundred forty seven pregnant women were consecutively selected in a community based study on violence during pregnancy carried out in León, Nicaragua. Women were interviewed twice during pregnancy. Standardized scales to measure partner violence, social resources, perceived stress and socioeconomic conditions were used. Two saliva cortisol samples were collected per each pregnant woman and drawn am and pm the same day. For analysis multivariate regression and PATH-modelling were applied.

Results: Intimate partner violence during the pregnancy, low social resources and perceived maternal stress were associated with high level of salivary cortisol. Pregnant women having high cortisol values were significantly more likely to give birth to SGA babies and also associated with preterm babies but non-significant. A substantial decrease of birth weight, 121-186 gr, was estimated to be associated with increase in cortisol due to violence exposure.

Conclusion: The results are consistent with the argument that neuroendocrine response to stress is part of the mechanism through which intimate partner violence during pregnancy is associated to adverse child outcomes.

Or 27

Increase matrix metalloproteinase activity from cultured endothelial cells exposed to venous cord plasma from high birth weight newborns

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Background: The causal links between fetal nutritional status and later risk of disease remain obscure. The vascular endothelium is a target in the pathogenesis of cardiovascular diseases. Already at the fetal stage may nutritional status affect the endothelium. Matrix metalloproteinase (MMP) activities are indicators of endothelial activation.

Hypothesis: Umbilical cord plasmas of various-sized infants have different effects on MMP activity in endothelial cultures (HUVEC).

Materials and methods: HUVECs from indifferent donors were exposed for 48 h to 20% venous cord plasma from uncomplicated term pregnancies (caesarean section). The activity (gelatinase) and amount (ELISA) of MMP in HUVEC supernatants were determined. Cord plasma from High Birth Weight (HBW, > 4000g) and Normal Birth Weight (NBW, < 4000 g), infants were compared.

Results: The MMP activity of HUVECs exposed to HBW-plasma was nearly 3 times higher compared to that obtained by NBW-plasma. The difference was attributed to MMP-9, and not MMP-2, since protein amount and gene expression were increased only for MMP-9. The increased MMP activity and mRNA expression of MMP-9 could be inhibited by about 70% using specific MMP inhibitors and siRNA, respectively. Cord lipid levels were similar among the two groups.

Conclusion: Cord plasma from HBW newborns induced more MMP-9 activity in HUVECs compared to plasma from NBW infants. Although not identified, cord plasma of HBW infants may specifically contain MMP-activators which in turn are related to nutritional status in utero.

Or 28

Melatonin reduces inflammation and cell death in white matter in the 0.65 gestation fetal sheep

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The premature infant is at increased risk of cerebral white matter injury, often referred to as periventricular leucomalacia, PVL. There is an urgent need for development of a neuroprotective strategy for PVL. Melatonin is neuroprotective in adult models of focal cerebral ischemia and it also attenuates ibotenate-induced white matter cysts in neonatal mice. Clinically, melatonin has been used to treat sleep disorders in children and no major side effects have been observed. The aim of this study was to investigate the possible protective and anti-inflammatory effects of melatonin in the immature brain following intrauterine asphyxia. Fetal sheep at 90 days of gestation were subjected to 23.5 minutes of umbilical cord occlusion. Melatonin (n=9) or vehicle (n=10) was administered intravenously starting 10 min after the start of reperfusion and continued for 6 hours. Four days after the insult, fetal brains were examined for morphological injury, amoeboid microglia cells and TUNEL-positive cells were counted. In the melatonin treated group, there was a reduction of activated microglia cells and TUNEL-positive cells suggesting a protective effect of melatonin. In conclusion, this study shows that melatonin attenuates the increase in activated microglia and TUNEL-positive cells in the cerebral white matter following intrauterine asphyxia in midgestation fetal sheep.

Or 29

Baseline blood pressure (BP) and maternal body mass index (BMI) : Association with late onset preeclampsia (LatePE) and non-proteinuric pregnancy induced hypertension (NonPPIH), but not with early onset preeclampsia (EarlyPE)

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Background/Hypothesis: EarlyPE may constitute a pathogenic entity different from LatePE and NonPPIH.

Objective: To investigate risks of various forms of pregnancy induced hypertension (PIH) in relation to first trimester BMI and BP.

Methods: 4025 Caucasian pregnant women in a prospective cohort study. EarlyPE and LatePE was defined as proteinuric PIH with delivery < or ≥37 wks gestation, respectively.

Results: 1. trimester BMI and systolic BP (SBP) were associated with risk of LatePE and NonPPIH, but not EarlyPE (adj. for each other and age, parity and smoking):

	EarlyPE OR(95%CI)	latePE OR(95%CI)	NonPPIH OR(95%CI)
1.trimBMI			
≤20	1.0	1.0	1.0
20-25	0.9(0.3-10.7)	4.5(1.1-18.9)	1.9(0.8-4.4)
25-30	0.6(0.1-3.5)	5.7(1.2-25.9)	3.2(1.3-8.0)
>30	1.9(0.3-10.9)	8.1(1.5-43.2)	4.8(1.8-12.8)
p trend	0.83	0.01	0.001
1.trimSBP*			
Q1**	1.0	1.0	
Q2	1.6(0.4-5.7)	1.2(0.4-3.5)	1.0***
Q3	0.6(0.1-3.3)	2.5(1.0-6.6)	4.8(2.0-11.2)
Q4	1.8(0.5-6.0)	3.2(1.3-7.8)	12.8(6.0-27.0)
p trend	0.56	0.002	0.001

*Similar results for diastolic BP;** Q=quartiles; ***Reference group: Q1+2

Conclusions: We have previously reported that women with EarlyPE and LatePE differ metabolically already in early second trimester (BJOG 2001). The present data support the notion that EarlyPE and LatePE represent at least partly different entities.

