2. INVITED SPEAKERS ABSTRACTS
THE GOLDEN HOUR FOR VERY IMMATURE INFANTS

Eduardo Bancalari

The minutes that follow birth are critical and can dramatically influence survival and subsequent quality of life. Because of respiratory depression or lung immaturity many premature infants need respiratory support immediately after birth. While many of the more immature infants require intubation and positive pressure ventilation evidence suggest that noninvasive respiratory support with N-CPAP or N-IPPV may reduce the incidence of death or BPD.

Early administration of surfactant is another therapy that has been shown to reduce severity of RDS, pneumothorax, and mortality. In infants who require early intubation for surfactant administration, rapid extubation to N-CPAP (InSurE) can also result in better respiratory outcome.

There is no conclusive evidence that sustained inflations or administration of surfactant in non-intubated spontaneously breathing infants improves long term outcome in extremely premature infants.

Evidence suggests that resuscitation with 100% oxygen in preterm infants is deleterious and increases the risk of oxidative damage and perhaps mortality. It is still not clear what the best inspired oxygen concentration is to start resuscitation in very premature infants but 30-40% with close titration to achieve the desired arterial oxygen saturation seems the most appropriate approach.

Cardiovascular support during the first minutes after birth has not been carefully evaluated. ELBW infants who require chest compressions and epinephrine in the DR have poor survival and neurodevelopmental outcome. Although volume expansion with blood or normal saline may be required in infants with suspected hypovolemia, rapid volume expansion may aggravate heart failure in asphyxiated infants and increase the risk for intracranial hemorrhage. Administration of vasopressors and inotropic agents shortly after birth should also be done with caution because of the potential side effects and lack of evidence for benefit.

Clinical evidence suggest that in the vigorous premature infant delaying cord clamping for 30–180 s following delivery improves blood pressure and decreases IVH and the need for blood transfusions. However, limited data is available regarding the risks or benefits of delayed cord clamping in the non-vigorous infant. Cord milking has been suggested as a more rapid alternative for placental transfusion when resuscitation cannot be delayed.

Maintenance of normal temperature and avoidance of excessive fluid losses during the first minutes of life is also critical in these infants. This can be achieved with the use of radiant warmers, hats and plastic wraps immediately after delivery.
BPD AND ADULT CHRONIC LUNG DISEASE: ARE THEY CAUSALLY LINKED?

Eugenio Baraldi

Bronchopulmonary dysplasia (BPD) is a chronic respiratory disease that develops as a consequence of perinatal/neonatal lung injury, and it is one of the most important sequelae of premature birth. Today BPD is mainly a developmental disorder in which the immature lung fails to reach its full structural complexity. Longitudinal studies on children with BPD identified, at all ages, increased rates of chronic coughing and wheezing, a greater need to use inhaled asthma medications and a significant airflow obstruction. Children who have survived BPD and children with asthma share some clinical and functional characteristics, but available evidence suggests that the two obstructive lung diseases do not have the same underlying airway inflammation. Spirometric values reflecting airflow, such as FEV1, are consistently lower in survivors of BPD into adolescence and young adulthood than in controls born at term rising the concern that the chronic lung disease after premature birth may predispose to the development of a chronic obstructive pulmonary disease (COPD)-like phenotype with aging. This is an open question that only follow-up and lung function studies extended to middle-age and beyond will answer. Unfortunately, no pathologic data are available elucidating which structural and pathophysiological alterations underlie the clinical and functional pulmonary abnormalities seen at long-term in some subjects delivered prematurely.

BPD is the earliest and perhaps longest-lasting obstructive lung disease in humans. During the early stages, BPD is characterized by a relevant burden of respiratory disease, with a significant impact on the quality of life of the affected children and their families. In grown-up BPD subjects respiratory symptoms cause less impairment, but on the functional side a persistent airflow limitation is documented and a possible early and steeper decline in lung function during adulthood has been hypothesized.

One of the major challenges for the research on BPD during next years is the investigation of the still largely unknown pathogenetic mechanisms underlying the functional and clinical picture presented on the long-term by BPD survivors. The characterization of such mechanisms may guide the development of novel targeted therapies or preventive strategies that could improve the overall respiratory health of these subjects.

References

CONTROVERSIES IN CORTICOSTEROID ADMINISTRATION – NEW DATA

Jose Luis Bartha

The reduction in neonatal morbidity after antenatal corticosteroid administration to women at high risk of preterm delivery has been proposed for long time as one of the best examples of Evidence –Based Medicine. However, there is still an open debate about many issues related with this topic. Concerning mechanisms of action most of studies have focused on the stimulation of the development of neumocytes, especially type 2, leading to changes in lung mechanic and function and, therefore, improving neonatal gas exchange. Also, the stimulation of development and maturation affects to tissues other than lungs. The main challenge now is to identify the genetic and molecular changes and the physiological pathways involved in these actions to better understand this mechanism.

Clinically, the most important recent controversy has been the use of repeated courses of therapy. Concerns about the use of weekly repeated doses of corticosteroids emerged after the demonstration of an increase in the rate of small-for-gestational age fetuses, impaired fetal growth, neurodevelopmental disability, and affected cognitive functions. This led to change protocols and clinical guides. But, on the other hand recent evidence has demonstrated that in comparison with a single dose, repeated courses reduced the risk of respiratory distress syndrome and other poor perinatal outcome variables without increasing maternal side effects. The use of a rescue dose after an initial course has emerged as a clear alternative that has been demonstrated to improve respiratory mechanics and function and reduce the rate of distress respiratory syndrome without significant side effects.

The use of this medication in the limits of viability is also another reason for discussion. While its use has been found to be useful between 24 and 25 weeks of gestation, the effects under 24 weeks are rather controversial. Along the same line, its use beyond 34⁰ weeks and even more after 34⁰ weeks is also debated. There are several randomized clinical trials finding contradictory results. Although currently the use of methods to assess fetal lung maturation is not generally recommended, some emerging ultrasound techniques may help in the future to identify those cases that can be beneficed from this therapy.

Finally, other issues such as the interval of time between administration and delivery, the fetal and infant side effects and its use in special populations such as in multiple gestation, preeclampsia and intrauterine growth retardation, diabetes and preterm premature ruptured of membranes, can be discussed.
GESTOSIS AND HISTOCOMPATIBILITY: FROM BIODIVERSITY PARADIGMA THE ENIGMA KEY?
HYPOTHESIS EVOLUTION AND BEYOND

Lorella Battini

The placental immunological barrier, between the mother and the fetal “graft”, allows mutual tolerance between two antigenically different organisms. Following a rejective hypothesis of the fetal graft in gestosis, we evaluated at placental and plasmatic level, the potential ethiopatogenetical role of the MHC-HLA antigens, which are implicated in tolerance and rejective reactions. Beyond this hypothesis, we studied the angiogenetic factors, as markers of placental endothelial cell disfunction and to assess the possible implication in dating delivery time.

Previously, placental endothelium from gestosis and physiological pregnancies was tested by immunohistochemistry and HLA-DR monoclonal antibodies. Subsequently, a placental ultrastructure and biochemical V-CAM1 plasmatic study followed. Furtherly, laser confocal and electron microscopy assessment was carryied out both through immunofluorescence and immunocytochemistry, for HLA-G1 antigen and ubiquitin.

Gestosic women, their partners and physiological control couples were also sero/genotyped for HLA-DR assessment, chronologically performed by Terasaki technique, low and high resolution PCR and DNA sequence-based typing.

Finally, placental angiogenic factor (PLGF), in gestosic patients and matched controls, was evaluated. The immunoistochemical study of placental endothelium showed a widespread expression of HLA-DR antigens, absent in normal pregnancy. Following, in placentae from gestosic women, we ultrastructurally demonstrated a placental barrier breakage, leading to the mixing of maternal and fetal blood. This condition could provoke a triggering of that maternal rejective reaction presumed to be at the basis of gestosis. Terasaki investigation of the Human Leukocyte class II DR Antigens (HLA-DR) showed a statistically significant increase of HLA-DR homozygosity and a reduced antigenical variety in gestosic women and their partners versus control couples. The following update, studying the 2nd exon of the human gene HLA-DRβ1 on the short arm of the chromosome 6, by DNA sequence-based typing (S-BT) PCR confirmed the significant excess of HLA-DR homozygosity in couples associated with gestosis.

