

elements in peritoneal fluid compartment may influence on disturbances in signal transduction.

278 Women's absence from work following hysterectomy. Results from a substudy in a randomised controlled trial.

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Background: Since 2000 an accelerated regime with focus on optimised patient information, refined anaesthetic techniques, multimodal analgesia, antiemetics, early mobilisation and oral nutrition has been used for all women referred to Hvidovre Hospital for a hysterectomy. As a result of this program, the length of hospital stay has been reduced. Recommendations for sick leave after hysterectomy are not evidence-based, but we chose to recommend a convalescence period of 14-21 days. The aim of this substudy was to estimate women's absence from work and to identify factors predicting a prolonged convalescence.

Methods: This substudy was a part of a randomised trial that included 59 hysterectomised women. They received a questionnaire 14 days after discharge about their need for health care counselling, experience of complications, self-estimated health, physical well-being and expectations about resumption of work and sexual life. Data about absence from work was obtained by phone calls three months after discharge from those currently employed (n=49).

Results: The median postoperative hospital stay was 1.5 days. The median recommended sick leave was 21 days, whereas the median actual absence from work was 28 days ($p < 0.01$). A longer period of absence than recommended was needed by 42% of the women, 12% stated that they managed with less than recommended and in 44% the recommended sick leave was suitable (response rate: 87.8%). The length of absence from work was independent of the type of hysterectomy. The sick leave was significantly longer in case of complications, poor self-estimated health, physically strenuous work, and estimation of the recommended sick leave as unrealistic.

Conclusions: After an uncomplicated hysterectomy women with physically non-strenuous jobs should have a recommended sick leave of 21 days. The results underline the necessity of an individualised recommendation for sick leave depending on the patients' self-estimated health, type of work and experience of complications.

279 Medical management of first trimester spontaneous abortion with a single dose of misoprostol

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Background: The efficacy of medical treatment of spontaneous abortion depends on the regimen and may depend on the ultrasonographic findings. The aim of this study was to estimate the efficacy of vaginal misoprostol for medical management of different types of spontaneous abortions.

Methods: A retrospective study based on a review of consecutive patients treated for a spontaneous abortion during the period December 2001 to August 2003. The medical regimen was 400 µg vaginal misoprostol followed by vaginal sonography after one, two or three days. The treatment was considered successful if a complete abortion (endometrial thickness ≤ 15 mm, no gestational sac and acceptable bleeding) was diagnosed at follow-up and no later evacuation was performed.

Results: The overall success rate was 38.1% (113/297) (95% CI: 32.5%-43.6%). Similar success rates were found after missed abortion and anembryonic pregnancy. The success rates were unaffected by the ultrasonographic size of the gestational sac or the embryo. However after blighted ovum (mean width of empty gestational sac ≥ 18 mm) the success rate was significantly lower day one (14.8%) (4/27) compared to day two and three (41.0%) (16/39), $p < 0.05$. In other types of spontaneous abortions the success rates were identical day one, two and three.

Conclusions: Medical management of spontaneous abortion reduced the need for surgical evacuation. Extending follow-up from one to two or three days increased the success rates of blighted ovum. The success rates of other ultrasonographic diagnoses were unaffected by the time of follow-up. The success rate may increase with larger doses of misoprostol or with a longer expectation time.

280 Physical therapy in the management of dyspareunia and vulvar vestibulitis syndrome

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Background: Vulvar vestibulitis syndrome (VVS) is an important cause of dyspareunia. The etiology and risk factors for VVS have been poorly defined. Therefore, the management of VVS patients is problematic. VVS is often associated with dysfunction of the pelvic floor muscles also known as vaginismus. The main goal of physical therapy is to rehabilitate the pelvic floor by increasing awareness and proprioception of musculature, by improving muscle relaxation, by normalizing muscle tone, by increasing elasticity of tissues at the vaginal opening and by desensitizing the painful area.

Methods: We systematically used physical therapy in the management of 52 patients referred to our Vulva Clinic because of severe VVS. VVS was diagnosed by uniform clinical criteria, and all patients had severe VVS. Physical therapy consisted of biofeedback, electrical stimulation and desensitization. The mean number of sessions was 7 (range 1-20). The sessions took place first at weekly intervals, subsequently at 3-4 weeks intervals. The mean duration of physical therapy was 3 months. Each session lasted approximately 1 hour.

Results: All except 1 patient learned to relax pelvic floor muscles. The resting pelvic floor muscle tension decreased from 23 μ V (range 13-48) to 10 μ V (2-22). Pain sensation was evaluated by visual analogic scale (VAS) which decreased from 7 (5-9) to 3 (1-9). of the 52 patients 34 (65%) had experienced sexual intercourse. of the 34 patients 23 (68%) experienced no dyspareunia.

Conclusions: VVS is a neglected and poorly understood cause of dyspareunia. Rehabilitation of the pelvic floor muscles by systematic physical therapy is a promising first line treatment modality for severe dyspareunia caused by VVS.

281 Infertility and subfertility in Norwegian women Results from the HUNT – study (Health Survey of Nord-Trøndelag)

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Background: Women's reproductive health has traditionally received little attention in large scale health surveys. Fertility patterns based on estimation of live birth in populations does not take into account the aspect of voluntary or involuntary childlessness neither infertility problems. The aim of this study was to estimate the magnitude of infertility problems in a general population and assess the sociodemographic correlates.

Methods: The total population of Nord-Trøndelag country (aged 20 and above) was invited to a health screening study between 1995-1997. The participants were asked to complete a questionnaire before attending the screening. Women were then additionally asked to complete a questionnaire on reproductive health. Women aged 50-69 were included in this study.

Results: Responder rate was 87 %. of the 10 359 participating women, 687 or 6.6 % reported infertility problems ("tried to become pregnant for more than a year without succeeding"). of these 183 (26.6 %) reported to be nulliparous, (1.8 % of all women). Proportionally more women reported infertility problems in the youngest age group (8.7% among women aged 50-54 compared to 5.0 % among women aged 65-69). High education was significantly associated to the reporting of infertility problems, also adjusted for age.

Conclusion: Infertility problems are common and seems to be increasing. A high proportion of these women remain nulliparous past their reproductive age.

282 Ultrasonographic findings in spontaneous abortion – relation to normal and abnormal karyotypes

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Background: Studies of the chromosomal constitution of first trimester spontaneous abortion have revealed that at least 50% of the abortions have an abnormal karyotype. There is no consensus as to whether endovaginal ultrasonographic findings can be used to predict the probability of abnormal karyotype in spontaneous abortions.

Methods: During the period October 1996 to June 1998, all women in Uppsala County, with a diagnosis of first trimester miscarriage, attending the Department of Obstetrics and Gynaecology, Uppsala University Hospital were recruited for the study. Inclusion criteria were a gestational age between 6 and 12 completed weeks, based on the first day of the last menstrual period, and a positive urine pregnancy test. Miscarriage was diagnosed after clinical examination, including endovaginal ultrasound. In cases where pregnancy structures (a gestational sac with or without embryo) could be identified at the time of diagnosis, a dilatation and curettage was performed. 576 women (578 embryos) were included in the study, among which 84 cases at the time of diagnosis were considered as complete spontaneous abortions. In 259 cases chromosomal analyses was possible and successful.

Results: of the chromosomal analyses, 100 cases revealed a normal karyotype and 159 cases an abnormal karyotype. Abnormal karyotypes were significantly more often found in cases where endovaginal ultrasound revealed an embryo smaller than expected, according to gestational length, $p < 0.05$.

Conclusion: More than half of the chromosomal analyses revealed an abnormal karyotype. Endovaginal ultrasound findings can be used to predict the probability of a chromosomal cause of a spontaneous abortion.

283 Sexuality education attitudes in Latvian schools

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Objectives: To investigate sexuality education in comprehensive schools of Latvia and to find out attitudes of different state authorities, parents and schoolchildren of pubertal age towards the investigation of menstrual cycle.

Methods: Meeting with state authorities, parents, adolescent girls. Organizing discussions in order to evaluate the overall attitude towards sexuality education in schools and investigation of menstrual cycle.

Results: Head of Education, Youth and Sports department considered filling bleeding cards as a project that “negatively influences adolescent girl psychological comfort”. Head of Riga Council indicated that such a project is “too intimate to be ever carried out in school settings”, whereas the Minister of Education and Science of Latvia –the highest instance to appeal- advocated and appreciated such a project that “promotes adolescent health education”. Some school teachers expressed their attitude as “I would never let such a intimate project through my hands. That would signify I favour that!” Several parents of adolescents wondered why to tell about “such things”. The most positive attitudes came from adolescents themselves, who told “at least there is a project that helps to realize that puberty occurs to everybody”.

Conclusions: Attitudes of leading Latvian authorities towards investigation of normal development in adolescents was surprisingly negative. State officers incompetence in health issues explains the insufficiency of the whole system in adolescent sexuality education. Family plays the most important role in adolescent health and sex education. However, family position is often narrow-minded, even in spite of information accessibility and opportunities of self-education. Radical changes in the field of sexuality education seem not to occur unless the government policy in public health education change. Positive attitudes towards normal phenomena and ability to talk freely about sexual development has to be the target.

284 Surgery after endometrial ablation and prognostic factors.

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Background: Treatment of meno-/metrorrhagia with endometrial ablation has a varying rate of success. Identification of women suitable for local treatment of the endometrium is a challenge. The aim of this study was to identify factors associated with treatment success or failure at long-time follow up.

Methods: Prospective standardised registration of data on 276 consecutive ablations performed from January 1, 1995 to December 31, 1998. Follow-up data were obtained from the National Case Registry (LPR). Mean follow-up time 6,25 years (range 4,5-8,5 years). Statistical analysis was performed using logistic regression.

Results: In the four-year period 261 women had 276 ablations. Mean age was 45 years (range 28-59 years). Two hundred and fifty six ablations were combined resection and rollerball treatment, 17 resection alone, and three rollerball

alone. Haemorrhage during operation led to acute hysterectomy in one patient (0,4%). A total number of 44 women (17%) had a second ablation (41 women had two ablations, three women had three ablations). Five women (2%) had a hysterectomy performed after diagnosis of complex hyperplasia/atypia. At follow-up 45 women (17%) had a hysterectomy; nine of these women had two previous ablations. When using backward logistic regression we identified two independent factors prognostic for treatment failure leading to re-operation or hysterectomy: age and submucosal fibroids (type 1 or 2). When testing for the effect of age a statistical significant inverse association was observed, regression coefficient 0,84, 95% CI [0,79-0,90] $p < 0,0005$. Presence of submucosal fibroids led to a two-fold increase in re-operation rate OR 2,23, 95% CI [1,15-4,3] $p < 0,02$. Rates of repeat ablation were affected by inexperienced surgeons OR 3,39, 95% CI [1,26-9,14] $p < 0,02$. Endometrial thinning agents and obesity had no statistical significant effect on re-operation rates in this study

Conclusions: The study showed that a young age at first ablation as well as submucosal fibroids were prognostic for treatment failure leading to new surgery.

285 Skills training of obstetric registrars

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Background: Aims: Introduction of skills training and evaluation of the programme at a compulsory course for obstetric registrars. Six skills (vaginal delivery of breech presentations, shoulder dystocia, ventouse delivery, amnion infusion, foetal blood sampling and handling of postpartum haemorrhage) were trained with systematic programmes and delivery manikins.

Material and methods: Participating registrars: 44. Questionnaires including registrar's self-assessment of confidence distributed before and after training. Statistical methods: Mann-Whitney test.

