At the Department of Obstetrics and Gynecology of Kaunas Medical University Hospital, a tertiary-care perinatal referral center the studies on preterm labour and infection were performed during last 8 year period.
We have shown that IAI and vaginal carriage of *C.trachomatis*, *E.coli*, *Staphylococcus aureus* are associated with an increased risk of preterm prelabour rupture of the membranes (PPROM). The presence of one or more of these conditions in late second or early third trimester may therefore be considered predictive of PPROM.
It was concluded that *E.coli* and *S.aureus* are significantly more prevalent in endocervical cultures from woman in preterm than from those in term labour.
Our results demonstrate that in pregnancies with PPROM cultures from the lower genital tract provide sensitive but nonspecific prediction of IAI.
One our study have shown that AF culture can identify patients with an increased risk of adverse maternal and neonatal outcome in patients with preterm PROM.
Our findings suggest that more vigorous oral antibiotic treatment of women with PTL latent phase, or intravenous early active phase would be justified. Such treatment would presumably be more efficient than symptomatic tocolytic treatment in setting where genital infections are prevalent.
A large body of clinical and laboratory information suggests that infection is major cause of preterm birth. This concept holds promise that new approaches can be used to treat or prevent preterm labour.

FM2.05.02
MATERNAL-FETAL INTERFACE
James Walker, Department of Obstetrics and Gynaecology, St James University Hospital, Leeds, United Kingdom

The baby is normally protected within the uterus by the closed environment. The Placenta acts as a barrier to bacterial infection and the cervix stops ascending infection. There is less protection against viral infections which can pass through the placenta relatively easily often with little maternal disease. These are less of problem to the late gestation fetus. The main problems come from the breakdown of the cervical barrier and the infection in the birth canal at delivery. Once there a rupture of the fetal membranes, bacterial infection can enter the amniotic cavity and directly infect the baby. There is evidence that the fetus can itself react by stimulating labour to reduce the damage that infection might bring but this in itself can lead to premature delivery. The mother also can react to intrauterine infection by stimulating labour to protect herself. Therefore both mother and fetus play a role in stimulating labour in response to infection. During birth, specific infections present in the vaginal can cause significant problem to the neonate, particularly chlamydia and gonorrhoea. These infections may be symptomless in the mother but cause serious neonatal infections. Viruses also cause problems at this time, particularly herpes and HIV. This has led to specific management protocols to reduce vertical transmission at the time of delivery by elective caesarean section.

FM2.05.03
MANAGEMENT OF HERPES INFECTION IN PREGNANCY
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Both HSV-1 and HSV-2 can be transmitted by contact with infected secretions on oral, genital or mucosal surfaces. After initial infection, HSV enters a period of latency, with possibility of recurrences throughout life, during which time it is contagious. HSV can be shed and transmitted in the absence of symptoms. Serious complications include encephalitis, meningitis, keratitis and neonatal disease. Genital HSV-2 infection has been epidemiologically linked as a risk factor in acquisition, transmission, and progression of HIV-related disease. Genital HSV infection is a common STD with prevalence reported 1% to 80% throughout the world.
Acyclovir, valacyclovir, and famciclovir have been approved for the treatment of primary and recurrent disease. They exert their action by inhibition of viral synthesis of DNA. Their use in the nonpregnant and pregnant woman can significantly alter the disease and influence transmission.
Management of pregnancies less than 29 weeks, patients with primary HSV may be treated with antiviral agents as non pregnant patients. Beyond 30 weeks, the infant is more susceptible to acquiring HSV infection. Type-specific serology should be obtained. Delivery by cesarean section can be considered but is not mandatory. From week 34 to term, if genital HSV lesions are present, the woman should be delivered by cesarean section to reduce the risk of HSV transmission to the infant. Specimens for viral culture should be taken from the cervix and any lesions within 24 hours of delivery. The use ofinvasive procedures during labor, such as fetal scalp monitoring and forceps, may facilitate transmission of HSV to the neonate.
In women with recurrent genital herpes who become pregnant, the risk of transmitting HSV infection to the neonate during pregnancy is very slight. If at delivery herpetic lesions are present, cesarean section may be considered.
If the child develops symptoms of neonatal herpes or culture results are positive, empirical therapy with intravenous aciclovir should be started. Use of acyclovir in infants, even in those that are premature, is very well tolerated, with a wide margin of safety.