Immunohistochemical and ultrastructural evidence of immunological activation and placental barrier disruption, support rejective hypothesis in gestosis. From serotyping and genotyping results, it emerges that HLA-DR homozygosity and reduced antigenical variety seem to be associated to a major risk for this syndrome, which furtherly appears to be a “couple’s disease”. HLA-G expression and localization data has been shown for discussion, to understand fascinating mechanism underlying tolerance/ rejection in pregnancy. The V-CAM 1 and PLGF values correlation with diagnosis and prognosis, confirmed the endothelial factor in pathogenesis and highlighted the route to delivery timing.
OBSTETRICAL AND PERINATAL OUTCOMES IN METHYLENE TETRAHYDROFOLATEReducerase POLYMORPHISMS

M. Sinan Beksaç

Objective: This study aimed to evaluate the effect of the methylenetetrahydrofolate reductase (MTHFR) polymorphisms as risk factors for obstetrical/perinatal complications.

Methods: We reviewed the records of pregnancies screened for MTHFR polymorphisms in our hospital between from January 2002 to December 2012. This cohort study is consisted of 617 patients including 227 patients with homozygous or compound heterozygous MTHFR polymorphisms (Group I), 257 patients with heterozygous polymorphisms (Group II), and 133 patients without MTHFR polymorphisms (Group III). Demographic data, obstetrical history, diagnostic laboratory parameters, pregnancy outcomes were recorded. A new obstetrics index (BOI) was used in order to compare the obstetrical backgrounds of the study groups.

Results: We have shown that patients who had homozygous or “compound heterozygous” mutations for MTHFR had adverse perinatal outcomes compared to control patients and patients with heterozygous mutations. We have found that obstetrical histories of patients with homozygous mutations are worse than the other groups. Besides, chromosomal abnormalities and structural anomalies such as neural tube defects, cardiac anomalies and urinary system anomalies are found to be more frequent in patients with reduced MTHFR activity. We have also demonstrated that when patients are prepared and treated preconceptionaly the pregnancy outcomes are better. Low dose low molecular weight heparin together with low dose salisilic acid and vitamin B supplementations are effective in pregnancy outcomes in this group of patients.

Conclusion: Patients with poor obstetrical history should be investigated in terms of the presence of MTHFR polymorphisms, so that necessary precautions can be taken preconceptionaly in order to prevent obstetrical/perinatal complications.
Pregnancy is associated with increased clotting potential, decreased anticoagulant activity, and decreased fibrinolysis; all these physiological changes play a role in the well-known prothrombotic phenotype of normal pregnancy. Thrombophilia, which refers to inherited or acquired disorders associated with a persistent hypercoagulable state and a tendency towards thrombosis, further contribute to an increased predisposition to thrombotic events during pregnancy.

Haemostatic disorders also play an important role in the pathogenesis of placenta-mediated pregnancy complications, in particular miscarriage, late pregnancy loss, placental abruption, preeclampsia, intrauterine growth restriction.

Conflicting results from retrospective and prospective studies do not easily allow to understand who should be screened for thrombophilias with laboratory tests. Furthermore, the optimal obstetric management of women affected by inherited or acquired thrombophilia is open to discussion, as thrombophilias are common, and many affected women will have a normal pregnancy outcome, while our ability to predict whether thrombo-prophylaxis will prevent adverse obstetric outcomes is controversial.

It is sometimes possible to identify women with an increased risk of adverse events by clinical history, such as personal or family history of venous thromboembolism, or prior adverse obstetric outcomes. In these cases, screening for thrombophilia should be considered.

Recommended screening tests for inherited thrombophilias should include factor V Leiden mutation; prothrombin G20210A mutation; and antithrombin III, protein S, and protein C deficiencies. Screening for acquired thrombophilias should include lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein antibodies.

For antiphospholipid syndrome (APS), it is presently well known that the treatment with heparin and aspirin improves pregnancy outcomes.

As a result, clinicians have begun to offer treatment with heparin and aspirin to patients with inherited trombophilia, even if data on its effect on obstetrics outcome are insufficient and need to be confirmed.

The anticoagulant of choice during pregnancy is low molecular weight heparin (LMWH), which is preferred to adjusted-dose unfractionated heparin (UHF) for its extended half-life, better bioavailability, ease of use and decreased incidence of bone loss in comparison to unfractionated heparin.
How Menudos Corazones Foundation Provides Support to Families Who Have Received a Prenatal Diagnosis of Congenital Heart Defect

Teresa Bordons

In Spain are born each year about 4,000 children with congenital heart defects (CHD). It is the birth defect highest in prevalence. Menudos Corazones emerged from a group of parents of children born with CHD, in order to support parents living through a similar experience. The foundation aims since 2003 to improve the quality of life of children, teenagers, and young adults born with CHD and their families and its programs are present in four public hospitals in Madrid.

Advanced medical technology has allowed in the past decades a significant increase of the rate of detection during pregnancy of structural heart defects or heart vessels malfunctions: psico-social parental care during the perinatal period is now an important goal. The emotional impact caused by a pre-natal diagnosis of CHD is profound and Menudos Corazones gives support to families in different ways, so that since the diagnosis is made they may have the opportunity to manage the news, and make well-informed decisions.

What Menudos Corazones provides?

- Psychological support aimed to generate coping strategies. It is essential a guide so to restructuring previous expectations on pregnancy and to support the control of emotions. Psychologists support parents in the process of making decisions being well informed.
- Contact if desired with parents of children born with a similar CHD diagnosis.
- Guidance on available social aids and resources adequate to their situation.
- Visits to the hospital units in which their child would be born in Madrid so to make the hospital environment familiar to parents.
- Use of the “Family Room” in 12 de Octubre Hospital close to the Intensive Care Unit ICU, an space to rest, and get some privacy in the hospital when children are in intensive care.
- Free accommodation in a shared apartment or a hotel room for pregnant women deferred to a hospital in Madrid from their place of habitual residence in order to provide adequate care in the perinatal period.

Menudos Corazones’ experience indicates that a pre-natal diagnosis of CHD makes a very significant difference in the way well-informed parents develop empowering strategies to cope with the diagnosis of a heart disease.
CIRCULATING ENDOTHELIAL CELLS, CIRCULATING ENDOTHELIAL PROGENITOR CELLS AND VON WILLEBRAND FACTOR AS A MARKERS OF ENDOTHELIAL DYSFUNCTION IN PREGNANCY COMPPLICATED BY HYPERTENSIVE DISORDERS

Grzegorz H. Bręborowicz

Background and aims
Endothelial cells dysfunction plays an important role in the pathogenesis of hypertension in pregnancy. We tested the hypothesis that there are altered number of circulating endothelial cells (CECs) and circulating endothelial progenitor cells (CEPCs) in pregnant woman with hypertensive disorders, when compared to pregnant healthy controls. Moreover, we assessed CECs: CEPCs ratio, as an effect of imbalance between regenerative and degenerative endothelial processes. Furthermore, we evaluated von Willebrand factor (vWf) level as a specific plasma marker of endothelial dysfunction/damage.

Methods
Venous blood from the first tube was used to determine vWf level by commercial ELISA. Second tube of blood was used for flow cytometric analysis. CEPCs were defined as CD45 (-) CD34 (+), CD146 (+) and CD133 (+). CECs were defined as CD45 (-) CD34 (+), CD146 (+) and CD133 (-). The evaluation of Doppler flow velocimetry was performed in the uterine arteries, umbilical artery and fetal middle cerebral artery.

Results
The highest mean number of CECs were found in the peripheral blood of pregnant women with chronic hypertension, and the lowest were found in the control group. The highest mean number of CEPCs were found in the peripheral blood of healthy pregnant women, and the lowest mean number were found in group of pregnant women with chronic hypertension. Mean level of vWf was the highest in women in pregnancies complicated by pre-eclampsia. CEPCs/CECs ratio reached the lowest values in pregnant women with chronic hypertension, and the highest in control group.