Results: Self-assessment scores before and after training were: Vaginal delivery of breech presentations: median 2 versus 4 – mean 2.23 versus 3.45. Shoulder dystocia: median 3 versus 4 and mean 2.53 versus 3.68. Ventouse delivery: median 4 versus 4 and mean 4.0 versus 4.25. Amnion infusion: median 1 versus 4 and mean 1.84 versus 3.95. Foetal blood sampling: median 4 versus 5 and mean 3.81 versus 4.43. Postpartum haemorrhage: median 4 versus 4 and mean 3.58 versus 4.0. Among the registrars 84 % reported lack of obstetric skills training during their previous clinical training. Before training the skills ‘vaginal delivery of breech presentations’, ‘shoulder dystocia’ and ‘amnion infusion’ had low scores and appeared not related to the amount of months the registrars had been working in the speciality. ‘Ventouse delivery’, ‘foetal blood sampling’ and

'postpartum haemorrhage' scored high before training, and appeared to increase with the number of months the registrars had been working in the speciality.

Conclusion: The changes in median self-assessment before and after training were statistically significant for all skills except ventouse delivery and foetal blood sampling, indicating that a systematic skills training of obstetric registrars is effective.

286 No difference in responsiveness to a low dose of alcohol between healthy women and men

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Background: The purpose of the current study was to examine gender-related differences in alcohol responsiveness by comparing the effect of a low dose intravenous alcohol infusion upon saccadic eye movements, self-rated sedation and intoxication scores.

Methods: The functional sensitivity to a low dose of alcohol in twelve healthy women and twelve healthy men was evaluated by comparing the effects of an intravenous alcohol infusion on a number of saccadic eye movement measures, including saccadic eye velocity (SEV), saccade latency, saccade accuracy, saccade deceleration, and self-rated levels of intoxication and sedation.

Results: The infusion of a low dose of alcohol induced a decrease in SEV, and increased saccade deceleration, and self-rated scores of intoxication in both males and females. Saccade accuracy was also significantly deteriorated by alcohol in both groups. The alcohol infusion did not induce any main gender-related differences in the saccade or visual analogue scale measurements.

Conclusions: According to the findings of the present study, no gender differences in the responsiveness to a low-dose alcohol infusion were found.

287 The incidence of ectopic pregnancy in Finland, 1995-2000

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Background: The change in the incidence of ectopic pregnancy (EP) in Finland showed an epidemic in the 1980's and a levelling-off from the early 1990's. Following to that the aim of the present study was to continue the evaluation of the incidence of EP during years 1995 to 2000.

Methods: The data from Hospital Discharge Register and Social and Health Organisation (STAKES) considering the

number of EP, miscarriage, pregnancy termination and delivery was analysed from 1995 to 2000. The incidence of EP was calculated per 100 pregnancies, 100 deliveries and 100 000 women aged 15 – 44 years and presented also in 5-year age-specific rates.

Results: During all the studied years the total incidence of EP was declining. In 1995, 1345 ectopic pregnancies was diagnosed in Finland while the corresponding figure was 851 in 2000. In 1995, there were 2.2 EPs per 100 deliveries and 1.7 EPs per 100 pregnancies and in 2000 the corresponding figures were 1.5 and 1.2, respectively. The total incidence of EP declined from 127.8 to 83.8/100 000 women. A decline of the incidence of EP was found in all 5-year age groups except in women aged 15 – 19 years where in 1996 and 1998 a slight increase was found.

Conclusions: A continuation in a declining trend of the incidence of EP which began in the early 1990's can recently be observed in Finland up to 2000.

288 The incidence of hysterectomy in Finland, 1987-2000

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Background: There has been quite a lot discussion about the incidence of hysterectomy between Nordic countries. The Finnish hysterectomy rates have been accused because they have been almost double compared to e.g. Swedish rates. In the present study we describe the trend and recent figures of hysterectomy in Finland and face the possible reasons for changes in these figures.

Methods: The data considering different types of hysterectomy for benign indication was obtained from the Finnish Hospital Discharge Register during years 1987 – 2000. The annual incidences of hysterectomy were counted by 100 000 women and presented also in 5-year age-specific rates. The relative changes were compared to the index year 1988.

Results: The total incidence of hysterectomy in Finland increased from 340 to 457/100 000 women during years 1987 – 1998. Since that a slight decline in the incidence has occurred and in 2000 it was 429/100 000 women. In all studied years the incidence was highest in women aged 45-49 years. Since 1988 the incidence has increased especially in women over 55 years (up to 79 years). Compared to the year 1988 the risk of hysterectomy was 2.1 in women aged 55-59 years in 2000 while among women aged 30-49 years the risk was varying from 0.7 to 0.9.

Conclusions: During the studied years the risk of hysterectomy was increased especially in women over 55 years which may reflect the increased use of hormone replacement therapy and a desire to obtain a bleeding free treatment. However, in the total incidence of hysterectomy a slight decrease was observed since 1998.

289 Sexual health service for adolescents in Internet

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Background: www.seksuaaliterveys.org -site was published in October 2001. The goal of this service is to improve the capability of adolescents to take care of their sexual health and also to provide consultation for those professionals who work with adolescents. By this service we reach even those who live in remote areas.

Methods: Virtual counselling gives the possibility to ask anonymously whatever one wishes to know about sexuality. All the answers are carefully considered in a multi-professional team and all professionals have long experience of sexology. The questions and answers are in an open file available to all who visit the sites. Internet services includes also the possibility for a free of charge anonymous appointment of sexual counselling, One-to-one chat in Internet. Monthly we have approximately 3500 visits and 150-200 questions. There are approximately 20 One-to-one -sessions per month. In 2002 we received questions equally from boys and girls. 100 questions of girls and 100 questions of boys were analysed regarding content.

Results: The most frequently asked questions were about anatomy, body and different symptoms (boys 66 %, girls 36 %). Girls (32%) wanted to know much more than boys (6%) about sexual health services and medicines. Girls also asked more about pregnancy (girls 27%, boys 4%) and contraception (girls 24%, boys 14%) than boys. Boys were more interested about masturbation (boys 17%, girls 4%) and performance pressure (boys 21%, girls 10%) than girls.

Conclusions: The Internet service is a needed and used way to give and get advice and information about sexuality and sexual health. The Internet service has the lowest threshold, and is a useful complement to phone services and visits, which often follows later.

290 Effects of a monacaprין-hydrogel on the vaginal mucosa and bacterial colonisation

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Background: Hydrogels containing 1-monoglycerid of capric acid (monacaprין) are potent inactivators of sexually transmitted viruses and bacteria in vitro. Monocaprins are widely found natural food substances and are not inactivated in an acid environment. This study was done to investigate tolerance of an intravaginal monacaprין hydrogel and its effect on the vaginal microflora.

Methods: In all 48 women seeking early pregnancy termination were randomised to receive either 5 ml intravaginal monacaprין or placebo hydrogel after informed consent. Vaginal swabs were taken to assess lactobacilli semi-quantitatively and detect bacterial vaginosis (Thomasson and Nugent criteria). A questionnaire was filled out detailing vaginal discharge and discomfort after application. There were two study phases: 20 women where gel was given 3-5 days before suction TOP and sampling repeated before the operation and 30 where gel was inserted by the woman 7-10 hours before preoperative sampling. In this group there was additional sampling for GBS and E.coli. Two women did not apply the gel (one each active substance and placebo).

Results: A short burning sensation or itching was experienced by 10 women in the monacaprין and two in the placebo group ($p=0.02$) and vaginal discharge in a chlamydia-infected woman receiving placebo. There were no other adverse effects. Half of each group had bacterial vaginosis. In the first phase there was no change in lactobacilli quantity nor an effect on vaginosis. In the second phase bacterial vaginosis was less evident in 5 cases, while others were unchanged. In one case quantity of lactobacilli diminished. Four women had GBS, three at the later sampling and one only at the first. No effect was seen on yeasts.

Conclusion: Monocaprין gel produces mild, shortlived discomfort in almost half the women and did not affect normal vaginal flora or bacterial vaginosis in this group of women.

291 Assessment of somatic p53 loss and gain in endometriosis using quantitative real-time PCR

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Background: Endometriosis is the presence of endometrial glands and stroma outside the uterine cavity and musculature. The disease is essentially benign, but shares some common features with cancer. To investigate aspects of this, the frequency of somatic DNA alterations involving the tumor suppressor p53 locus (17p13;exon 1) was determined.

Methods: Subjects treated for endometriosis in Iceland ($n=26$) and USA ($n=45$) were studied. The Icelandic cases included paraffin-embedded tissue from 19 affected matched endometriosis cases and 7 unaffected endometrial controls. The USA cases consisted of fresh surgical tissue from 17 matched endometriosis cases and 28 unaffected controls. DNA isolation and PCR using the Taqman assay were done to quantify the number of copies present at both the p53 tumor suppressors and GAPDH (16p; control) gene locus.

Results: For the endometriotic tissues the mean normalised p53 values were 1.16 (Icelandic cases) and 3.46 (USA cases) copies/reaction. Significant differences were observed between 1) normalised p53 values in the control blood and affected tissue for the USA samples ($p=0.008$); 2) endometriosis cases from Iceland and USA ($p=0.007$); but not 3) normal endometrium from Icelandic and USA samples ($p=0.7$).

Conclusions: In agreement with previous studies it appears that similarly to what can be seen in cancer, somatic p53 alterations/instability may be involved in the pathogenesis of endometriosis. The data support that underlying genetic mechanisms may be influenced by environmental/ population factors.

292 Vulvovaginal candidiosis - a mainly hidden problem for the gynaecologist, including many remaining diagnostic and therapeutic problems

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Background and objectives: Vulvovaginal candidiosis (VVC) and such recurrent infections (RVVC) is generally believed to be common and easily diagnosed and treated. To explore the epidemiology of genital candida infections by studying the consumption of antifungal drugs aimed for treatment of VVC/RVVC by analysing data from all prescriptions and all over-the-counter (OTC) products sold in a Swedish county over a ten-year-period. To study the value of diagnostic methods to detect various candida species in genital samples of women, referred with the diagnosis of RVVC (i.e. having had at least 4 attacks previous year).

Material and methods: The database of Apoteksbolaget was used for the antifungal drug consumption studies. A large number of factors that might have influenced the consumption pattern, were also investigated. Introital and vaginal samples from 113 women with a history consistent with RVVC, were studied by microscopy of stained smears and wet mounts. Cultures were made on Sabouraud and chromogenic agar and tested by a PCR assay. History was uniformly taken with regard to a large number of parameters.

Results: Of the antifungal products sold, 93% were purchased as OTC products. Many of the remaining 7 % of the sales were purchased by prescriptions made by midwives. There was a 20% increase and then after a 20 % decrease in the sales volumes over the study period. At the peak, the annual sales volume could have been enough to distribute one package to every fourth woman in childbearing age in the county. There was a correlation between the amount consumed per woman and the population density in the (33) municipalities in the county. The same pattern was not found for the overall consumption of medical drugs. Neither the number of pharmacies (all state-owned and the only ones allowed to sell the drugs under study and which

register every drug sold) and their exposure of OTC products, nor the number of inhabitants and health providers in the county, could explain the great changes in the antifungal consumption. Chromogenic agar could directly identify as to species all candida strains isolated as judged from the outcome of biochemical tests and an automatic speciation system. PCR missed some culture-positive patients, but was, on the other hand, the only positive test in another small number of cases. Dilution of samples resulted in a few more PCR positive cases. Roughly half of the suspected RVVC cases remained candida negative even after extensive laboratory tests. Those being negative were significantly more often consumers of yoghurt, but did not differ in a large number of other characteristics.

Conclusions: The gynaecological society has very little insight in the extent of the VVC/RVVC epidemiology, as self-treatment is dominating. The diagnosis is wrong in up to half of cases of RVVC, even when 'diagnosed' by gynaecologists. What the candida-negative 'RVVC' cases suffer from is still unknown.

293 Catheter-directed thrombolysis for the management of postpartum deep venous thrombosis

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Background: Catheter-directed thrombolysis that removes thrombus and restores patency of the veins appears to be a safe and effective management of acute deep venous thrombosis (DVT). It has been shown to reduce long-term post-thrombotic morbidity and improve quality of life. Pregnancy and postpartum period are generally considered as contraindications for thrombolysis. However, catheter-directed thrombolytic therapy of DVT may reduce long-term sequelae in these young patients by restoring the patency of veins. The purpose of this pilot study was to evaluate the efficacy of catheter-directed thrombolysis in treating acute symptomatic postpartum DVT.