FM2.06 INTRAPARTUM CARE - MOTHER

FM2.06.02
PAIN RELIEF IN LABOUR
Mohamed. Radhouane Rachdi, Dept. Gyn. & Obst., Military Hospital, Tunis, Tunisia

Pain during labour is usually defined as an unpleasant sensory and emotional experience. The management of pain in labour must have a beneficial effect on both mother and foetus.
What techniques are available?
- Non pharmacological methods methods of pain relief :
  *Education
  *Transcutaneous nerve stimulation (TENS)
  *Acupuncture
-Pharmacological methodes of pain relief.
The ideal analgesic would have the following proprieties: effective and controlable analgesia, safety to mother and foetus, mobility, no effect on labour.
- Opioids: pethidine (neonatal side effects), morphine, sufentanil.
- Inhalation agents: nitrous oxide (rarely used)
- Regional analgesia: comonly used.
  *Caudal analgesia and paracervical blocks used in the second stage for instrumental delivery.
Epidurals and spinals give excellent pain relief in labour.
*Epidural analgesia provides high-quality pain relief but is not instant in onset and may be associated with motor block.
*Spinal analgesia: it`s advantage is instant in onset but has a limited duration of action.
*Combined spinal-epidural analgesia (CSE): provides the advantage of a spinal and the epidural analgesia.
*Patient controlled epidural analgesia (PCEA) consists of self administration to minimize drug dosage and reduce demand on professional time.
*Continuous spinal analgesia with microcatheters. The safety and efficacy of delivering sufentanil and / or bupivacaine into the intrathecal space via a 28g catheter is being in evaluation. The effects of this technics on mother, foetus and labour are analized with a review of literature and personal experience.

FM2.06.03
THE USE OF MISOPROSTOL IN THE THIRD STAGE OF LABOUR: RATIONALE AND EXPERIENCE.
Hazem El-Refaey, Department of Obstetrics and Gynaecology, Chelsea and Westminstter Hospital, London, UK

Misoprostol, an orally administered PGE1 analogue, has acquired a place in the management of miscarriage, induction of abortion and labour. Within the last several decades scientific dogma prevented the investigation and use of enterally (oral and rectal) administered prostaglandins in the management of the third stage of labour. The background for this research programme will be presented and data from a randomised trials will be discussed.
Although it is well established that the routine use of uterotonic agents after delivery reduces the incidence of postpartum haemorrhage, the currently available agents have several drawbacks. Administration is invasive and

associated with unpleasant side effects. Syntometrine, the most widely used parenteral agent, is contraindicated in around 15% of women, as it can cause a rise in blood pressure. Syntometrine is deactivated by heat and light; it therefore requires specific conditions, including continuous refrigeration, for storage and transfer. Hence its routine use is confined to countries with good medical infrastructure and is unaffordable in the developing world. In developed countries there is need to offer patients a wider choice in the third stage of labour.
The efficacy of misoprostol in the third stage of labour was investigated in a comparative trial. One thousand women randomised to 500 ug misoprostol given orally or to a standard regimens of oxytocin, with ergometrine, or ergometrine. The main end points of the study were Incidence of postpartum haemorrhage; and. Incidence and severity of the side effects. Postpartum haemorrhage occurred in 12% of women given misoprostol and in 11% of women given standard oxytocic drugs (relative risk (RR) 1.10, 95% confidence interval (CI) 0.79, 1.55). Blood loss of 1000 mL or more occurred in 2% of women in each group. The main side effects of misoprostol were shivering (RR 1.95, 95% CI 1.69, 2.25) and a rise in temperature (difference in mean rise 0.34 C°, 95% CI 0.26, 0.42).

FM2.06.04
CAN THE PERINEUM BE PROTECTED?
Henri-Jean Philippe, CHU Limoges, St-Germain, France

During many years, guidelines for preventing third-degree laceration and damage to the pelvic floor have been recommended. And for instance, in France, between 1972 and 1981, the episiotomy rate increased from 8.1 to 32.1%.
Since this period, a lot of studies show that the restrictive use of episiotomy does not increase incidence of severe perineal tears than the liberal use.
Frequency of episiotomy is going to decrease from 60% to 25-30% in most of delivery-rooms.
The second question is about technic of episiotomy: mediolateral or middle episiotomy?
"midline episotomy remains the most important risk factor for perineal damage for both nulliparous and parous women".
La deuxième question concernait la pratique d'une épisiotomie latéro-médiane ou médiane. La plupart des équipes ont mis en évidence que la pratique d_une épisiotomie médiane majorait le risque de déchirure périnéale sévère.
Others questions are not resolved: which the best or the less worst?
- Forceps or vacuum delivery,
- squatting, standing or sitting position,
- with or without peridural,
- antenatal or postnatal pelvic muscle exercice,
- perineal massage?
And, the main question is : Is cesarean for preventing perineal damage justified ?
- statistically, there are some benefits in early postpartum period,
- psychologically, it is questionned,
- medically, there are less maternal complications in cas of elective cesarean section.
In conclusion, we need to improve our knowledges about mecanisms of delivery.