In group of women in pregnancies complicated by pre-eclampsia we found a positive correlation between mean systolic and diastolic blood pressure and CEPCs/CECs ratio. In pre-eclamptic women with abnormal Doppler flow velocimetry which indicated insufficiency of the placenta, vWf level was significantly higher.

Conclusions
1. The number of CECs depends on type of hypertension complicating pregnancy.
2. Number of CEPCs reflects indirectly degree of endothelial damage and possibilities to its regeneration.
3. The number of CEPCs in women with preeclampsia may reflect the insufficient or impaired repair mechanism of endothelial damage.
4. Hypertensive disorders in pregnancy are associated with endothelial dysfunction with incorrect numbers of CECs and CEPCs.
5. The longer duration of exposure to elevated blood pressure and more extensive damage to the endothelium, the lower CEPCs / CECs ratio.
6. Endothelial injury in pre-eclamptic patients, expressed by the higher levels of vWf, showed the relationship with ultrasound features of placental insufficiency.
PSYCHOLOGICAL SUPPORT OF THE FAMILIES IN PERINATAL MEDICINE

Evelyn Cano Giménez

The arrival of a newborn infant to the family unit is always a source of joy, but sometimes this state of satisfaction of the parents and the close relatives is interrupted when the baby is born and has to be admitted to the Neonatal Intensive Care Unit (NICU). This situation can happen for various reasons. One of the most common reasons is being born prematurely or being born with a serious health problem that endangers their life. This unexpected situation provokes high levels of stress, anxiety and possible depression to the family. Moreover, combined with the fact that the expectations of having a healthy baby are not fulfilled, they have to live with the uncertainty as to whether their baby will survive and the sudden changes they might find in their lives as parents. Further, parents have to adapt themselves to a different environment, a specialized language, and sometimes they also have to move to cities where they do not reside. All these circumstances cause the disappearance of normalcy in the family dynamics. We should clarify that this situation does not only affect parents, but also affects the immediate family (siblings, grandparents, uncles, aunts, friends, etc.). For all the above situations, it is important to provide psychological support to the whole family from the admission of the mother to the discharge of the baby in order to guide and help them through different situations, and therefore reducing levels of stress and anxiety. In this way, when the baby is discharged, parents might be predisposed to interpret, pamper and take care of their baby. That will not be possible if they leave the hospital confused, afraid, stressed, anxious or depressed, and this, surely, will influence the mental and psychomotor development negatively.
HOME HOSPITALIZATION OF THE EARLY DISCHARGED PRETERM NEWBORN STRENGTHENING TIES BETWEEN PARENTS AND CHILDREN

Xavier Carbonell-Estrany

Introduction.
Increasing prematurity generates prolonged hospitalization, which makes the parent–child relationship difficult. Preterm newborns may be discharged at home earlier if they are followed by domiciliary nursing care (early discharge, ED). ED is considered if the premature reaches 34 weeks of postmenstrual age, is fed by mouth and is not receiving any medication.

Patients.
During a 12 year period (December 2002 till December 2014) a total of 7403 patients were admitted in the Neonatal Service. Of them, 1474 (20%) accepted to be in the program of ED. 73% were premature, 50% with weight under 1500 g at birth and only 11% were term babies included in the program for associated pathological or social conditions. The results of the ED program during this 12 years period are described.

Results.
Of the total of premature under 1500 g (n=1627) admitted in the unit in this period, 414 (26%) were included in the ED program. Infants born with gestational age ≤ 36 weeks in the ED program (n=1223) had a mean birth weight of 1615 ± 381g. (IQR:1355-1910g.) and a mean birth gestational age of 32.6 ± 2.34 (IQR:31-34).
The weight at the time of ED was 1870 ± 130 g (IQR:1795-1950). In the whole group of ED, 34 patients (2.4%) required rehospitalisation and the average of nursing visits was 3.43 ± 1.5 (IQR 2-4) with a length of stay of 29.01 ± 6.92 (5-60) minutes.
A randomized survey of satisfaction was performed to the parents in 448 cases (30% of total) and in over 90 % of the cases the score obtained was ≥ 9 over10.

Other considerations.
In 2007, ED premature were compared with the premature with late/conventional discharge (LD). There were significant differences between the ED vs LD groups in birth weight (1166.75 ±236.23 LD versus 1129.03 ± 252.17 ED; p =0.027), GA (29.59 ± 2.64 LD versus 30.60 ± 2.45 ED; p=0.000), rate of intrauterine growth retardation (ED: 107 -36.1 %-; LD 311 -27.1 %-; p=0.002). The ED patients had significantly less morbidity and invasive procedures than the LD.
In 2008, 65 LD premature were compared prospectively with 65 ED premature group. No statistical difference in any demographic item was observed in both groups, neither there were differences in mother’s pathology or in perinatal/neonatal diseases or procedures use in both groups. There was a significant decrease in the total of hospital days (34 vs. 23; p<0,001) in ED group. Also the ED group showed a superior increase in weight (g/Kg/day) in the week post discharge at home in comparison with control group in the hospital (21.5 g/Kg/day vs 17 g/Kg /day; p<0,001).

Conclusion.
The 12 years balance of the ED program implemented in our Service has been highly successful with extremely low rate of readmissions and complications and very high acceptance by the parents .The VLBW patients involved in the early discharge have less pathology in the neonatal period. The total number of hospitalization days is significantly reduced. The increase in body weight is statistically faster in the premature in the home care program.
The ED program is effective, shortens the hospital stay, saves money and is very well accepted by parents and health providers.
SUPPORT TECHNOLOGIES FOR MEASUREMENT OF BASAL TEMPERATURE AND CERVICAL SECRETION

Candela Cardero De La Puente

- In addition to observation of the cervical secretion and the measurement of Basal Temperature there are different support devices that help the personal detection of signs, reinforce and/or give security to the observation and charting.
- The aim of these devices is to determine the possible fertile days of the cycle and some of them -with more accuracy- detect the ovulation period.
- The use of these devices must not substitute completely the self-observation of the natural signs, that always express with more accuracy the “fertility window”.

FERTILITY MONITORS

A. HORMONAL DETECTION IN URINE: (Oestrone and LH).
   - Detection of the amount of LH by ovulation tests:
   - ACOFAR / FIDETEST / UNITEST / FELCONTROL.
   - Combined detection of the Oestrone and LH, by ovulation monitors:
   - PERSONA / CLEAR BLUE.
   - CICLOTEST 2 PLUS… and CICLOTEST BABY (they also register the body basal temperature).
   - LADY COMP BASICA, PLUS or BABY (they personalize the detection with individual indicators).

B. DETECTION BY THE CRYSTALLIZATION IN SALIVA
   - With optical microscopy:
   - OVULATOR / PG53 / FERTIL CONTROL EASY
   - With electrolytic changes in saliva:
     - OVA CUE (electric monitor).
NOVEL OBSERVATIONS ABOUT THE BIOLOGY OF THE PLACENTA IN IUGR

Irene Cetin

Intrauterine growth restriction (IUGR) occurs when fetal growth rate falls below the genetic potential. This condition affects a significant number of pregnancies (7-10% depending on the population), although its severity ranges from intrauterine demise to occasional recognition at delivery with birthweights below the 10th centile. Most IUGR are born from otherwise healthy mothers, although preeclampsia is often associated with this condition. Incorrect early implantation of the placenta may lead to mismatches in oxygen delivery to different areas of the placenta. A malfunctioning or “insufficient” placenta has been recognized as the “cause” of IUGR, leading to altered placental transport of nutrients, mainly amino acids and lipids, but also micronutrients such as iron and folate.