Methods: Patients enrolled had symptomatic acute DVT (< 3 weeks duration) within 42 days of childbirth. Thrombolysis was performed using a recombinant human tissue plasminogen activator, Alteplase 5 mg IV bolus followed by an infusion at 0.01mg/kg/hr for next 20-24 hours. Unfractionated heparin 5000 IU bolus followed by 300 IU/kg/24 hour was infused concomitantly into an arm vein. Fibrinogen and Cephotest were obtained every 6 hours and maintained at >1g/L and between 50 -70 sec, respectively by adjusting heparin and Alteplase infusion. Venography was repeated after 20-24 hours and angioplasty (\pm stenting) was performed if stenosis was present. In case of partial thrombolysis infusion was continued for a maximum of 96 hours. Lysis

was considered complete if there was less than 5% residual luminal area narrowing. The treatment was considered successful if there was complete or partial resolution of lower extremity pain and oedema, and recanalization of vein with less than 30% residual luminal area narrowing. Following thrombolytic therapy, patients were fitted with graduated compression stockings, anticoagulated with oral warfarin for one year (or lifelong in case of stent implantation).

Results: Five women with postpartum DVT (four iliofemoral DVTs, and one renal and ovarian vein thrombosis on the left side) had catheter-directed thrombolysis. The treatment was successful in all four cases of iliofemoral DVT and symptom relief achieved in all five cases. However, despite partial thrombolysis and restoration of some flow in the patient with renal and ovarian vein thrombosis, the renography performed one month later showed absent left kidney function.

Conclusion: Where expertise exists, endovascular therapy consisting of catheter directed thrombolysis with angioplasty and stenting in selected cases could be considered as a primary therapeutic procedure in patients with acute postpartum DVT.

294 Management of Menorrhagia with MIRENA®-LNG-IUD: A Retrospective Study

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Objective: To estimate the efficiencies of progesterone intra-uterine releasing at stabile dose through Mirena®-LNG-IUD in women with uterine fibroids, associate with menstrual disorders. A secondary objective was the contraceptive performance.

Methods: During 2002-2004, 143 insertions were performed in fertile women aged between 31-44 years for treatment of menorrhagia – 103 cases (72,03%) with uterine fibroids (clinical/ultrasonographic confirmed) and for contraceptive purposes – 40 cases (27,97%); patients were followed-up at 1-3-6-12-24 months following insertion.

Results: After 2-3 months of treatment, women with menorrhagia has reported a significantly improvement of catamenial characteristics [regularly cycles (78,64%), greatly reduced bleeding (90,29%) and extinction of dysmenorrhoea (100%)]. After 4 months we observed by ultrasound that for 71 of the patients (68,93%), the dimension of fibroid and of the uterus was reduced, in average by 10-17%. Hormonal side effects such as mood-changes, headache, sleepiness and mastalgia were reported at 6 patients (4,20%). All insertions were successfully. Neither complications (infection, expulsion or perforation) nor pregnancies occurred. The Mirena®-LNG-IUD was well tolerated by all patients. We suggest that LNG intrauterine releasing is capable of reducing the size of the myomas in reproductive aged women. As

a result, the LNG-IUD is a very useful, effective, non-surgical and reversible treatment of idiopathic menorrhagia and prevents menorrhagia-related anaemia (the most common cause of anaemia in fertile women).

Conclusions: Our study suggests that LNG-IUD has great rates of removal for amenorrhoea, reduce bleeding and PID episodes. Strong endometrial suppression is the principal mechanism explaining the effect on menstrual blood loss and the contraceptive performance. Mirena® is a fertility-conserving alternative to both hysterectomy and endometrial resection, even if the uterus is enlarged (17 women with adenomyosis hysteroscopic confirmed) or in the presence of small intramural and sub-serous fibroids. LNG-IUD may be a highly attractive cost-effective treatment option to many women and avoid the high cost of surgery and other invasive treatment procedures.

295 Adiponectin gene haplotype is associated with preeclampsia

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Objective: We determined whether the polymorphism of the gene encoding adiponectin contributes to individual differences in the susceptibility to the development of preeclampsia.

Methods: The study involved 133 Finnish women with preeclampsia and 245 healthy control subjects who were genotyped for two single nucleotide polymorphisms (SNPs), SNP45 in exon 2 and SNP276 in intron 2, in the adiponectin gene. χ^2 analysis was used to assess genotype and allele frequency differences between the preeclamptic and control groups. In addition, the pair of loci haplotype analysis, employing the expectation-maximization (EM) algorithm, was used to examine the estimated haplotype frequencies of the two SNPs, among the two groups.

Results: The TT genotype versus pooled G genotypes in SNP276 was associated with protection against preeclampsia ($P=0.012$) at an odds ratio of 0.27 (95 % CI: 0.09–0.80). Also the genotype and allele frequency distributions of SNP276 differed significantly between the preeclampsia and control groups ($P=0.035$ and $P=0.043$, respectively). Single point genotype and allele distributions in SNP45 of the adiponectin gene were not statistically different between the groups. In the haplotype estimation analysis, pooled G haplotypes versus the TT haplotype were significantly over-represented in the preeclampsia group ($P=0.042$).

Conclusions: Polymorphisms of the adiponectin gene show weak, but statistically significant, haplotype association with susceptibility to preeclampsia in Finnish women.

296 Fetal age assessment based on femur length at 10-25 weeks of gestation, and reference ranges for femur to head ratios

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Background: The aim of the present study was to establish new reference charts for gestational age assessment based on fetal femur length, and new reference ranges for femur to head ratios at gestational weeks 10-25, and to determine the effect of maternal and fetal factors on these charts.

Methods: 650 low-risk women with regular menstrual periods and singleton pregnancies were recruited to a prospective cross-sectional study after written consent. Femur length, outer-outer biparietal diameter and head circumference were measured at 10-25 weeks of gestation. We used regression analysis to construct mean curves and assess the effect of maternal and fetal factors on age assessment.

Results: The new chart for age assessment using femur length was based on 636 measurements. The 95%CI of the mean corresponded to <1 day. The variation between the mean and the 90th percentile was 5, 6 and 7 days at 13, 18 and 23 weeks, respectively, similar to the results when using biparietal diameter or head circumference. Maternal age modestly influenced gestational age assessment (1.3 days/10 years, $p=0.005$), whereas smoking, height, body mass index, multiparity, fetal gender, Cephalic Index and breech presentation had no impact. Reference charts for femur length to head ratios are presented. Maternal age, fetal gender and Cephalic Index influenced the femur length/biparietal diameter ratio, while fetal gender only influenced femur length/head circumference.

Conclusions: Fetal age assessment based on femur length is an equally robust method as measuring head circumference. Femur length/head circumference is a more robust ratio to characterize fetal proportions than is femur length/biparietal diameter.

297 Fetal age assessment based on ultrasound head biometry and the effect of maternal and fetal factors

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Background: Maternal height and weight have increased during the past 20 years, and so has birth weight. The aim of the present study was to establish new reference charts for gestational age assessment using fetal biparietal diameter (BPD) and head circumference (HC), and to determine the effect of maternal and fetal factors on age assessment.

Methods: This was a prospective, cross sectional study of 650 healthy women with regular menstrual periods and singleton uncomplicated pregnancies, recruited after written consent. BPD (outer-outer) and HC were measured at 10-24 weeks of gestation. We used regression analysis to construct mean curves and assess the effect of maternal and fetal factors on age assessment.

Results: BPD and HC were successfully measured in 642 participants. Using BPD and HC before 20 weeks, the new charts gave 3-8 days higher gestational age assessment than the charts presently in use, and <1day difference compared to other recently established charts. Maternal age, multiparity, fetal gender, breech position, and shape of fetal head affect gestational age estimation by 1-2 days when using BPD ($p = 0.0001-0.02$). Only maternal age and fetal gender affected estimation when using HC (< day, $p = 0.001$).

Conclusions: Our new charts for assessing gestational age based on fetal head biometry are notably different from charts presently in use. Maternal and especially fetal factors affect gestational age assessment when using BPD, but less so for the HC-method, which is suggested as the more robust method.

298 Professional Development through a Distance Learning Program in Evidence Based Perinatal Care

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Background: Modern perinatal care should be based on scientific evidence and continuously updated. Traditional medical training does not give the tools for critical reading or appraising clinical practices in use.

Method: A distance learning web platform is used for a program for training of obstetricians and neonatologists in a network of centers in the Baltic countries, Saint Petersburg, Donesk in Ukraine and Västerås in Sweden, coordinated by Uppsala University. The web platform allows interaction between the participants and teachers such as asking questions about the material and discussing topics in groups. In the program emphasis is put on providing tools for critical reading, starting with material about information seeking and evidence based medicine. In the clinical part participants use these tools to seek evidence-based solutions to clinical problem situations and clinical guidelines. For each teaching unit the participants are asked demonstrate EBM thinking by fulfilling a written assignment. Each participant is also responsible for a clinical project to improve quality of care.

Conclusions: The interactive distance learning program seems to be a feasible and effective tool for professional development. However, an occasional personal encounter

between students and teachers probably strengthens the process.

299 Normal Amniotic Fluid Index by Gestational Week in a Korean Population

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Background: To obtain a gestational reference range for the amniotic fluid index (AFI) among Korean women.

Methods: An analysis of AFI estimations was undertaken in 1,089 Korean women with normal pregnancy between 20 and 40 weeks of gestation. It was a prospective study conducted in an Inha University Hospital. Women with fetal anomalies, pregnancy-induced hypertension, diabetes mellitus, and other maternal complications were excluded from the study. The median, the 5th and the 95th percentile values were calculated for each gestational week.

Results: The median reached its peak at the 29th week of gestation with 12.5 cm and declined to 8 cm at 40 weeks. We observed approximately 6 cm as the lower limit of normal (5th percentile) and approximately 15 cm (95th percentile) as upper limit of normal AFI at term for our population.

Conclusions: We standardized the reference values for normal AFI in Korean women.

300 Increased risk of complications during pregnancy in CADASIL

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Background: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary small-vessel disease caused by mutations in the Notch3 gene on chromosome 19. It is characterized by migraine-like headache and recurrent ischemic attacks due to lacunar infarcts, which lead to cognitive decline and finally subcortical vascular dementia. Maternal pre-existing microvascular diseases are known to predispose to pre-eclampsia. The main purpose of this study was to assess the risk of stroke and other complications during pregnancy and puerperium in CADASIL patients. CADASIL has not been previously reported as a cause of ischemic episodes during pregnancy or puerperium.

Methods: In Finland we have so far identified 39 female CADASIL patients, who have had pregnancies. Among them we were able to examine the clinical course of pregnancy

(both obstetrical and neurological) in 25 consecutive patients on the basis of a detailed questionnaire and/or medical records.

Results: 12 patients suffered from neurological symptoms and/or pre-eclampsia in 19 (44%) of their 43 pregnancies and/or puerperia. These complicated pregnancies comprise 24% of all 78 pregnancies in the examined 25 CADASIL females. CADASIL manifested for the first time during pregnancy or especially during puerperium in 82% of the patients. Transient neurological episodes were present in 17 of 43 pregnancies; the most common symptoms were hemiparesis (76%), hemiparesis (35%), aphasia (65%), visual disorders (47%) and headache (89%). Altogether 8 (42%) of 19 complicated pregnancies were associated with pre-eclampsia-like symptoms, which unusually occurred more often in later pregnancies.

Conclusion: In CADASIL, complicated course of pregnancy was remarkably common compared to stroke or pre-eclampsia incidence in pregnancy generally. Pregnancy increases the risk of transient neurological symptoms and pre-eclampsia in CADASIL in all age groups but especially in females over 30 years old. CADASIL may be underlying cause of neurologically complicated pregnancy of unknown etiology and an independent risk factor for pre-eclampsia.