Or 30

Apoptosis in human umbilical vein endothelial cells induced by preeclamptic serum can be attenuated by addition of either folic acid or N-acetylcysteine

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Background: Preeclampsia complicates 2% of all pregnancies, and it is a major cause of maternal and perinatal morbidity and mortality. The cause of the syndrome remains to be fully elucidated, but endothelial dysfunction is a central event in the maternal disease. Endothelial dysfunction founds several of the clinical manifestations of the syndrome e.g. hypertension, proteinuria, oedema and increased coagulation. Clearly, the basis of the endothelial dysfunction has to be investigated to understand the pathogenesis and to optimize potential therapeutic intervention.

Objective and hypothesis: In preeclampsia, several of the blood-components that are involved in mediating endothelial dysfunction, could potentially also induce apoptosis. We hypothesised that increased apoptosis of the maternal endothelium could be a cause of the wide-spread endothelial dysfunction seen in advanced preeclampsia.

Methods: We stimulated Human Umbilical Vein Endothelial Cells (HUVECs) with serum from preeclamptic and healthy pregnancies. Apoptosis was monitored by Hoechst staining, immuno analysis and caspase 3-assay. Involvement of the NF-κB pathway was determined using a luciferase reporter-assay.

Results: Preeclamptic serum induced increased apoptosis in HUVECs and activation of NF-κB compared to addition of healthy pregnancy serum. Furthermore, the apoptotic effect induced by preeclamptic serum was enhanced when co-stimulating with neutrophil granulocytes. In contrast, addition of either folic acid or N-acetylcysteine attenuated the apoptotic response induced by preeclamptic serum.

Conclusion: These results suggest that apoptosis in endothelial cells is a specific mechanism involved in the endothelial dysfunction in late preeclampsia. Additionally, both folic acid and N-acetylcysteine seem to have beneficial effects on endothelial stability.

Or 31

Longitudinal reference ranges for flow velocities and waveform indices of the ductus venosus

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Background: Serial Doppler measurements of the ductus venosus are suggested as part of the monitoring of growth-restricted fetuses. However, reference values for flow velocities and waveform indices are based on cross-sectional studies and less suitable for the purpose.

Objective: To establish longitudinal reference ranges for ductus venosus flow velocities and waveform indices and provide the necessary terms for calculating conditional reference ranges for serial measurements.

Methods: A total of 160 low-risk pregnancies were recruited to a longitudinal study after written informed consent. Starting at 20-22 weeks of gestation, pulsed Doppler ultrasound was used to record the ductus venosus blood flow velocities at monthly intervals. Statistical analysis included regression analysis and the use of multilevel modeling.

Results: With a success rate of 93% 547 measurements (4-5 in each fetus) were used to establish the reference ranges. The time averaged maximum velocity was 50.3 cm/s at 21 weeks of gestation, increasing to 59.8 cm/s at 32 weeks and remaining stable towards term. The peak-systolic velocity increased from 59.3 cm/s at 21 weeks to 71.4 cm/s at 31 weeks, followed by a slight decrease towards term. The diastolic velocity showed a continuous increase from 31 cm/s at 21 weeks to 42.6 cm/s at 40 weeks. The pulsatility index for veins decreased from 0.57 at 21 weeks to 0.44 at 40 weeks.

Conclusion: The new reference ranges reflect the development of the ductus venosus blood velocities and velocity indices during the second half of pregnancy and are thus appropriate for the serial measurements required when monitoring growth-restricted fetuses.

Or 32

Metformin reduces pregnancy complications in PCOS women - Could increased flow in the uterine arteries be an explanation? - Results of a prospective, randomized, double-blind study

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Background: Metformin seems to reduce pregnancy complications in PCOS women. Neither changes in androgen levels, CRP nor indices of coagulation seem to explain this. It has also been shown that metformin passes freely over the placenta. Reduced uterine artery blood flow predicts pregnancy complications such as PIH and PE at midgestation.

Objective and hypothesis: Our aim was to investigate the changes in blood flow of the uterine artery in PCOS women treated with metformin or placebo. We hypothesized that metformin would decrease the pulsatility index (PI) in the uterine artery leading to increased blood flow to the placenta.

Methods: A prospective, randomized, double blind, placebo controlled clinical intervention study. Forty women, 18 - 40 years with PCOS, and with singleton pregnancies were included at gestational week 8 (in average). Patients were treated with metformin 850 mg twice daily or identical placebo capsules from inclusion until delivery. PI of the uterine artery was measured (under standardized circumstances) at gestational week 12, 19, 24, 32 and 36.

Results: Women randomized to metformin had higher PI at week 12 than those in the placebo group. The PI was significantly more reduced in the metformin group than in the placebo group at week 19 and week 24.

Conclusions: Metformin seems to improve uterine artery blood flow from week 12 to week 24 in pregnancy. This could possibly explain the reduction of pregnancy complications in pregnant PCOS women. If our results can be confirmed in larger studies, this could be important in understanding metformin action and pathophysiology of pregnancy complications in PCOS women.