Maternal nutritional status, diet and exposure to environmental factors are increasingly acknowledged as potentially affecting fetal growth both by altering nutrient availability, as well as by modulating placental gene expression, thus modifying placental function. However, the reason why placental development fails to be appropriate in these pregnancies is still not known. Mitochondrial DNA (mtDNA) copy number is positively correlated with the number of mitochondria and its control is essential for normal cell function. We have previously reported altered mitochondrial content and function in intrauterine growth restricted (IUGR) placentas, as well as higher mtDNA levels in IUGR maternal blood. Moreover, we have measured by respirometry the functionality of the respiratory complexes, in order to assess potential alterations in placental energetic metabolism. More recently, we have investigated placental mesenchymal stromal cells (p-MSCs) in IUGR compared to appropriate for gestational age (control) pregnancies. Proliferation rate was lower in IUGR compared to control cells, both in placental membranes and basal disc. Moreover, expression of hematopoietic (CD45), hematopoietic stem (CD133, CD34, CD117), endothelial (CD31) and mesenchymal (CD105, CD29, CD44, CD73, CD90) markers evaluated by flow cytometry showed an earlier shift towards homogeneity in IUGR than in controls. In vitro findings also demonstrate that multipotency of IUGR-derived p-MSCs is restricted, as their capacity for adipocyte differentiation is increased, whereas their differentiation ability towards endothelial cell lineage is decreased.

The potential role for p-MSCs in intrauterine growth restriction, as well as the striking mitochondrial changes involved in energy production, open new perspectives for the early diagnosis and treatment of IUGR.
MICRONUTRIENT REQUIREMENTS AT CONCEPTION AND DURING PREGNANCY

Irene Cetin

Awareness has increased during recent years that a healthy balanced diet, rich in antioxidants and fish, provides the best basis for optimal pregnancy outcome. Adequate nutrition is very important for adequate intake not only of macronutrients like proteins, carbohydrates and fats, but also of micronutrients and essential fatty acids like omega 3, for which we may more easily incur into deficiencies or inadequacies.

Micronutrients are vitamins and minerals required in minute amounts for metabolism and normal organism functioning. With their numerous functions in the body, micronutrients are essential for growth and development. Micronutrients, particularly folate, are required to provide the basis for conception, implantation and embryo development in the first weeks of pregnancy. Their requirements increase exponentially during pregnancy in order to meet the growing demands of the feto-placental unit. Moreover, nutritional needs for micronutrients are increased during pregnancy not only to support fetal growth and development but also for adaptations occurring in maternal tissues and metabolism. This is because while energy needs increase only about 10% during the course of pregnancy, the need for certain vitamins and minerals in pregnancy shows a much greater increase. Supplementation with omega 3 and specifically DHA during pregnancy has also been shown decrease risk of premature delivery and to improve some eurodevelopmental outcomes in childhood.

Micronutrient deficiencies have been associated with significantly high reproductive risks, ranging from infertility to fetal structural defects and long-term diseases. On the other side, healthy dietary patterns and micronutrients supplementation, particularly during the peri-conceptional period, are related to improved birth outcomes, probably through alterations in maternal and fetal metabolism due to micronutrients role/involvement in enzymes, signal transduction, transcription pathways, oxidative stress and epigenetic modifications. Since different pregnancy stages represent a continuum, from the pre-conception to the post-partum period, an injury acting before conception or in early pregnancy may have long-lasting effects on the well-being of the mother and the fetus, and may further influence the health of the baby at a later age.

There is a growing interest in the role of micronutrients and DHA in pregnancy, because of the increased needs and greater vulnerability of pregnant women to the effects of deficiency or imbalance. This is particularly important for those micronutrients such as folate, iron, vitamin D and iodine, i.e. those micronutrients that are at greater risk of deficiency and for which effects have been shown on outcomes of pregnancy.
PLANNED HOME BIRTH IN THE DEVELOPED WORLD: A CHALLENGE TO PERINATAL MEDICINE

Frank Chervenak

This presentation addresses the recrudescence and new support for planned home birth in the United States and the other developed countries in the context of professional responsibility. Advocates of planned home birth have emphasized patient safety, patient satisfaction, cost effectiveness, and respect for women's rights. We provide a critical evaluation of each of these claims and identify professionally appropriate responses of obstetricians to planned home birth. Planned home birth has unnecessary, preventable, irremediable and therefore unacceptable increased risk of harm for pregnant, fetal, and neonatal patients. We show that the persistently high rates of emergency transport undermines patient safety and satisfaction, the raison d'etre of planned home birth, and that a comprehensive analysis undermines claims about the cost-effectiveness of planned home birth. We then argue that obstetricians should understand, identify and correct the root causes of the recrudescence of planned home birth; respond to expressions of interest in planned home birth by women with evidence-based recommendations against it; refuse to participate in planned home birth; but still to provide excellent and compassionate emergency obstetric care to women transported from planned home birth. We explain why obstetricians should not participate in or refer to randomized clinical trials of planned home vs. planned hospital birth. We call on professional organizations of obstetricians and midwives not to support planned home birth when there are safe and compassionate hospital-based alternatives and to advocate for professional responsibility in obtaining a safe home-birth-like experience in the hospital.
NONINVASIVE PRENATAL TESTING: STATE OF THE ART

Carmina Comas Gabriel

The recent development of non-invasive prenatal testing (NIPT) for aneuploidies with cell-free (cf) DNA marks the beginning of a new era for prenatal screening. Several recent studies have demonstrated that the most effective method of NIPT for trisomy 21, with detection rates above 99% and false positive rates (FPR) of about 0.1%, is derived from the examination of cfDNA in maternal plasma. Conventional first trimester combined screening including serum markers and nuchal translucency has 85–90% detection rates with 5% FPRs. Consequently, cfDNA testing is far superior to screening methods that are currently in use, and should lead to widespread future use of the test in routine clinical practice. Clinical trials have demonstrated the effectiveness of NIPT for main autosomal trisomies in high-risk women. More recent studies in low risk populations provide some, albeit limited, evidence suggesting that cfDNA screening may be as effective in the general population as it is in those already scheduled for invasive testing. As NIPT has transitioned from clinical trials to clinical care, reports are beginning to be published on laboratory screening performance in clinical settings. Considering all these experiences, there is no doubt that NIPT is here to stay and its scope will broaden. The question remains as to how should it be used and implemented in routine clinical care. Moreover, in the past two years, various labs have introduced panels and technological advancements that have expanded the clinical applications of cfNIPT. This talk will cover the evolution of NIPT from the preliminary experience to its current state, focusing on what the clinician should know when counseling. Main topics we are going to discuss are what are the facts, some important misconceptions, important and practical concepts to be aware of when counselling, some still unsolved questions (from a technical, clinical, economical and ethical point of view), what are the current scientific recommendations and what is the future we can expect regarding this technology.
Cerebral palsy is the most common motor disability in childhood. Population-based studies from around the world report prevalence estimates of cerebral palsy ranging from 1.5 to more than 4 per 1,000 live births or children of a defined age range. In the Unites States, about 1 in 323 children has been identified with cerebral palsy. Preterm birth is a major risk factor for cerebral palsy, and the risk increases markedly with decreasing gestational age. In 1995, Nelson and Grether reported that in utero exposure to magnesium sulfate was associated with a lower prevalence of cerebral palsy in infants with a birthweight <1500 g. Since then, several observational studies have reported an association of antenatal treatment with magnesium sulfate for preterm labor or preeclampsia with a decreased risk of cerebral palsy in low birthweight or preterm infants. Now, there is compelling evidence from several high-quality meta-analyses of randomized controlled trials that antenatal magnesium sulfate has a neuroprotective effect in very preterm infants. In fact, magnesium sulfate administered to women at risk of preterm birth before 32 weeks of gestation reduces in their children the risk of cerebral palsy by ~30%, moderate or severe cerebral palsy by ~35%, and substantial gross motor dysfunction by ~40%. Importantly, magnesium sulfate does not have any effect on the risk of total pediatric mortality which indicates that the reduced risk for cerebral palsy does not appear to be due to selective mortality of magnesium sulfate-exposed infants. Recent evidence has shown that antenatal magnesium sulfate is associated with a decreased risk of neonatal cranial ultrasound abnormalities such as echodensities and echolucencies among infants born at <32 weeks, which could partially explain the effect of magnesium sulfate on cerebral, palsy. The number of women at risk of preterm delivery before 32 weeks of gestation who need to receive magnesium sulfate to prevent 1 case of cerebral palsy is about 50. This intervention is cost-effective and it is estimated that ~600 new cases of cerebral palsy could be prevented annually in the United States if all women at risk of preterm delivery before 32 weeks of gestation receive antenatal magnesium sulfate. Recently, the World Health Organization has recommended the use of magnesium sulfate for women at risk of imminent preterm birth at <32 weeks of gestation for preventing cerebral palsy in the infant and child.
THE PREVENTION OF PRETERM BIRTH IN TWIN GESTATIONS