301 Specificity of antenatal ultrasound

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Background: One of the main reasons for ultrasound screening is to detect fetal anomalies. The most important concern is the possibility and the risk that termination of pregnancy is performed where the fetus is either normal or has less severe anomalies than those diagnosed by ultrasound.

Method: About 330 cases of fetal examinations in Uppsala and Southern Stockholm between 1992-2003 were included. The results from 136 analysed cases are presented here. For inclusion, the pregnancy had to be terminated only due to ultrasound findings and not primarily due to chromosomal aberrations. The last ultrasound finding was compared with the fetal examination (autopsy) in four groups:

- A. Ultrasound findings exactly matched postnatal findings.
- B. Major ultrasound findings confirmed by postnatal findings, but other anomalies were either misdiagnosed or missed.
- C. Ultrasound findings were not confirmed; but the postnatal findings were at least as severe as the prenatal ones.

D. Postnatal findings showed a less severe abnormality than ultrasound findings, which meant that termination may not have been carried out.

Results: The number of cases in group A was 65(48%), in group B 53(39%), in group C 15 (11%) and in group D 3(2%). The specificity according to clinical aspects was 98%. Invasive fetal diagnostics was done in 85(62%) cases. Chromosomal aberrations were found in 20 (15%). In 71(52%) of the cases, fetal examination provided further important diagnostic information and in some cases a syndrome was discovered.

Conclusions: Termination of pregnancy is not always based on a correct prenatal diagnosis.

Autopsy of the fetus by an experienced perinatal pathologist is necessary to provide relevant additional information, which is used to counsel the parents in forthcoming pregnancies, feedback to obstetrician and others in the fetal-medicine team and importantly to make sure that a high quality is obtained.

302 ADAM12: A first-trimester maternal serum marker for pre-eclampsia?

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Objectives: ADAM12 (A Disintegrin and Metalloprotease) is produced by the placenta, and is present in pregnancy serum but not in serum from healthy non-pregnant women. We have recently demonstrated that ADAM12 is a promising first-trimester marker for Down syndrome (Laigaard et al., Prenatal Diagnosis 23: 1086, 2003). The goal of this study was to determine whether ADAM12 concentration in 1. trimester maternal serum could be used as a marker of pre-eclampsia as well.

Methods: We developed a semi-automated, time-resolved, immunofluorometric assay for the quantification of ADAM 12 in serum. The assay range was 78 to 1248 µg/l. 1 trimester serum samples from normal pregnancies (n=324) and pregnancies that developed pre-eclampsia (n=160) were all from the Copenhagen trial. Serum levels were converted to multiples of the mean after linear regression.

Results: We found that ADAM12 in pregnancies with pre-eclampsia had a mean log MoM of -0.066, which is significantly lower than normal pregnancies with a mean log MoM of 0.001 (p=0.008). Pre-eclamptic samples with a fetal weight under 2500g (n=27) had a mean log MoM of -0.12, which was nearly significant (p= 0.053). Magno gradu pre-

eclamptic samples had a log MoM of -0.028, which was not significant.

Conclusion: ADAM12 in the first trimester is significantly reduced in pregnancies that later develop pre-eclampsia. The clinical relevance will need to be assessed in larger studies.

303 Biochemical markers of chromosomal pathology as markers of complicated pregnancy

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Background: The aim of the present work was according to the retrospective analysis to study interrelation of parameters of biochemical screening with complications of pregnancy.

Materials and methods: We had analyzed data about 60 pregnancies. Pregnancy at 45 women after natural conception and 15 pregnancies after IVF. Biochemical markers that were measured: pregnancy associated plasma protein – A (PAPP-A) in 11 - 12 weeks of pregnancy and beta-chorionical gonadotropin (b-hCG), alfafetoprotein (AFP) en unconjugated estriol (E3) in 17 - 18 weeks in peripheral blood (V.Z.). This tests was made with ELISA method with standard sets of system ' DELFIA ' by the analisator 1420 VICTOR2 "Wallac OY", (Finland).

Results: On our data, parameters of biochemical screening at women after IVF and spontaneous abortions did not differ. The received results testify to authentic difference of concentration PAPP-A and the tendency to authentic difference of concentration b-hCG depending on current of the first trimester. At pregnant with the complicated current of the first trimester concentration PAPP-A was authentically lower. The analysis of results of biochemical screening depending of pregnancy flow of the second trimester testify to authentic difference of concentration both PAPP-A, and AFP. At presence of complications of current of the second trimester concentration PAPP-A was authentically lower, and concentration AFP - authentically is higher. At presence of complications of the third trimester of pregnancy concentration PAPP-P in the first trimester was authentically lower, also as the concentration E3 in the second.

Conclusion: Thus, the received data give the basis to speak about presence of precise authentic changes in concentration of biochemical markers investigated by us depending on current of pregnancy. On the basis of the results received by us, and also the data of the literature we can fairly notice, that with biochemical screening of chromosomal pathology we can make diagnosis or prognosis concerning complications of pregnancy.

304 Caesarean section rate of 70 % < 28 gestational week – why, how, then?

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Background: According to the “better baby” hypothesis, 1/3 of mortality decline of very preterm could be attributed to improved high-risk obstetric care. The position of a more liberal use of abdominal delivery on foetal indication for extremely preterm is not yet settled. The North of Sweden has a higher C.S. rate for deliveries < 26 w than the South.

Methods: Eligible cases were all women delivered by caesarean section < 28 gestational week of Umea University Hospital 1997-2003. For each case two referents were selected having planned term first time caesarean matched by age and month of delivery.

Results: The C.S. rate for all deliveries was 16 %. The rate for 26-27 w was 76 % (n: 48), and for < 26 w the rate was 66 % (n:47). In 37 % of the cases maternal complications, as eclampsia/preeklampsi and abruptio placenta, were the reason for the abdominal delivery. Foetal indication prevailed for 63 %. The major part of foetal indication was PROM with complications as amnionitis or abruptio placenta, while breech, transfusion syndrome, threatening foetal asphyxia added to the rest. T-incision of isthmus (15) or corporal incision (1) was performed for 16 %. A difficult extraction of the children occurred in 17 %. Wound infection and postpartum endometritis were noted for 4 %, and haemorrhage > 1 000 ml for 8 %, with no significant differences to elective term abdominal delivery. of the children (n: 113) 41 %, 9 % and 7 % had Apgar Score < 4 at 1, 5 10 minutes. 14 died as neonates.

Conclusion: Extremely preterm abdominal delivery concerns severe pregnancy and birth complications and could be a more difficult surgical procedure than term caesarean. However, no increase in haemorrhage or major postoperative morbidity could be perceived.

305 Decrease in early neonatal mortality rates in Obstetrics-gynecology clinic, Prishtina university hospital, after war (1999-2003)

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Background: Number of deliveries in Kosova is 45000-50000 per year. OGC is the only tercial referral centre where approximately 13000 deliveries take place. ENMR in OGC is one of highest in Europe (22/1000).

Methods: For this study we used retrospective, epidemiological-clinical trials. ENMR were followed-up monthly and yearly. In mean time we implemented all the necessary

actions for prenatal improvement. In statistical analysis we included all viable newborns with birth weight >500 g and gestative age >22 weeks. We classified them by bithweigh and cause of death. The statistical analysis was done using confidence interval.

Results: ENMR in 1999 was 31/1000, in 2000 29.5/1000, in 2001 28.3/1000, in 2002 23.3/1000 and during 2003 it was 21.7/1000. Most common cause of newborn death was prematurity (47%), followed by congenital anomalies (22.3%) and obstetrics causes (17.6%). Perinatal mortality rates didn't show any significant decrease because of increased number of stillbirths referred from the regional hospitals and maternity houses.

Conclusions: Supplying OGC with new diagnostic equipment, reconstructing maternity ward, applying new protocols for treatment of risked pregnancies helped in gradual reduce of ENMR. We have to organize informing campaigns involving adequate perinatal care and optimal antenatal visits which should be supported by Ministry of Health. Genetic consultation should take place also. There should be an improvement of OGC drug supply, which are very often missing. There should be an increase in the number of neonatologists and an improvement in their training. We have to cooperate and communicate more with all European and worldwide Ob/Gyn associations, especially with those which are advanced in these aeries.

306 Arterial embolization and prophylactic catheterization for treatment of severe obstetric hemorrhage

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Background: Pelvic arterial embolization is an alternative method in treating massive post-partum hemorrhage. In this study we wanted to evaluate the indications, efficacy and complications associated with pelvic arterial embolization and prophylactic balloon catheterization in the management of peripartum hemorrhage at a university hospital.

Methods: Twenty-one women underwent arterial embolization between February 2001 and October 2003 for treatment of primary peripartum hemorrhage due to placenta previa or accreta (n=10), uterine atony (n=7), retroperitoneal hematoma (n=3) and disseminated intravascular coagulopathy (n=1). Mode of delivery was spontaneous vaginal in 9, elective or emergency cesarean section in 12 patients. Blood loss rated between 3,2 and 15 liters. In seven cases placenta previa or accreta was diagnosed prenatally. In these cases arterial balloon catheterization was performed prophylactically before the elective cesarean section.

Results: of the seven cases who underwent prophylactic catheterization, embolization was successful in five, and

diminished bleeding in other two cases. Hysterectomy was performed in three of these patients. The other fourteen patients were treated with embolization in emergency. In eight cases embolization was performed as a primary operation, and succeeded in six. In other six cases hysterectomy was performed as an emergency primary operation but bleeding continued, and embolization was performed. Of these, in five cases embolization was successful. Overall complication rate due to embolization was 3/21. The complications were thrombosis of popliteal artery, necrosis of proximal vagina, and ischemia of sciatic nerve.

Conclusion: Embolization is of significant value in treating obstetric hemorrhage. Insertion of arterial balloon catheters prophylactically before cesarean section in patients with anticipated placental problems seems to be a safe and effective method in controlling bleeding. In cases with persistent bleeding following cesarean section and hysterectomy embolization could be a primary procedure prior to re-operation.

307 Intrapartum fetal monitoring by CTG + ST-analysis of fetal EKG. A 4 years experience from risklabours at Haugesund Hospital

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Background : At Haugesund hospital, with about 1500 deliveries per year, we have been using ST-analysis of the fetal-EKG as a mode of fetal surveillance during labour since 1990.

Methods: From 1999 we used STAN-ESST, with automatic detection of ST-changes.

From 2001 we have used STAN-S21, with automatic detection and warning of significant ST-waveform changes. We have also from 1999 had strict documentation of every delivery, including neonatal data. From 2001 we started systematically re-education and certification of the staff, both midwives and doctors.

Results: When analysing the data from 1999-2000 we found that 6 of the babies in the STAN-group had metabolic acidosis in the umbilical artery (2,4 %). When looking into the CTG+ ST-analysis from these deliveries, we found significant ST-changes indicating delivery in 5 of 6 deliveries, but the midwife or doctor did not react adequately on the signals. In the period 2001-2002 there was only one new-born with metabolic acidosis in the STAN-group (0,27 %). The baby was delivered by emergency caesarean section soon after admission because of biphasic ST, but was stillborn. Operative intervention for fetal distress in this risk-group surveyed by STAN was 14,5 % in the first period, 15,2 % in the second. In 2002 our department had a caesarean section-rate of 10,3 %, being the lowest in Norway. Operative intervention for fetal distress was totally 3,5 % (2,3 % opr.vag., 1,2 % sectio)

Conclusion: It seems that CTG+ST-analysis gives us a tool to detect fetuses at risk of hypoxia during labour, and gives us the opportunity to deliver them early enough to prevent damage.

At the same time it helps us to avoid unnecessary operative deliveries for fetal distress, thus giving the mother, the father and the new-born a much better experience.

308 Bacterial vaginosis in pregnant women in Denmark. Prevalence and association with preterm delivery

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Background: The aim of the study was to examine the prevalence of bacterial vaginosis in the second trimester of pregnancy, and to examine, whether the occurrence of bacterial vaginosis was associated with subsequent preterm delivery and perinatal infections.