ON2.02 OVARIAN CANCER TREATMENT: CHEMOTHERAPY

ON2.02.02
IS THERE A ROLE FOR SECOND-LINE CHEMOTHERAPY IN EPITHELIAL OVARIAN CANCER?
Kevin B. Knopf, Medicine Branch, National Cancer Institute, Bethesda, MD, Unites States

Although many patients with epithelial ovarian cancer are curable with surgery and chemotherapy the majority of patients who present with advanced stage disease will eventually relapse and die of their disease. Second-line chemotherapy can achieve significant prolongation of survival in patients with relapsed epithelial ovarian cancer for those who remain platinum-sensitive at the time of their relapse. In women who are platinum-refractory very modest gains in survival and significant palliation have been observed with available agents. Despite the introduction of a number of new chemotherapeutic agents significant gains in survival in platinum-refractory ovarian cancer have been limited. Our original analysis examined trends in progression-free survival and overall survival with the use of second-line chemotherapy as reported in the literature from 1980-1997. Publications that contained the words "refractory", "resistant", or "second-line" in the title combined with "ovarian cancer" were reviewed. We limited our search to peer-reviewed studies of phase II or phase III oral or intravenous agents that had a minimum of 20 evaluable patients. We calculated an estimated median overall survival of 9.5 months from initiation of second-line chemotherapy. More distressing, however, was that over this time period we estimated an improvement of overall survival in patients with platinum-refractory ovarian cancer of 3.6 months. We have now extended this analysis to include all relevant published trials from 1980-2000 and will present these findings and their implications for future research. Because of the difficulty of treating relapsed ovarian cancer, issues of quality of life and cost effectiveness with second-line chemotherapy are vital and will also be discussed. Possible future research directions in this area will be offered.

ON2.02.03
GENE THERAPY FOR OVARIAN CANCER : DEVELOMENT OF NOVEL TREATMENT STRATEGIES
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In the last decade, advances in molecular biology have led to the development of techniques that permit the manipulation of mammalian cell DNA for diagnostic and therapeutic purposes. Gene therapy has subsequently evolved as a treatment option in patients with malignancies. The ability to transfer genes into cell, has opened a new spectrum of therapeutic possibilities. Various novel molecular strategies have been developed in recent years to inhibit tumor growth directly or to stimulate a systemic immune response against the cancer.
Several methods are currently used to tranfer genes into mammalian cells. Physical methods like electroporation, gene gun, or chemcal methods have been used in a variety of cell systems. DNA that is transferred by these techniques is usually in the form of plasmid DNA. Recent improvment in the development of liposomes have led to an increased interest in physical methods. Human ovarian cancer cells have also been found to be readily infectable in vitro and in vivo with a variety of viral vectors.
Important requirements for gene delivery systems are the accuracy of gene delivery to the target cell, the efficiency of tranfection, and the subsequent level of transgene expression. For in vivo use, the current most efficient gene transfer is accomplished using recombinent adenoviruses.
The absence of a specific antigens for ovarian cancer makes specific targeting of ovarian cancer cells inside the peritoneal cavity difficult. Tissues specific trangene expression using, for example, an erbB-2 sensitive promoter, restrics expression of the transgene to erbB-2 expressing cancer cells.
Several cytokines, for example, interleukin-2 are important in the generation of antitumor immunity. In order to circumvent the problem of severe toxicity associated with high doses of systemic cytokines, the transfer of cytokine genes into tumor cells to copresent tumor associated antigens and the amelioratory cytokine have been proposed.
Immunosuppressive factors such as transforming growth factor beta (TGFß) is an important Immunosuppressive factor in ovarian cancer. This molecule can inhibit the generation of lymphokine activated killer cells in vitro via the effect of TGFß. We have recently examined the effect of TGFß and IL-2 gene therapy using in vivo models and have developed a human trial.
Targeting the p53 tumor suppressor gene, which is mutated n approximately half of epithelial ovarian cancer, has been studied in Phase I-II trials. A phase II trial using transfection with a wild-type p53 using an adenoviral vector given systemically along with the chemotherapy and is being selectively administered to women whose tumors contain p53 mutations. Other strategies involve the use of herpes simplex virus thymidine kinase (HSV-TK) gene followed by exposure to the antiviral drug, gancyclovir.
Targeting ovarian cancer charasteristic factors like overexpression of oncogenes, growth factors, or mutated tumor suppressor gene products offer an array of targets for gene therapy. For the effective transfer of genes in vivo, improvements in gene delivery strategies must be made in order to achieve specific tumor targeting combined with high and long lasting gene expression.