Agustín Conde-Agudelo

Twin gestation is associated with an increased risk of adverse perinatal outcomes which are mainly driven by prematurity. Several interventions have been proposed to prevent preterm birth in twin gestations. There is insufficient evidence to support the use of prophylactic tocolytic agents, bed rest, and specialized diets or nutritional advice. Current evidence indicates that cervical cerclage, 17α–hydroxyprogesterone caproate (17-OHPC), vaginal progesterone and cervical pessary are ineffective for preventing preterm birth and associated perinatal morbidity and mortality in unselected twin gestations. Cervical cerclage is associated with a significantly increased risk of very low birthweight and respiratory distress syndrome in women with twin gestations and a short cervix. The use of 17-OHPC is contraindicated in twin gestations because there is a trend towards an increase in the risk of adverse perinatal outcomes among women treated with 17-OHPC. In addition, the administration of 17-OHPC in women with a cervical length >25 mm before 24 weeks of gestation is associated with a significantly increased risk of adverse perinatal outcomes. Two individual patient data meta-analyses have shown that among women with a twin gestation and a cervical length ≤25 mm at midgestation, vaginal progesterone is associated with a 44% significant reduction in the risk of neonatal morbidity and mortality and a 30% non-significant reduction in the risk of preterm birth at <33 weeks. However, a small number of patients with twin gestations were included in these analyses. The efficacy of cervical pessary in women with a twin gestation and a short cervix remains unclear. A post-hoc analysis of a randomized controlled trial (RCT) from the Netherlands reported that pessary reduced significantly the risk of preterm birth at <32 weeks of gestation and adverse perinatal outcomes among women with a cervical length <38 mm. Another post-hoc analysis from a multicenter RCT showed that pessary does not reduce the risk of preterm birth and adverse perinatal outcomes in women with a cervical length ≤25 mm. Finally, a RCT conducted in Spain reported that the insertion of a cervical pessary reduces the rate of spontaneous preterm birth at <34 weeks of gestation in women with a CL ≤25 mm without effects on neonatal morbidity and mortality. In conclusion, further RCTs of vaginal progesterone and cervical pessary in women with a twin gestation and a short cervix are urgently needed to clarify whether these interventions can reduce the risk of preterm birth and perinatal morbidity and mortality.
**FETAL CARDIAC FUNCTION – EVALUATION OF SYSTOLIC AND DIASTOLIC FUNCTION**

Fatima Crispi

Fetal echocardiography was initially employed to detect congenital heart disease, but its use in fetal cardiac function assessment has recently been proposed. Fetal cardiac dysfunction may be due to an intrinsic myocardial disease or to a secondary adaptive mechanism. The latter is particularly important because the heart seems to be a central organ in the fetal adaptive response to a variety of insults. Consequently, fetal echocardiography including assessment of systolic and diastolic function may be useful in the detection, monitoring and prognosis of diseases that may affect fetal cardiac function. The primary function of the heart is to eject blood in order to provide adequate perfusion of organs. The heart achieves this function by contracting its muscular walls around a closed chamber to generate sufficient pressure to eject blood from the ventricle through the aortic/pulmonary valve and into the aorta/pulmonary artery (systole). An adequate filling of the ventricle from the atria (diastole) is also essential. In order to maintain normal cardiac function, both systolic and diastolic processes must be preserved and time events must occur in a synchronized manner. The use of 2D, M-mode, conventional and tissue Doppler, 2D-speklae tracking and 4D-statio temporal image correlation permit to evaluate ejection fraction, ventricular inflow and outflows, stroke volume and cardiac output, ejection and isovolumetric times, myocardial performance index, and myocardial displacement, velocity, strain and strain-rate of the fetal heart. In spite the obvious difficulties of assessing a small and moving organ within a small, moving, and changing patient, fetal echocardiography has demonstrated to by a feasible and reliable tool for assessing fetal cardiac function with adequate equipment and specific training. Functional echocardiography may be useful to select high-risk populations and to monitor several fetal conditions including intrauterine growth restriction, twin-to-twin transfusion syndrome, maternal diabetes, and congenital diaphragmatic hernia. In addition, given the substantial evidence indicating the occurrence of programming of adult cardiovascular disease in fetal life, cardiac function assessment might help to predict perinatal and long-term cardiovascular outcomes.
METHODS OF CARDIAC EXAMINATION (2D, M-MODE, SPECTRAL DOPPLER, COLOR DOPPLER)

Fatima Crispi

Recent advances in fetal echocardiography enable the assessment of structural and functional integrity of the fetal heart. 2D and color Doppler are the essential tools for obtaining the systematic transverse planes for the detection of congenital heart disease (abdominal, four-chamber, right outflow, left outflow, three-vessel and trachea views). The use of M-mode and spectral Doppler permit a more advanced evaluation including the assessment of cardiac rhythm and function by evaluating timing events, ventricular inflow and outflow, myocardial displacement and ejection fraction. An combined and integrate use of the available techniques is essential for the adequate evaluation of the fetal heart structure and function.
THE RELATIONSHIP TO MATERNAL AGE & PREGNANCY OUTCOME

Snezana Crnogorac

During the last forty years there has been an increasing trend among women in the industrialized world to delay childbearing. The mean maternal age at the birth of the first child increased between 1970 and 2000 in many countries, from 21.4 to 24.9 years in the United States and from 25.6 to 28.0 years in Japan with very similar changes in Europe countries. The proportion of first births to women aged 35 years and over in the United States increased nearly eight times from 1970 to 2006. In the last several decades women are more often using the latter part of their reproductive period to have all their children, they tend to be well educated of higher socio-economic status and of lower parity than older mothers from the recent past. Fertility potential decreases with advancing maternal age. For over 30 years assisted reproductive technology and oocyte and embryo donation has been used to treat age-related infertility. This practice has become increasingly common and today a significant percent- age of older women all over the world undergo oocyte donation. Multifetal pregnancies are often and associated with significant maternal and fetal complications. Advanced maternal age are associated with a range of adverse pregnancy outcomes including low birth weight, pre-term birth, stillbirth, unexplained fetal death and increased rates of Caesarean section. Some studies have demonstrated an increased incidence of antepartum haemorrhage, operative vaginal delivery, preeclampsia, and placenta praevia. The risks of aneuploidy and fatal congenital anomalies increase with maternal age. About 16 million adolescent girls aged 15-19 give birth each year. Almost 95% of these births occur in developing countries. Adolescent childbearing has a negative impact on the health of the adolescents and their infants. Accounting for about 11% of all births worldwide, maternal conditions in adolescent’s cause 13% of all deaths and 23% of all disability adjusted life years. Studies have shown rates of newborn death to average about 50% higher to adolescent mothers versus mothers in their 20s. The adverse impact of poor newborn health due to adolescent pregnancies can have inter-generational effects and also long term effects leading to adulthood disease. Key words: advanced maternal age; adolescent pregnancy: complication; adverse perinatal outcomes.
FETAL BRAIN TUMORS, CYSTS AND HEMORRHAGE

Vincenzo D’Addario

Most fetal brain anomalies can be diagnosed during the second trimester scan performed to screen for fetal malformations. However there are some cerebral pathologies which become evident only during the late second and third trimester of pregnancy. Occupying space lesions, such as tumors, cysts and hemorrhages frequently appear as late onset complications in a fetus diagnosed as normal during the second trimester anomaly scan.

The most common type of congenital brain tumor is teratoma whose prognosis is extremely poor: the survival rate at 1 year of life is only 7% and falls to 3% in cases diagnosed before 30 weeks of gestation. The outcome is better in cases of lipomas of the corpus callosum or in cases of isolated resectable masses.