Methods: A total of 3364 pregnant women, aged 18 years or more, were included in a cohort study at their first antenatal visit. A sample of the fluid in the upper part of the vagina was taken and smeared onto a glass slide. The smear was air-dried and stored for subsequent diagnosis of bacterial vaginosis. After re-hydration with isotonic saline the smear was examined in a phase-contrast microscope at 400 X, and the numbers of lactobacilli and small bacteria were counted. The presence of clue-cells was recorded. A score for bacterial vaginosis was calculated according to the method described by Schmidt. Main outcome measures were spontaneous delivery at less than 37 weeks of gestation, preterm labor, premature rupture of membranes, clinical chorioamnionitis and postpartum endometritis.

Results: The prevalence of bacterial vaginosis was 16 %. Smoking during pregnancy was associated with bacterial vaginosis ($p < 0.001$). The frequency of spontaneous preterm delivery among women with singleton pregnancies was 4 %. A history of previous preterm delivery was associated with spontaneous preterm delivery in singleton pregnancies, both in univariate and multivariate analysis (OR 2.0 95% CI 1.4-3.0). Smoking and bacterial vaginosis was not associated with spontaneous preterm delivery. Bacterial vaginosis was associated with clinical chorioamnionitis among all women in the study (OR 2.3 95% CI 1.2-4.4).

Conclusions: The prevalence of bacterial vaginosis in the early second trimester of pregnancy was comparable to that found in other studies. Bacterial vaginosis was associated with clinical chorioamnionitis among all women in the study, but not with spontaneous preterm delivery among women with singleton pregnancies.

309 Sugar intake among pregnant women in Oslo

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Background: The sugar intake is increasing rapidly in western countries. The health consequences of high sugar intake have therefore gained much interest. We have earlier shown that high sugar intake is associated with increased risk of early onset preeclampsia (Clausen et al, AJOG 2001). Recommended sugar intake in Norway is < 10 % of total energy intake (E%). The aim of this study was to investigate sugar intake among pregnant women in Oslo, Norway.

Methods: In 1995-97 we collected dietary data (quantitative food frequency questionnaire) from 3133 pregnant women in early second trimester. 83 percent of the women who were asked filled in the questionnaire.

Results: 37.9 percent of the pregnant women reported sugar intake above 10 E%, 14.2 % reported intake > 15 E% whereas 5.2 % had an intake > 20 E%. Low age, low education and smoking were all factors independently and positively associated with high sugar intake. Among women 20 years or younger as much as 27 percent reported sugar intake > 20 E%. Sugar containing soft drinks was the most important source of high sugar intake. The intake of sugar containing soft drinks was 800 ml/d for women with sugar intake > 20 E% compared to 52 ml/d for women with sugar intake < 10 E%. Pregnant women with high sugar intake had higher total energy intake, but lower intakes of important vitamins (vitamin A, C, D, E) and important foods like fish, fruits and vegetables than women with recommended sugar intake.

Conclusions: Almost 40 percent of pregnant women in Oslo had a sugar intake above recommended intake. Young pregnant women had an exceptionally high intake. Women with high sugar intake had a diet composition with less fish, fruits, vegetables and vitamins than women with normal sugar intake.

310 Human placental growth hormone (hPGH) and growth hormone binding protein (GHBP) during a twin pregnancy compared to singleton pregnancies

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Background: During pregnancy, placental growth hormone (PGH) gradually replaces pituitary growth hormone (GH) in the maternal circulation. Peak levels are reached in gesta-

tional week 34 – 37. Serum PGH has been found to be positively correlated to birth weights and is therefore presumed to be involved in the regulation of substrate supply to the placenta. Also, serum levels of insulin-like growth factor I (IGF-I) appear to be regulated by hPGH. Theoretically, levels of hPGH should be increased in twin pregnancies, due to the increased fetal and placental mass.

Methods: 12 healthy women participated, 11 had a singleton pregnancy and 1 had a twin pregnancy. Fasting blood samples were withdrawn during pregnancy and post partum. Blood samples were analysed for serum hPGH, GH, IGF-I and GHBP.

Results: Both serum hPGH and IGF-I levels peaked in the third trimester. Levels of serum hPGH and GH were higher in the woman with twin pregnancy in the last half of pregnancy, whereas serum IGF-I was at similar levels. Interestingly, levels of GHBP in the third trimester were at their lowest in the twin pregnancy. An inverse relationship was observed between serum GHBP and hPGH, both with ($r = -0.72$, $p = 0.008$) and without ($r = -0.62$, $p = 0.041$) including the twin pregnancy. Analyses revealed no significant correlations between serum hPGH and IGF-I at any gestational age, though trends were observed. This was probably due to the low number of data for analysis. Third trimester hPGH levels correlated positively to birth weights when including the twin pregnancy ($r = 0.78$, $r = 0.003$), but only showed a trend without ($r = 0.52$, $p < 0.1$).

Conclusion: Serum hPGH levels appear to be increased during twin pregnancy. Twin pregnancy may be a potent stimulus for increased maternal energy turn-over during pregnancy, influencing the GH-IGF-axis.

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Pre-eclampsia and intrauterine growth retardation in women taking part in early and midtrimester ultrasound screening programme: A prospective study in a big Finnish university hospital district

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Background: Although pre-eclampsia (PE) and intrauterine growth retardation (IUGR) are common, only few prospective studies exist on their development. We studied the occurrence of PE and IUGR in women participating the double ultrasound screening programme, with the ultimate goal to develop biochemical or ultrasonographic means for the prediction of PE and IUGR.

Methods: We studied 4427 women with singleton pregnancies who had US in the first and second trimester. The findings in US and clinical examination were recorded, and sera samples were collected for future analyses. The pregnancies were followed up to the delivery. Pure PE was defined as a blood pressure elevation (> 140/90 mmHg, or a rise of 20/15 mmHg, systolic/diastolic) in previously normotensive

women, without or with proteinuria (> 0.3 g/24hrs or dipstick >0.3 g/l), and IUGR as a birth weight below 5 percentiles of national average.

Results: Pure PE developed in 128 pregnancies (2.9%) (proteinuric in 88 and non-proteinuric in 40). PE started before 32 weeks in 15 women. PE was accompanied by IUGR in 27, by intrahepatic cholestasis in 5 and by glucose intolerance in 19 women. In addition, 13 women with pre-existing hypertension showed elevation in blood pressure fulfilling the criteria of superimposed PE. Thirty-four women without any evidence PE gave birth to IUGR infants.

Conclusions: The risk of PE in this prospective study (2.9 %) is smaller than that reported in many retrospective or cross-sectional studies (4-5 %). This difference may be due to stricter criteria we employed for the diagnosis of PE. The risk of IUGR in PE was also lower than often reported. US findings and various biomarkers, their basal values or changes from the first to second examination, may reveal useful means for the prediction of PE and/or IUGR.

312 Introducing a fast-track recovery programme in relation to acute caesarean section

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Background: Studies have shown that introduction of a fast-track recovery programme reduces the post-operative stress reaction of the body when applied to planned operations. The fast-track recovery programme includes improved anaesthetic, pre-operative patient information, administration of post-operative pain therapy, and early post-operative nutrition and mobilisation. Reduction of the post-operative stress reaction enables the patients to regain their normal activity level earlier, reduces post-operative complications, and reduces costs due to reduced hospitalisation and convalescence. The objective of this study was to evaluate the health related effects of implementation of a fast-track recovery programme for women who deliver by acute caesarean section.

Methods: The study was a non-randomised prospective cohort study on two fixed samples with a follow-up until two months after discharge. One hundred consecutive women entered the study allocated to either the reference group or the intervention group. The evaluation used the women's own assessment of physical abilities, physical and mental well being, ability to breastfeed and to provide care to the newborn and need for Primary health Care contacts. Data was collected using structured interview guides, self-administered questionnaires and information from patient records.

Results: Significantly less women in the intervention group experienced pain on the third post-operative day. The intervention led to a reduced average length of hospitalisation by one day without causing an increased number of contacts to the Primary Health Sector or an increased number of

readmissions for the mothers and newborns postpartum. The reduced hospitalisation did not reduce the number of women who were breast-feeding two months after the discharge.

Conclusion: The average length of stay can be reduced introducing a fast-track recovery programme after acute caesarean section without an increase in health related complications.

313 Maternal mortality in Denmark, 1985-1994

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Background: Maternal death is a rare but very serious event. In Great Britain a national confidential enquiry into maternal deaths has taken place since 1952 assessing suboptimal cases. In Denmark there are no reviews on maternal mortality. Assessing maternal deaths is useful in development of research in critical obstetric incidences and in development of training for healthcare personnel.

Methods: Linkage of data from the Danish Cause of Death Registry, Medical Birth Registry and National Patient Registry identifying all female deaths in Denmark (1985-1994) with a pregnancy registered < 12 months prior to the death. The cases were classified using the British classification as either obstetric (direct, indirect) or non-obstetric (suicide, murder/violence, accident, cancer, others non-obstetric, unknown) related deaths.

Results: We present preliminary data and a complete update will follow. There were 304 pregnancy related deaths. Of these 71 (23 %) were obstetric (30 direct (42%), 35 indirect (49%), 6 unknown obstetric cause) and 233 non-obstetric (60 suicide (26%), 13 murder/violence (6%), 54 cancer (23%), 53 accident (23%), 31 other non-obstetric causes (13%), 22 unknown cause (9%)). Mean age was 30 years for the obstetric and 31.2 (NS) for the non-obstetric cases. Time from pregnancy related contact to the health care system and death was 71 days for the obstetric and 233 days for the non-obstetric cases ($p < 0.05$).

Conclusions: Using registry data on pregnancy, delivery and death it is possible to get important information on maternal mortality. However time delay, validation and qualitative evaluation must be considered. Using personally reported data (as in Great Britain) the time span is shorter, but especially non-obstetric and late indirect obstetric deaths may be underreported.

314 An intervention program for reducing morbidity and mortality associated with neonatal allo-immune thrombocytopenic purpura (NAITP)

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Background: The incidence of NAITP has been reported to be 1 of 1,000 to 2,000 pregnancies and is most frequently caused by antibodies against the human platelet antigen (HPA) 1a. According to retrospective studies, 10-30% develop intra cerebral haemorrhage (ICH) and the outcome is fatal in 10% of these cases. The objective of the present study is to identify pregnancies at risk, i.e. HPA 1a negative women, and to offer them an intervention program aimed to reduce morbidity and mortality of NAITP.

Methods: All pregnant women in the Northern and Southern parts of Norway are HPA 1 typed. The HPA 1a negative women are screened for anti-HPA 1a every fourth week during pregnancy, and anti-HPA 1a is quantified when present. Immunised women are referred to a university hospital for clinical follow up and cerebral ultrasound, and caesarean section is performed in gestational week 38. Prior to delivery, platelets from HPA 1bb donors are harvested and reserved for transfusion of the neonate. Platelets are transfused immediately if petechiae are present and/or if platelet count is $< 35 \cdot 10^9/L$.

Results: Data from 62,176 pregnancies who delivered has revealed that 2.3% of the women are HPA 1bb and 10% of these have anti-HPA 1a. Approximately 1/4 of the immunised women gave birth to a severely thrombocytopenic child. There have been one case of ICH, which was clinically insignificant and no NAITP-associated intrauterine deaths.

Conclusion: In this prospective intervention study the morbidity and mortality associated with NAITP are far less than previously reported.

315 Intrahepatic cholestasis of pregnancy and ADH1C genotype

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Background: The pathogenesis of intrahepatic cholestasis of pregnancy has been related to abnormalities in the metabolism and disposition of sex hormones and/or bile acids. The severity of disease varies and familial clustering and endemic occurrence strongly indicate a genetic basis. The main consequences of ICP are an increased risk of fetal distress, with stillbirths and premature deliveries. The class 1 alcohol dehydrogenase 1C (ADH1C) was recently shown to be the sole bile acid 3 β -hydroxysteroid dehydrogenase in human liver cytosol and is thus suspected to be involved in cytosolic bile acid binding and transport processes. In the present study we investigated the polymorphism of the ADH1C gene as a potential candidate predisposing to cholestasis of pregnancy.

Methods: 112 Finnish women with established ICP were genotyped for the ADH1C by a PCR-RLFP method.

Results: The distribution of ADH1C genotypes were: ADH1C*1/*1: 25.9% (n=29), ADH1C*1/*2: 49.1% (n=55) and ADH1C*2/*2: 25.0% (n=28). The allele frequencies: allele 1: 0.504 (n=113) and allele 2: 0.495 (n=111). Distributions were in Hardy-Weinberg equilibrium $p=0.85$. The genotype and allele frequencies did not differ from those previously reported for other European populations.

Conclusions: According to these data the genetic variation in the ADH1C gene appears not to be associated with susceptibility to ICP. This, however, does not rule out that it may play a role in modifying the severity of the disease.

316 Recurrence of hypertensive disorder in a second pregnancy in women at increased risk

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Background: The risk of any recurrence of hypertensive disorder in pregnancy is higher in a familial material. This was investigated further with reference to the type and severity of the hypertensive complication and the risk modulating effect of overweight and interbirth weight gain.

Methods: Maternity records from family clusters with 784 multiparous women who had hypertensive disorder in their

first pregnancy were reviewed to reclassify disease status and calculate odds ratios for risk of recurrence in singleton pregnancy.

Results: Recurrence was seen in 56-88% of second pregnancies dependant on the type of disorder in the first pregnancy. Concordance between diagnosis in a first and second pregnancy was most frequent in women with chronic and gestational hypertension. In women with gestational hypertension and preeclampsia the recurrence risk increased with earlier diagnosis and increasing severity of hypertensive disorder in the first pregnancy (OR 1.69 for gestational hypertension and 5.55 for preeclampsia). Overweight and inter-pregnancy weight gain (BMI > 2 units) doubled on average the risk for any recurrence (OR 2.14 and 2.39 resp.) in women with gestational hypertension.

Conclusions: Recurrent hypertensive disorders in pregnancy are common in women with a family connectivity to the disorder. Early onset of hypertension is an independent risk factor, most evident in women with preeclampsia in a first pregnancy, while being overweight and gaining weight between pregnancies confers risk for women with gestational hypertension.

317 Genetics of hypertension in pregnancy: A follow-up study on Icelandic patients

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Background: Hypertension in pregnancy varies from gestational hypertension to preeclampsia/eclampsia. An added complication is chronic hypertension. A genetic component has been implicated. We have previously reported on a locus of genome-wide significance on chromosome 2p13.

Methods: A material of 4489 women with hypertension in pregnancy, including chronic, was used. The population is well defined and extensive genealogical information allowed family clustering of affected women (5 affected/cluster related within 6 meioses) with detailed phenotypic data. A genome-wide linkage scan with 1100 markers was done and the material fractionated by phenotypes into chronic primary hypertension, gestational hypertension, preeclampsia, eclampsia, superimposed preeclampsia. Gestational hypertension phenotypes were further defined by ponderal index and highest diastolic pressure. A framework of 1100 micro-satellite markers was used with additional markers for chromosome 2. Multipoint, affected-only allele-sharing methods gave evidence for linkage and calculating lod scores by the Allegro program.

Results: A locus on the short arm of chromosome 2 was confirmed. Patients with chronic hypertension alone did not contribute. Restricting the analysis to severe disease forms did not reveal a single major locus. However, when

combined with the gestational hypertension phenotype they contributed to the lod score on Chr. 2p. Ponderal index did not increase the lod score on Chr. 2p, but patients with highest diastolic BP > 110 mmHg contributed to a slightly higher score. A new locus on Chr. 5q appeared.

Conclusion: By careful phenotyping of different forms of hypertensive disorders in pregnancy it seems that gestational hypertension and preeclampsia reflect the same genetic disorder. Chronic hypertension is probably an unrelated pathology. Some mild and severe forms of hypertension in pregnancy share a causative genetic factor located on Chromosome 2p. Additional factors may be involved in severe forms of hypertension in pregnancy, including on Chromosome 5q.

318 Increased fetal hemodynamic response to maternal NE after pharmacological inhibition of norepinephrin uptake

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Background: Norepinephrine (NE) in particular have been shown to be elevated in pregnancies complicated by preeclampsia and intra-uterine growth restriction (IUGR). Specific uptake of norepinephrine, by membrane bound transporters, norepinephrine transporter (NET), plays a central role as a regulator of extracellular level of this vaso-active transmitter. We have recently demonstrated a reduced expression of the NET gene in placenta from preeclamptic pregnancies. In order to study the potentially adverse effects of a reduced NET expression on placental buffering capacity we pharmacologically blocked NET with a specific uptake inhibitor-reboxitine.

Objective: Evaluate effect of pharmacological NE uptake inhibition on maternal and fetal hemodynamic responses to increasing maternal doses of NE.

Methods: 11 fetuses (127 days) were chronically instrumented with arterial catheters. After stabilization (48 h), maternal BP and fetal arterial BP were monitored continuously during repeated maternal iv administration of NE (5- 500 g NE). Fetal and maternal hemodynamic responses to NE were recorded before and after administration of 100 mg reboxitine sc to the ewe. Fetal and maternal serum concentrations of reboxitine were measured using established HPLC analysis.

Results: Mean fetal arterial BP response to maternal NE was significantly higher after reboxitin administration as compared to before reboxitin administration at each given dose of NE. Mean response of maternal BP to NE was significantly augmented with increasing dose of NE after reboxitin treatment.

Conclusions Pharmacological inhibition of NET appears to decrease the buffering capacity of the placenta, thereby giving rise to sympathetic vascular effects in the fetus. Reuptake by NET appears to be an important mechanism to protect the fetus from fluctuating levels of maternal NE. A reduced buffering capacity in preeclamptic pregnancies due to reduced NE uptake may lead to increased fetal exposure to circulating maternal monoamines.

319 Breech deliveries in Iceland. Infant outcome.

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Background: Vaginal breech deliveries are questioned in many western countries since the publication of Term Breech Trial (TBT) of Hannah et al. year 2000. Local results (internal audit) are valuable for every obstetric unit and constitutes the ground on which the local policy can be built. The aim was to describe the mode of delivery and infant outcome in breech deliveries during a ten year period at Landspítalinn University Hospital.

Method: A retrospective study, performed 2002-2003. The study group consisted of all women who gave birth to infants in breech presentation. During the study period the criteria for vaginal delivery were as follows: (a) pelvic outlet greater than 34.5cm and (b) estimated fetal weight less than 4kg. The mode of delivery (planned and actual) and Apgar scores were registered. Infant outcome was compared according to planned mode of delivery. An exclusion was made of infants with diagnoses that can lower Apgar scores (i.e. congenital heart diseases)

Results: 647 infants were delivered in breech presentation. 108 (18%) were planned to occur vaginally, 539 (82%) were planned to elective c.s. Twenty four (22%) of the planned vaginal deliveries ended as emergency c.s. There was a significant difference in 1 minute Apgar scores with median value =7 in the planned vaginal group but median =8 in the planned c.s. group. There was no difference in the 5 minute Apgar scores, both groups having a median value =9. There was no difference in admission days at NICU between the groups.

Conclusions: Vaginal delivery did not increase the risk of perinatal asphyxia. The frequency of emergency c.s. in the planned vaginal group was low indicating strict criteria for vaginal delivery. These results should encourage us to consider the possibility of vaginal breech deliveries in the future.

320 What determines analgesic effect at paracervical block?

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Background: The objective of our study was to evaluate the analgesic effect of paracervical block (PCB) in labour pain relief and to find out the determinants, which are associating with good analgesia.

Population and methods: In a prospective trial 341 women received PCB for pain relief in the first stage of labour, either with 25 mg of levobupivacaine or 25 mg of racemic bupivacaine. The analgesic effect of PCB was measured by Visual Analogue Scale (VAS). The factors associating with good pain relief (> 50 % decrease of VAS within 30 minutes) were analysed statically by Student's t-test or Mann-Whitney test in continuous variables and by Fisher's exact test in categorial variables, and after univariate analysis by logistic regression analysis. Main outcome measures Main outcome measure was to find out the clinical factors associating with good pain relief 30 minutes after PCB.

Results: Good pain relief was achieved in 47.2 % of the cases. In univariate analysis, primiparity, PCB given by a specialist obstetrician, higher pain score before PCB (VAS>8) and longer duration of labour were found to be significant for good pain relief. Age of the mother, length of the gravidity, level of the dilatation of cervix, amount or efficacy of the contractions before PCB, induction of labour, analgesic agent (bupivacaine or levobupivacaine), weight or sex of the infant or time of the day when PCB was given did not affect on the level of pain relief. In logistic regression analysis primiparity OR 3.06 (1.86-5.06), higher pain score before PCB OR 1.99 (1.24-3.19) and PCB given by a specialist doctor OR 1.76 (1.07-2.88) were found to affect on the level of pain relief 30 minutes after PCB.

Conclusions: The best pain relief after PCB was achieved among the parturients who were primiparas, whose pain score before PCB was high and whose PCB was given by a specialised obstetrician.

321 Fetal echocardiography during routine first trimester screening: a feasibility study in an unselected population

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Background: First trimester ultrasound screening is a routine in many institutions. It is generally performed at 12 -14 weeks to confirm the number of pregnancies and fetal viability, to measure the crown-rump length (CRL) and the nuchal translucency (NT). Early detection of fetal structural anomalies has been reported including cardiac defects in high-risk population. However, feasibility of fetal heart scanning in an unselected population at this early gestational age has not

been properly evaluated. The objective of our study was to evaluate the feasibility of identifying fetal heart structures by two-dimensional transvaginal sonography during routine first trimester screening in an unselected population.

Material and Methods: This is a prospective study of 545 pregnant women attending Tampere Health Center, Finland between November 2002 to February 2004. Viable pregnancies at 12+0 to 13+6 weeks gestation (CRL, 54 to 84 mm) were included. All examinations were done by a single perinatologist (TV) using a 7.5 MHz probe. After confirming the fetal viability, CRL and NT were measured. Fetal heart structures were examined systematically by obtaining standard views. The largest transverse diameter of both ventricles was measured in diastole in the four-chamber view. The origins and the crossing of aorta and pulmonary artery were examined and their diameters were measured at the semilunar valve levels in systole. Whether the aortic and ductal arch views were satisfactory or not was also recorded. These women had a further screening at around 20 weeks by other sonographers. Outcome of pregnancy and information on neonates were recorded in all cases. The outcome data are available for 202 fetuses to date.

Results: The average age of the women was 29 (17-44)y, BMI 25 (17-44)kg/m² and the mean gestational age was 13+0 weeks, 555 fetuses were examined. Five fetuses had a NT measurement ≥ 8.0 mm and were karyotyped. One of them had trisomy 21, parents decided to continue the pregnancy. The four-chamber view was satisfactorily visualized in 385 (69%), the aorta in 376 (67%), the pulmonary artery in 361 (65%), and the aortic arch in 323 (57%) cases. The mean diameters of right ventricle, left ventricle, aorta, and pulmonary artery were 2,6 (SD 0,40), 2,7 (SD 0,40), 1,3 (SD 0,20) and 1,4 (SD 0,23)mm, respectively. One atrio-ventricular septal defect was diagnosed at 13+5 weeks. In addition, this fetus had hydrops, but the karyotype was normal. However, intrauterine fetal demise was diagnosed at 16+3 weeks. At autopsy, proper examination of the heart was not possible due to autolysis. None of other fetuses were diagnosed to have a heart defect or any other major congenital malformation antenatally. A total of 201 babies have been delivered to date. The average birth weight was 3532 (range, 1510 to 4770)g. No neonate had a five minute Apgar score < 7 , but five required admission to the neonatal intensive care unit due maternal diabetes (two), maternal hyperthyroidism (one), neonatal sepsis (one) and prematurity (one). Two babies were diagnosed to have VSD postnatally.