According to their location brain cysts may be differentiated into two main subgroups: extra-axial (or arachnoid) cysts and periventricular cysts. Arachnoid cysts are mainly supratentorial and in case of huge size cause displacement but not destruction of the surrounding brain structures. The postnatal outcome is independent from the size and location of the cyst, but mainly depends on the integrity of the surrounding cerebral structures. In most cases, however the prognosis is good.

Periventricular subependimal cysts are usually located at the level of the germinal matrix below the frontal horns of the lateral ventricles. They may be the natural evolution of a small subependimal hemorrhage, the consequence of an hypoxic-ischemic event, or may be the result of post-infectious germinolisis caused by neurotropic viruses; in a high percentage of cases, however, they have no clinical consequence and may regress spontaneously in utero or after delivery.

Hemorrhages are rare events in the fetus; they are mainly due to altered intracranial blood flow and pressure, secondary to hypoxia/hypercapnia (i.e: severe IUGR, placental abruption) or may be consequence of TTTS complicating a monochorionic twin pregnancy or may be due to severe fetal anemia or alloimmune trombocitopenia. The prognosis is extremely variable: the fetus may die in utero, the hemorrhage may evolve in periventricular leukomalacia, but small hemorrhages may resolve without any sequela.
In 2012, the World Health Organization (WHO) adopted a Comprehensive Implementation Plan on maternal, infant and young child nutrition. The Plan aims to alleviate the double burden of malnutrition in children, starting from the earliest stages of development. Substantial benefits can be obtained by concentrating efforts from conception through the first two years of life, but at the same time a life-course approach needs to be considered so that good nutritional status can be maintained. The Plan established six global targets to be achieved by 2025 from baseline levels estimated between 2010 and 2012. Global targets are important to identify priority areas and to catalyse global change. The six targets, many of which are inter-related, address nutrition conditions that are responsive for a large burden of nutrition-related morbidity and mortality from conception through the first two years of life. Target 1 on Stunting, calls for a 40% reduction of the global number of children under five who are stunted. Target 2 on Anaemia, entails a 50% reduction of anaemia in non-pregnant women of reproductive age (15-49 years). Target 3 on Low Birth Weight calls for a 30% reduction of low birth weight. Target 4 on Overweight, implies a halt in overweight rates of under-five children by 2025. Target 5 on Breastfeeding, requests an increase in the rate of exclusive breastfeeding in the first six months up to at least 50%. Last, Target 6 on Wasting implies that the global prevalence of childhood wasting should be reduced to less than 5% by 2025 and maintained below such levels. The six targets have been set at global level and they need to be translated into context-specific national targets – a process that is currently ongoing – taking into consideration country nutrition profiles, risk factors trends, demographic changes, experience with developing and implementing nutrition policies, and health system development. This presentation will review the rationale for setting the six global targets and present current progress towards their achievement.
**LONG TERM OUTCOME IN HIE**

Linda S. De Vries

Hypoxic-ischemic encephalopathy (HIE) occurs in 1-6 of 1000 full-term live births and is a major cause of neurodevelopmental disability. Long-term neurodevelopmental outcome depends on the severity of HIE with rarely an adverse outcome following mild HIE, more common following moderate HIE, and invariably present following severe HIE.

Numerous previous outcome studies of children with HIE have focused on major adverse outcomes, including death, cerebral palsy (CP), or severe cognitive impairment. However, deficits in the absence of CP or major disability may include intellectual impairments, as well as specific memory and behavioural problems. Data on long-term follow-up is limited and mainly based on infants born before the era of hypothermia. Childhood outcome from the TOBY trial showed that significantly more children in the hypothermia group than in the control group survived without neurological abnormalities and were significantly more likely to survive with an IQ score of 85 or higher at 6 to 7 years of age than children who did not undergo such therapy. Infants who were cooled performed significantly better on tests for attention and executive functions.

Magnetic resonance imaging (MRI) performed during the neonatal period will identify the main two patterns of brain injury, basal ganglia/thalamic injury (BGT) a marker of acute asphyxia and white matter/watershed (WM/WS) injury a marker of more prolonged or repetitive injury. Therapeutic hypothermia has been shown to be associated with a reduction in lesions in the basal ganglia or thalamus, white matter and abnormal signal intensity of posterior limb of the internal capsule. The predictive value however of these MRI abnormalities for subsequent neurological impairment is not affected by therapeutic hypothermia. BGT injury is most likely to result in dyskinetic cerebral palsy or quadriplegia and WM/WS injury in impaired intellectual performance at a later age. Children with HIE who survive without a major disability are at increased risk for long-term cognitive and/or neuromotor deficits and follow-up should be continued till school age and adolescence also in the era of hypothermia.
BRAIN IMAGING AND PROGNOSIS OF NEURODEVELOPMENTAL OUTCOME IN PRETERM INFANTS

Linda S. De Vries

Extremely preterm infants are at a high risk for neurodevelopmental impairments, especially cognitive and behavioural problems. Neonatal neuro-imaging techniques, especially sequential cranial ultrasound and magnetic resonance imaging (MRI) enables detection of brain injury and altered brain development and assists in the prediction of high-risk infants who need early intervention and long-term follow-up.

The focus in brain imaging has shifted from severe lesions such as large intraventricular and parenchymal haemorrhages and cystic periventricular leukomalacia to assessing and understanding the etiology of more subtle noncystic white matter injury, punctate white matter lesions, and cerebellar lesions. The more severe lesions that dominated the early period of preterm neonatal brain imaging occur less often but are still associated with major disabilities, such as, cerebral palsy, while subtle white matter injury and cerebellar lesions are more often associated with cognitive and behavioral problems, which have become the most prevalent issues among the survivors of extremely preterm birth. As there is a decline in mortality and severe brain lesions, especially cystic white matter injury, MRI plays an important role in identifying more subtle white matter lesions as well as lesions in the cerebellum. Severe brain lesions are most often reliably detected with sequential cranial ultrasound, allowing prediction of the majority of infants who develop cerebral palsy. More centres are also performing a single MRI at term equivalent age. Conventional MRI will identify lesions that may have been missed with cranial ultrasound, especially lesions within the cerebellum. Additionally 2-dimensional measurements can be made and several scoring systems are now available which show an association with later motor and cognitive outcome. A limited number of centres have started to use more routinely quantitative rather than qualitative MRI, including diffusion tensor imaging and resting state functional MRI to study connectivity. With these advanced imaging techniques, which require post-imaging analysis, more information has become available on (deviant) brain development in this at risk population. These advanced quantitative analysis techniques are currently predominantly research tools; however, with increasing automated systems, they have the potential to become clinical tools in the near future.
The international Child Health Nursing Network (Red ENSI) is the strategy for cooperation among institutions involved in training nurses and aimed at enhancing national health systems. Set up in 2006 under the auspices of the Pan American Health Organization (PAHO), the ENSI network is based on the principle that the development of professional competencies in attending children and adolescents is fundamental to implementing policies to attend a population’s health needs. Red ENSI (Spain) was set up in 2011 at the 5th International Meeting of Nursing Networks in Portugal at which PhD Carmen Sellán was appointed network coordinator. PhD Sellán is also a member of the Research Secretariat.

Its main goals include:

- Foster cooperation among members to broaden and strengthen activities in the fields of healthcare, teaching, research and technical cooperation in child health.
- Highlight the current situation and trends in child health nursing by identifying priorities for change and development.
- Promote the use and production of scientific and technical knowhow in caring for children and adolescents.
- Exchange experiences and teaching methods/methodology in child health.
- Promote the rights of girls and boys of all ages in any circumstances.
- Ensure healthy surroundings and settings for boys and girls at all stages of their development.

The ENSI network currently has 19 Member Latin American States. Spain has both institutional and individual members, with professionals from several fields and nursing students at under- and postgraduate levels. It is currently carrying out the project “Gender Construction in Girls and Boys for Integrated Health”. Future projects include mapping the emergence and prevalence of illnesses in neonatal, pediatric and adolescent populations; the analysis and methodology assessment of the Integrated Management of Childhood Illness Strategy (IMCI); as well as highlighting and disseminating the network’s activities.
INFORMATION ON THE OVARIAN CYCLE PROVIDED BY BODY BASAL TEMPERATURE. SYMPTOTHERMAL RECORD

Lourdes Durango

During the ovulation cycle, progesterone derivatives act on thermoregulation centres, raising women’s body temperature by tenths of a degree (Celsius).