Conclusion: It was possible to obtain standard echocardiographic views and identify fetal heart structures in a majority of fetuses during routine 12-14 weeks scan. Although confirmation of normality may not always be possible during this early stage in the developing fetus, absence of abnormal findings may be reassuring.

322 Identification of HPV DNA in precancer lesions of uterine cervix in Bulgarian women population by different variants of the PCR assays

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Human papillomaviruses (HPVs) are associated ethiologically with premalignant cervical lesions and cervical carcinoma. Laboratory diagnosis of HPV infection depends on molecular techniques as DNA hybridization or nucleic acid amplification. We have used different PCR systems by means of which clinically significant HPV types can be successfully detected and identified. Consensus and type-specific primer sets were used in a simple (conventional) type of PCR, multiplex PCR and real-time PCR assays. Fresh clinical samples (cells from different parts of uterine cervix) were submitted to treatment with DNAzol[®] for extraction of cellular and viral DNA, which was used as a template for amplification of specific nucleotide sequences in the regions of HPV-L1, E1, E2 and E5 genes. of 53 eligible women 43 (81%) were found to be positive for different genotypes of HPV and 10 women (19%) were negative. of 43 positive for HPV infection women; 6 (14%) were found to be positive for HPV 16; 14 (33%) – for HPV 18; 12 (28%) – for HPV 16 and 18; and in 11 (25%) were detected low-risk HPVs (6 or 11 type). Multiplex PCR, the technique of running several reactions simultaneously, has been shown to be very sensitive and specific. On the other hand, rapid real-time PCR can distinguish different HPV types on the basis of amplification followed by melting temperature analysis. We believe that the use of such molecular-based diagnosis in the routine work of virology laboratories will enhance definitely the opportunity for objective assessment of the individual carcinogenic risk and will contribute to the quality of treatment approach of the physicians.

323 Early stage cervical cancer, radical hysterectomy and sexual function: a longitudinal study

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Background: Limited knowledge exists regarding the impact of treatment on the sexual function of early stage cervical cancer patients. We investigated the longitudinal course of self-reported sexual function after radical hysterectomy (RH) alone.

Methods: 173 patients with lymph node-negative early stage cervical cancer who had undergone RH and pelvic

lymphadenectomy alone were assessed prospectively using a validated self-assessment questionnaire 5 weeks and 3, 6, 12, 18, and 24 months after RH. Results were compared with an age-matched control group from the general population. At 12 months post-surgery, the patients completed an extended version of the questionnaire with additional items assessing the patient's perception of changes in sexual function compared with before the cancer diagnosis.

Results: Compared with control women, patients experienced severe orgasmic problems and uncomfortable sexual intercourse due to a reduced vaginal size during the first 6 months after RH, severe dyspareunia during the first 3 months, and sexual dissatisfaction during the first 5 weeks after RH. A persistent lack of sexual interest and insufficient vaginal lubrication were reported throughout the first 2 years after RH. Long-term lack of sexual interest and insufficient vaginal lubrication were confirmed by the patient's self-reported changes at 12 months after RH compared with before the cancer diagnosis and by a pre-post comparison within patients. However, most of the patients who were sexually active before their cancer were sexually active again 12 months post-surgery (91%), although with a decrease in sexual frequency reported.

Conclusion: RH had a persistent negative impact on the patients' sexual interest and vaginal lubrication whereas the majority of other sexual and vaginal problems disappeared over time. Sexual and vaginal problems in the short-term and long-term after RH should be discussed with the patient before and after surgery.

324 Longitudinal study of uro-gynecological morbidity and quality of life after radical hysterectomy

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Background: Radical hysterectomy (RH) and pelvic lymphadenectomy is widely used as the primary treatment for lymph node negative early stage cervical cancer. Little knowledge exists concerning the impact of RH on self-assessed urological and gynecological adverse effects as well as the impact of RH on the patients' level of functioning.

Methods: 173 lymph node-negative, early stage cervical cancer patients who had undergone RH and pelvic lymphadenectomy alone, were assessed prospectively using validated self-assessment questionnaires at 5 weeks and 3, 6, 12, 18, and 24 months after RH. Results were compared with scores from an age-matched control group from the general population.

Results: Compared with the control group, patients reported long-term pain and urological adverse effects: frequent voiding, bladder insensitivity for micturition, and burning sensation or pain during micturition for 6 to 12 months post-surgery, whereas urine retention problems and pain in the pelvic area were reported throughout the first 24 months post-surgery. Temporary (up to 3 months post-surgery) adverse effects were also reported: fatigue, sleep disturbances, constipation, appetite loss, impaired physical, emotional, cognitive, role, and social functioning, and impaired global health status/quality of life. Comparison with an age-matched control group proved useful as it elucidated the prevalence of symptomatology and level of functioning in the general population and thus prevented over-interpretation of the level of problems attributable to the surgery.

Conclusion: RH for early stage cervical cancer is associated with both short and long term urological and pain symptomatology besides having a short-term negative impact on many aspects of the patients' level of functioning. The latter suggests that, over time, patients adapt well to the morbidity after RH.

325 The endogenous estradiol metabolite 2-methoxyestradiol may be an effective preventive agent for breast cancer in postmenopausal high risk women

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Background: Epidemiological trials support the evidence that tamoxifen may be useful as chemopreventive agent for breast cancer in high risk women. However, tamoxifen therapy is associated with serious side effects such as increase in uterine cancer. Furthermore therapy resistance may develop in the long-term as observed for breast cancer treatment which is characterized by an increased sensitivity of cell proliferation to growth factors. 2-methoxyestradiol (2ME), an endogenous estradiol metabolite, is an effective inhibitor of cell proliferation and angiogenesis. We compared 2ME with tamoxifen on its ability to suppress cell proliferation of normal human epithelial breast cells.

Methods: The cell line MCF-10A was used for the experiments. 2ME and 4-hydroxytamoxifen (4OH-Tam), the main effective metabolite of tamoxifen, were tested at 1, 5 and 10 μ M. Cell proliferation was measured after 7 days incubation in the presence or absence of a growth factor mixture (GFs; EGF, FGF, IGF-I, each 1pM).

Results: The GFs mixture elicited a nearly 100% increase in cell proliferation as compared to controls. In the absence of GFs, 2ME inhibited cell proliferation by 30% at 10 μ M as compared to controls, whereas 4OH-Tam showed no significant effect. In the presence of GFs 2ME still reduced cell proliferation by 30 and 60% at 5 and 10 μ M as compared to GFs, whereas 4OH-Tam again did not show any significant effect.

Conclusions: Our results indicate that 2ME may be superior to tamoxifen in preventing human epithelial cell proliferation. Since 2ME is well tolerated even in high dosages, this estradiol metabolite may be useful as a novel chemopreventive agent for postmenopausal women at high risk for breast cancer.

326 Expression of proliferation markers (Ki-67 and PCNA) in human mammary gland tissue culture

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Background: The human mammary gland progresses through tissues proliferation, differentiation, and regression as the circulating levels of sex hormones change with stage of the menstrual cycle or with the age. The studies have resulted in controversial findings about proliferative effects of steroids on the normal human mammary gland. It is highly likely that ovarian hormones play a key role in the etiology and biology of breast cancer, which is the leading cancer form among women in western country. Limited data are available on the differential role and importance of estrogens and progestins with regard to breast cancer risk; hence, new experimental models are needed to understand better the role and mechanism of action of different hormones in breast epithelium. The aims of our work were to establish culture condition for freshly isolated human breast tissue and compare the proliferative activity by using PCNA and Ki-67 gene expression in explants, which were pre-treated with different hormones.

Methods: Human mammary gland explants were obtained from female patients who underwent surgery because of breast carcinoma. The organ culture method by Trowell was used with some modifications. The peritumoral tissues were organ cultured for 3 weeks in chemically defined medium with 17 β -estradiol (E2) or medroxyprogesterone (MPA) or combination of E2 and MPA.

Results: Histological analysis of breast tissues, which were pretreated with different hormones, revealed differences in the appearance of the epithelium. E2 is associated with increased epithelial proliferation, documented by PCNA and Ki-67 indices.

Conclusion: The tissue culture provides a method to investigate the proliferation-inducing activity of steroids in human mammary gland. Further investigation is needed to assess the possible association between the proliferation-inducing activity of steroids and their combinations in the normal breast and in the breast cancer tissue.

327 A protective and randomised public-health trial on neural network assisted screening for cervical cancer in Finland

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Background: To evaluate the feasibility and relative validity of interactive neural network assisted screening (Papnet®) in primary mass screening for cervical cancer as a public health policy (routine screening).

Methods: A randomised, ongoing trial involving in the first three years (1999-2001) with ca. 150-170 000 invitees and 100-110 000 attendees per year in the routine organised mass screening in Finland. While drawing invitations from the population registry, the women were two to one randomised at an individual level to have their smear analysed either conventionally or with Papnet®. The distribution of smears to different cytological categories, detection rates of dysplasias, in situ carcinomas and cancers were estimated with smears analysed either conventionally or by Papnet®. The trends in cervical cancer incidence will finally be the end points of the study.

Results: Altogether 330445 smears were screened and 1291 were histologically confirmed as dysplasias and carcinomas in three years time period. The detection rates for histologically verified carcinoma in situ/severe dysplasia, moderate and mild dysplasias were 0.13%, 0.14% and 0.11% with conventional and 0.13%, 0.12% and 0.12% with Papnet®, respectively. The detection rate of invasive cancer was 0.011% (N=25) with conventional method and 0.013% (N=14) with Papnet®. None of the differences were statistically significant ($p > 0.05$).

Conclusion: Papnet® screening was feasible as a part of routine screening and performed equally well compared to conventional one as used in Finland there organised mass screening was practised very successfully in the last 38 years. We are going to continue the trial as planned to study the potential trends in cervical cancer incidence in both study arms.

328 Preoperative serum hCGbeta as a prognostic marker in primary fallopian tube carcinoma

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Background: Primary fallopian tube carcinoma (PFTC) is a rare disease. Only few articles have been published concerning serum tumor markers in patients with this disease. We

assessed the clinical value of the serum concentration of hCGbeta and CA125 as prognostic markers in PFTC.

Methods: 91 consecutive patients treated for PFTC in Helsinki University Central Hospital between 1985-2000 were studied. 60 preoperative blood samples were available, the rest 31 patients served as control patients. The overall and relapse-free survivals were studied and the prognostic value of tumor markers were evaluated.

Results: Elevated concentrations of hCGbeta ($>2\text{pmol/L}$) and CA125 ($>35\text{IU/L}$) were observed in 37% and 86%, respectively. The overall 5-year survival was 33%. The overall 5-year survival was significantly longer, if residual tumor size was $<1\text{cm}$ than if it was $>1\text{cm}$, 51% and 20%, respectively ($p=0.002$). When hCGbeta was elevated the overall 5-year survival was 18% and if normal 38% ($p=0.052$), the corresponding figures being 39% and 14% ($p=0.009$) for CA125. In stage IV the overall survival was 0%, if hCGbeta was elevated and 28% if it was normal ($p=0.013$). In a univariate Cox regression analysis residual tumor size ($p=0.004$), CA125 (75 percentile cut-off point) ($p=0.012$) and stage IV ($p=0.018$) were associated with overall survival. Serum hCGbeta (75 percentile cut-off point) ($p=0.019$), stage IV ($p=0.025$) and residual tumor size ($p=0.019$) correlated with relapse-free survival. In multivariate analysis hCGbeta, stage IV and histology emerged as independent prognostic factors.

Conclusions: This is the first study to evaluate the prognostic value of serum hCGbeta in PFTC. The current data indicates that hCGbeta is an independent prognostic factor in patients with PFTC.

329 The net effect of HRT on breast cancer morbidity and mortality in Danish women. Results from a prospective observational study

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Background: Epidemiological studies have suggested that users of hormone replacement therapy (HRT) more often develop breast cancers with favourable prognostic characteristics, implying a better prognosis. We have investigated the risk of developing both prognostic favourable and non-favourable breast cancers and the risk of fatal breast cancer in users of HRT.

Methods: The Danish Nurse Cohort started in 1993, with all Danish nurses above 44 years, receiving a mailed questionnaire, which provided information on HRT use, reproductive and lifestyle related factors. (Response rate 86%). Women with previous cancer, hysterectomy, missing information on

HRT, surgical- and premenopausal women were excluded, leaving 10,874 women for analysis. Breast cancer cases, pathological details and deaths, were ascertained using the Danish national registries. Follow-up for incident cases ended by 31.Dec.1999 and for death on 21.Oct. 2001.

Results: A total of 244 women developed breast cancer. Current users of HRT had a higher risk of developing a hormone-receptor positive than negative cancer ($p=0.013$) and low malignant compared to high malignant cancer ($p=0.063$). For tumour size, lymph node involvement and stage of disease the risks were equally increased 2-3 fold for both the favourable and non-favourable type. Fatal breast cancer in the entire cohort was increased by 80% for current users of HRT although not statistically significant; RR 1.80 (0.93 -3.46). Based only on cases, the risk of dying from breast cancer with HRT-use was reduced by 40%; RR 0.60 (0.31-1.53).

Conclusion: The net effect of HRT on breast cancer morbidity and mortality should be investigated in the entire study-population. The risk developing both favourable and non-favourable types of breast cancer is increased in HRT-users. Despite a higher risk of developing hormone-receptor positive and low malignant breast cancer and a lower case-fatality, the risk of fatal breast cancer seems to be increased with the use of HRT.

330 Comparison of ploidy and immunohistochemically detected p53, Her2/neu, ER, PR and Ki67 expression in epithelial ovarian cancer in premenopausal (<40 years) and postmenopausal (>60 years) cancer patients

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Background: Epithelial ovarian cancer (EOC) is rare in young women. Only 10 percent of patients with EOC are younger than 40 years, and in these patients the tumours are mainly borderline tumours or well differentiated cancers. Hormonal factors, such as prolonged FSH-stimulation, have been implied in the etiology of EOC. In regard to hormonal factors, young patients differ greatly from typical postmenopausal EOC patients. We examined, whether cancers in young women differ from cancers detected in older women.

Methods: 37 patients with EOC diagnosed at the younger than 40 years were matched by histological cancer subtype, grade and stage with 37 patients older than 60 years at the time of diagnosis. The paraffin-embedded tumour samples from these patients were analysed with flow cytometry for DNA ploidy and with immunohistochemical staining for p53, Her2/neu (erbB2), Ki67, ER (estrogen receptor), and PR (progesterone receptor). Differences between the groups were estimated by Odds Ratios using logistic regression and the

Genmod procedure, which allows for comparison between matched pairs.

Results: The groups consisted of 19 borderline tumors and 18 invasive cancers. There was no difference between immunohistochemically detected p53, Her2/neu, ER, PR or Ki67 expression between young and old patients. In old patients, the tumors were significantly more often aneuploid than in young patients (OR 6.1, P 0.01).

Discussion: In young patients, tumors were mostly euploid, indicating that these tumors have less severe DNA damage than histologically similar tumors from old women. Regarding the other biological tumor characteristics examined here, no difference was found between tumors from premenopausal and postmenopausal patients.

331 Matrix metalloproteinases (MMP-2, MMP-9) and their inhibitors (TIMP-1, TIMP-2) in low malignant potential ovarian tumors

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Background: Ovarian tumors of low malignant potential (LMP), also referred to as semi-malignant or borderline tumors, account for about 15% of all ovarian epithelial malignancies. LMP tumors constitute a special group of tumors with clinical behavior and histopathology between benign and malignant neoplasms. This study aimed to analyze the expression of matrix metalloproteinase-2 (MMP-2) and -9 (MMP-9) and their tissue inhibitors TIMP-1 and TIMP-2 on LMP ovarian tumors and compare these values with those recorded for benign and malignant ovarian neoplasms.

Materials and methods: A total of 53 ovarian tumors (16 benign, 15 LMP and 22 malignant) were evaluated by immunohistochemistry for the expression of MMP-2, MMP-9, TIMP-1 and TIMP-2. The patients were treated in the Department of Obstetrics and Gynecology between the years 1984 and 1998. Formalin-fixed, paraffin-embedded tissue samples from ovarian tumors were obtained from the files of the Department of Pathology, and their histology was verified. The avidin-biotin-peroxidase method was used for immunostaining.

Results: MMP-2 expression was found in 50% of the benign, 40% of the LMP and 90% of the malignant ovarian tumors (benign vs malignant, $p=0.02$; LMP vs malignant, $p=0.002$). The expression of MMP-2, TIMP-1 and TIMP-2 was lower in the benign and LMP tumors compared to the malignant ones. There was a correlation between MMP-9 and TIMP-2 in the malignant group ($p=0.02$). Twenty (91%) of the malignant cases died of the disease and none of the benign or LMP cases died of the disease.

Conclusion: In conclusion, our results show that MMP-2, MMP-9, TIMP-1 and TIMP-2 expression is low in LMP and benign ovarian tumors. These findings further support the view that LMP ovarian tumors are more similar to benign than malignant ovarian tumors.

332 Establishment of a human ovarian carcinoma taxol-resistant cell lines OC3/TAX3, OC3/TAX5 and their biological characterization

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Background: Ovarian carcinoma is one of gynecologic malignancy that cause the highest death rate. Taxol plus platinum (TP) therapy is gaining extensively acceptance as the standard regimen in clinical chemotherapy of ovarian cancer nowadays. Development of tumor cell resistance to this drug is often encountered. Presently, the most research on the drug-resistance tumor cell lines were carried out in vitro by stepwise sequential exposure to increase concentration of taxol. It's much different from the schedule which the anti-cancer drugs were used repeatedly and intermissive in clinical practice.

Methods: Using the corresponding dosage calculated from clinical chemotherapy, we established two taxol-resistant human ovarian carcinoma cell sublines. OC3/TAX3 was exposed intermissive and repeatedly to high-level concentration of taxol at 300 $\mu\text{g/ml}$ for 2 hours each time. OC3/TAX5 was exposed intermissive and repeatedly taxol at 50 $\mu\text{g/ml}$ for 24 hours each time. The drugs sensitivity were examined by tetrazolium dye test (MTT). Distribution of cell cycle, DNA content analysis, and P-Glycoprotein (P-gp) expression were detected with flow cytometry (FCM).

Results: OC3/TAX3 cells were established after 5 months with stable resistance and the drug resistance index (RI) was 6.70. It displayed significant cross-resistant to topotecan (TPT). Distribution of cell cycle revealed a higher percentage of G_2+M ($P<0.01$), less percentage of S-phase ($P<0.05$), and over-expression of P-gp ($p<0.01$). OC3/TAX5 was established after 4.5 months with stable resistance and the drug resistance index was 2.52. Besides the drug resistance to taxol, the cell exhibited cross-resistant to methotrexate (MTX).

Conclusions: Both of OC3/TAX3 and OC3/TAX5 cell lines are ideal models for investigation the mechanism of taxol resistance. Taxol resistance in those cells could be related to over-expression of P-gp and the change of cell cycle profiles. The drug-resistance degree of the taxol-resistant cell lines were stable and might serve as a model for screening the drug-resistant gene and selecting the reversal agents of drug-resistance.

333 Grand multiparity and risk of gynaecological cancers; population-based study in Finland

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Background: The aim of this national cohort study was to assess the significance of parity, age at first birth and interval between the births to the risk of breast, endometrial, cervical and ovarian cancer of grand multiparous (GM) women with at least five full-term pregnancies.

Methods: The population register of Finland with complete family information since 1974 included nearly 90,000 GM women. The linkage of the GM women with the data (until 1997) of Finnish Cancer Registry revealed 1508 breast, 419 endometrial, 388 ovarian and 220 cervical cancers and 178 CIN3 cases. Standardized incidence ratios (SIR) were calculated by dividing the number of observed cases by the number of expected cancers. Poisson regression analysis was used in the relative risk (RR) estimations. The HPV16 and C.trachomatis seroprevalence of GM women were studied in cervical cancer cases by linking GM cohort to Finnish Maternity Cohort, where serum samples from all pregnant women since 1983 have been collected.

Results: In the GM cohort, the incidences of breast (SIR 0.55, 95% CI 0.52-0.58), endometrial (SIR 0.57, 95% CI 0.52-0.63) and ovarian (0.65, 95% CI 0.58-0.71) cancers were lowered and cervical cancer (SIR 1.13 95% CI 0.98-1.29) and CIN3 (SIR 1.37, 95% CI 1.17-1.58) slightly increased. The RR decreased significantly from 5-paras to 8-paras only in the breast cancer while in ovarian and endometrial cancer it remained quite stable. In breast cancer young age and in endometrial old age at first birth was protective. In cervical cancer and CIN3, the SIR was lowest for 8+ -paras, and the RR highest for those with young age at first birth. The seroprevalence of HPV16 of GM women with first child under the age 19 years was higher than in the controls.

Conclusions: Our study confirmed that grand multiparity is a significant factor in the pathogenesis of gynecological cancers. Pregnancies after the 5th birth, however, have only minimal influence in this respect. The age at first birth also appeared important risk factor. The variation in the significance of different reproductive factors in the etiology of gynecological cancers is a reflexion of the differences in the hormone dependency of the host tissues of these cancers. The effects were strongest in breast and endometrial cancers.

334 Screening for Y microdeletions in men with testicular cancer

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Background: Infertility might be a presenting symptom of testicular cancer and show a high incidence - ranging from 0.4 to 1.6% - of carcinoma in situ in infertile men. In the present study, we investigate a possible association between Y microdeletions, which have been shown to be a cause of male infertility, and testicular cancer to clarify whether Y microdeletions could be one of the common causal factors in these cases.

Material and method: The study was designed as a retrospective study. A total of 180 DNA samples from men diagnosed as testicular cancer were screened for Y microdeletions. Fertile men (n=200), who had fathered a minimum 4 children spontaneously, were included in the study as a control. A fluorescent multiplex PCR protocol with 25 sequence-tagged sites (STS) was performed for screening for Y microdeletions in interval 5 and 6 of Yq11.

Result(s): A single STS missing (sY153) was found in 7 men; 1 from control group, 6 from cohort population. Using lower annealing temperature in the PCR, the presence of PCR products with expected sizes were demonstrated indicating that these single missing STSs were not due to a real Y microdeletion, but probably due to a sequence variation in the primer binding site.

Conclusion(s): Since no contiguous, real Y microdeletions were found in the study population, it seems Y microdeletions are not a likely common etiological cause of poor spermatogenesis in testicular cancer. However, it remains to be determined whether the men having a single STS missing have a potential risk factor for testis cancer.

335 No excess mortality due to high age in vulvectomy women in Sweden 1980-2000

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Background: High age has negative impact on survival after cancer treatment. the aim of this study was to analyse the possible excess mortality, taking the expected mortality into account, due to high age in vulvectomy women in Sweden 1980-2000.

Methods: Data were obtained from the Swedish Cancer Register and the Swedish Hospital Discharge Register. Relative survival was analysed using a computer program package for cancer survival studies¹. The relative survival rate is the ratio of the observed to expected survival in a comparable general population, taking into account population, age and calendar period². The excess mortality rate is 1- the relative survival rate. We have used here the annual excess mortality rates.

Results: From 1980 to 2000, Swedish hospitals admitted 1366 women for vulvectomy, due to vulvar cancer, which corresponds to a mean of 15 cases/1,000,000 female population. Observed survival showed an inverse relation to age but no relation to calendar period. Excess mortality showed no relation to neither age nor calendar period. Excess mortality for all patients was observed mainly for the first five years after surgery.

Conclusion: Observed survival in vulvectomy Swedish women showed an inverse relation to age. No such relation was detected in excess mortality, taking the expected mortality into account.