Previous Researchers.
1928 Van del Walde relates biphasic temperature to ovulation.
1930 W. Hildebrand uses it for natural regulation of fertility.
1950 Rötzer (Austria) and Breault (Canada) define Symptothermal Methods.
1980 Freundl (Germany) and Flynn (UK) point out that body temperature is a precise indicator of ovulation.

Conditions
Basal: Before getting up in the morning.
Testing Site: In mucosa (mouth, vagina or rectum).
Thermometer: Preferably non digital.
Charting: Daily.
Every morning write down temperature readings on the cycle follow-up chart.
Temperature values must be rounded up in the following way:
• From 0.03 to 0.07 tenths of a degree (both included): Round up to 0.05.
• Below or above those values, round down or up to the closest tenth of a degree.
• Example: 36.22 into 36.20; 36.23 into 36.25; 36.27 into 36.25; 36.28 into 36.30.

Determining ovulation through body basal temperature:
• To identify the temperature rise: three consecutive temperature readings show higher values than the previous six readings.
• The third of these consecutive values must be at least 0.2 degrees above the highest value of the previous six readings.
• Draw on chart a baseline above the highest value of the previous six readings.

Exception 1: If the third value is less than 0.2 degrees above, a 4th day high reading will be necessary. It should be above the highest of the previous six readings (but not necessarily more than 0.2 degrees).

Exception 2: Among the 3 values after temperature rises, there is an interspersed value above or under the baseline. Both exceptions cannot combine.

Temperature rise confirms it has been an ovulatory cycle. It does no inform (like cervical secretion), that ovulation is going to occur, but that it has already taken place.

Further contributions.
Length and profile of the thermal plateau provide information on the quality of corpus luteum. From day +5 to day +7 (after ovulation) progesterone reaches peak levels, being World Congress on Perinatal Medicine Madrid, 3 - 6 november de 2015 the suitable period for hormonal studies. It also marks the day to begin a gestagenic treatment, and the response to hormone treatment. Length above 16 days indicates pregnancy diagnosis.
Clinical cases will be discussed to illustrate.

Pearl Index.
Dusseldorf Group (Germany) reports 3 unwanted pregnancies in 7.866 cycles (0.4%). In 2.3%, method was not followed correctly.
ANATOMICAL CHANGES IN THE CERVIX

Lourdes Durango

Anatomical changes are due to hormonal changes. World Health Organization (WHO), prescribes the use of two of the three biological indicators: cervical secretion and symptothermal tracking of body basal temperature. The so called third indicator should not be used on its own.

Previous research:
- 1930: Calkins tried to identify predicting factors of the duration of labour. By rectal tact, he realised it was much shorter when the neck was dilated and soft.
- 1955: Cocks identified five different types of uterine neck anatomy: Caesarea is more frequent when the cervical os is positioned towards the sacrum.
- 1958: Dutton considered this method useful to decide on labour induction.
- 1960: Garrett modified this classification.
- 1964: Bishop described a scoring system for decision-making on labour induction, which has proved to be the most effective method (1).

Labour begins due to a rise in oestrogen levels; the same that causes cervical changes during the cycle:
- As ovulation gets closer, the cervix rises, gets centred in the vagina, softer (like the lips or the ear lobule), and the external os is open.
- During the infertile phases of the cycle: The cervix is lateralized in the vagina, hard (like the point of the nose), and closed (2).

Cervical self-palpation: Introducing two fingers in the vagina (index and middle fingers). It should be done at about the same time every day, keeping a record of results. Changes will be gradual until ovulation, and there is a sudden new change after it.
2. Cómo reconocer la fertilidad.- Dra. A. Otte y cols. Editorial EIUNSA.
LESS INVASIVE SURFACTANT ADMINISTRATION (LISA)

Herting Egbert

The combination of surfactant administration with noninvasive ventilation was first practised in Scandinavia more than 25 years ago. Infants with Respiratory Distress Syndrome (RDS) were intubated, received surfactant and were extubated to Continuous Positive Airway Pressure (CPAP). However, this procedure named INSURE (INtubate-SURfactant-Extubate) still needed sedation, analgesia, classical endotracheal intubation and positive pressure ventilation. In contrast, spontaneous breathing, often with CPAP support, is maintained during the LISA procedure (LISA = Less Invasive Surfactant Administration) as a small diameter tube is passed through the vocal cords just for the time needed (1 to 3 minutes) to administer the surfactant. The catheters used vary in stiffness, material, length and diameter. Depending on personal preference and expertise the nasal or the oral route have been used with or without the help of a Magill forceps. Special catheters for LISA and application devices for this technique have recently been developed. There is ongoing debate about the optimal technique for LISA, the question of sedation and the ideal surfactant dose/surfactant preparation for LISA. LISA has been in clinical use in Germany for more than 10 years and there is evidence from randomised controlled trials (AMV trial, NINSAPP study) that LISA reduces the number of infants that need mechanical ventilation in the first days of life. The procedure is safe and first reports on long-term outcome are favourable even in studies reaching down to a gestational age of 24 weeks. First evaluations seem to indicate that LISA is less effective when RDS has already progressed to severe disease and also in infants that have not received lung maturation with glucocorticoids before delivery. Future studies should therefore include the prophylactic (or very early) use of LISA in preterm infants which are at high risk for RDS. So far only a single randomised controlled study (TAKE CARE study) resulted in a significant reduction in the incidence of BronchoPulmonary Dysplasia (BPD) at a gestational age of 36 weeks. Most of the studies published so far were underpowered to evaluate the effects on BPD. However, 2 metanalyses and a case control study in more than 1000 infants (matched pairs) demonstrated an increased number of infants surviving without BPD following LISA treatment. In consequence, LISA plays a crucial role in the maintenance of spontaneous breathing in infants with RDS and it has become an integral part in many neonatal units that manage preterm infants with a minimally invasive approach.
NEWBORN CARE IN THE DEVELOPING COUNTRIES: WHAT ELSE CAN WE DO?

Dolores Elorza

A great advance has been done in decreasing under-five mortality rate, mostly in infants older than 1 month of age, but in many regions of the world, especially in Africa, the decrease on neonatal mortality rate (NMR) has been slower. In some countries more than half of all deaths in children younger than 5 years occur in the neonatal period. Childbirth is a moment with enormous risk of death, disability and loss of development potential. Impact on development outcome of insults produced around birth or deficits in early nutrition, has not been clearly evaluated in low-income countries. Not only survival but also disability should be kept in mind.

Prematurity, intrapartum complications and infections are the main causes of neonatal mortality in low-income countries. Although every newborn is vulnerable, the risk is higher for small for gestational age and preterm babies. Nowadays, there are evidence-based interventions whose implementation in antenatal period, during labour and delivery or in the immediate postnatal care, can reduce mortality caused by prematurity in 58%, by intrapartum complications in 79% and by infections in 84%. It is estimated that a high coverage of current available interventions could save 1.95 million newborn lives. Antenatal steroids, training tools for resuscitation and low-cost equipments for respiratory support such as continuous positive airway pressure may improve survival in preterm babies. Skilled birth attendance, emergency obstetric care and immediate care for every newborn with delayed cord clamping, cord cleansing with antiseptics, skin-to skin care, early initiation of breastfeeding and vitamin K administration can reduce intrapartum complications. But is crucial the immediate care for small and ill neonates: resuscitation if perinatal depression and appropriate care for babies with neonatal encephalopathy; kangaroo care, topical emollient therapy, management of respiratory distress syndrome, nutritional support for preterm babies. Those strategies may reduce neonatal morbi-mortality. Finally, recognition and management of neonatal infection using antibiotics to treat neonatal sepsis, pneumonia, meningitis, and even facility-based supportive care with intravenous fluids, decrease mortality related to infections.

But the effect of these interventions on the population depends on the achievement of high coverage. The cause-specific risks of death in countries vary substantially by NMR level. In this post MDGs-era, The Every Newborn Action Plan aims to end preventable newborn deaths, helping to identify neonatal health status of the different countries, and motivating them to set their priorities, defining their specific goals and designing programmes to incorporate the interventions required.
THE CYCLE IN 3 PHASES: CHARACTERISTICS OF THE FERTIL PHASE

Hermelinda Estévez

The cycle in 3 phases is based on changes in cervical mucus, that were reported by John and Evelyn Billings, by what women can recognize their fertility or infertility (1).

1st fase of infertility. It is the period since the last day of menstruation until the first in which a change can be seen in the mucus pattern or in the sensation (dry to wet); length is variable, and is prolonged in cycles over 28-29 days, and can have no existence in short cycles.

Fertile phase. Changes are observed in the secretion: the quantity is abundant appearance is transparent (like egg white) and elastic (until 15-20cm). The sensation is: lubricant wetness. Odeblad conducted a study on 14 women, 18 to 25 years old, who have written down their sensations during 32 cycles, with the following results: both sensations, wetness and lubrication, end a few hours before ovulation (it can be 8 - 3 hours) (2).

Day peak/Summit: Last day of fertile secretion and/or sensation of wetness; it is the closest day to ovulation. It happens day 0:ovulation (80%) or since day -2 until day +2 (20%).The following 3 days are considered as probably fertile.

2nd phase of fertility. It is the most fixed phase of the cycle: 14 days; it has a duration of 10-16 days. It starts from the 4th day post-peak until next menstruation. There is not secretion or it has characteristics of infertility: little quantity, sticky, lumpy; daily sensation is dryness.

Hormonal alterations change the characteristics of the cycle: ovarian deficiency prolongs 1st phase of infertility and also shortens the second one and produces amenorrheic potholes; hyperprolactinemia can prolong the cycle; its action on progesterone reduces levels; stress can produce a cycle with anovulation or shorten it in an insufficient luteal phase.

CERVICAL SECRETION: TYPES ACCORDING TO ODEBLAD

Hermelinda Estévez

Physiology of cervical secretion. It is a complex mucoid secretion depending on circulating hormone levels. Its qualitative, quantitative and structural variations make it permeable or impermeable to sperm. It is made in the ciliated secretory epithelium that covers linings of the cervix duct consisting in secretory cells and ciliated. There are reserve cells at the base of the epithelium, to ensure its regeneration differing in one or the other cellular type when necessary.

Composition. It can be considered a hydrogel composed of a liquid phase consisting essentially of water with numerous components in solution or suspension: mineral salts, sugars, amino acids, lipids and proteins. The solid phase consists of polymerized protein, connected by non covalent links, forming fibrils.

Researches. Its description was made by Pouchet (1847) and Robin (1848). Marion Sims described its sperm permeability “when the cervical mucus is clear and transparent” (1). This rhythmic permeability was later investigated by Hühner.

Biophysical parameters. They are determined by variations during the cycle: quantity, appearance, fluidance, cervical opening, hydrogen potential and crystallization.

The Discovery of the forestation of the cervical secretion is due to Papanicolaou (2), and more in a deeper way to Rydberg that compares it with ferns or palm leaves. It is determined by its contents of chloride in dissolution. Gynaecologist Beck and Neuhaus, of the Mineralografía Institute of the University of Bonn, made contribution by saying that crystallisation is induced by mucoid content.

Secretion types: In 1968 Odeblad classified 2 secretion types: type E (estrogenic) and type G (gestagenic) that is not receptive to sperm (3). In 1976 Odeblad presented at the University of Surrey (England) 2 new types that depended on E: S (sperm transmission) and L (locking-in). G, L and S model explain the sperm ascent. In 1990 he defined the characteristics of the secretion P (peak fertility). Each of them has its own crystallographic pattern.

**THE SCIENTIFIC EVIDENCE FOR CCHD SCREENING AND ITS PRACTICAL APPLICATION USING PULSE OXIMETRY**

Andrew Ewer

The possibility of screening for critical congenital heart defects (CCHD) using pulse oximetry, is not a particularly new concept. However, it is only in the last five years of so, that there has been sufficient convincing evidence of the feasibility of such testing to allow clinicians to evaluate its universal introduction. The early data came from single centre studies which showed proof of concept but the numbers of patients with CCHD were too small to make any precise judgement regarding the test accuracy. Since 2008 several important studies, with much larger numbers of patients, have been published which demonstrate beyond reasonable doubt the accuracy of screening for CCHD with pulse oximetry. Although these studies employed different screening algorithms with significant variability in the timing of screening, all demonstrated that screening identified babies with CCHD who may otherwise have been missed and added value to existing screening. Over 90% of CCHD lesions were consistently identified if all screening methods were employed. In addition many babies with clinically important non-cardiac disease (such as respiratory problems and infections) were also detected and although technically false positives these babies often have conditions which may be life-threatening and therefore become important secondary targets of screening. Studies have also demonstrated that screening is acceptable to both parents and clinical staff and that it is cost-effective in a number of different health care settings.

The supportive evidence appears sufficiently robust to allow, not just individual groups of clinicians to consider the introduction of routine screening within their hospital setting, but also health policy advisors to recommend national screening programmes such as the one introduced across the United States of America in 2011. A number of countries now have pulse oximetry screening as national policy and a number of others are actively considering it.

Although it is clear that any form of pulse oximetry screening appears to offer an advantage, the debate continues about the ideal screening tool. Some algorithms involve using a single post-ductal (foot) saturation measurement while others include both pre- and post-ductal and repeat tests. The optimal timing of testing is also unclear; earlier testing (in the first 24 hours) may lead to more false positives but may also identify more seriously ill babies before they deteriorate and collapse.

The available evidence will be reviewed and set into context so that most appropriate form of testing in a particular clinical setting can be assessed.
PREVENTION AND MANAGEMENT OF POSTPARTUM HAEMORRHAGE

Dan Farine

Prevention of PPH:
RCTs have shown that oxytocin administration can eliminate about 2/3 of PPH, severe PPH and other parameters of blood loss. I suggest simplistic approach for prevention. In under-developed areas (no refrigeration) - Misoprostol (600-800 mg) either orally or preferably rectally would provide a good prevention with little side effects. In the developing world Oxytocin should be used. In the developed world – PPH is on the rise (reasons: Advanced maternal age, obesity, GDM, macrosomia, polyhydramnios, multiples etc). In this setting the Canadian (SOGC) guidelines call for the use of Carbetocin in women that undergo CS and in women that have 1 or more risk factors for PPH. About 80% of labours have risk factors so most labors will require Carbetocin.

Medical therapy (most are offf license or label):
1. Oxytocin – IV drip of concentrations of up to 40U/l. A single dose 5U could be administered slowly or IM. (this is different from the 10U recommended by the FIGO in 2003). Lower dose has lower the risk of hypotension. we found that the ED50 of oxytocin is 0.5 U (and not the recommended dose of 5U).
2. Misoprostol – May be added to oxytocin or used alone in low resource setting or home births. It is effective the skills required minimal skills in administration as the optimal route is rectal (Note that the FIGO guidelines recommended sublingual dose).
3. Prostaglandin F2 alpha – Best injected to the uterus. The operator may opt for the fundus if it is atonic or aim for the lower segment if the fundus is firm. PF2alpha may aggravate asthma and mimic amniotic fluid embolism as the clinical picture is of PPH and airway constriction.
4. Dinoprostone (Prostin E2) suppository. It is contraindicated in hypotension. It also needs to be thawed which may reduce its effectivity.
5. Methylergonovine - Should not be used in hypertensive patients as it may further aggravate the hypertension and was reported to cause strokes.
6. Methergin - A combination of oxytocin and Ergonovine. Should not be used in hypertensive patients similarly to ergonovine alone.
7. Transanemic acid – antifibronolytic with mixed results.
8. Factor VII – it is very expensive (few thousands dollars) ; requires fibrinogen to act ; requires consultation with hematologists.
9. Nano particles – This is a very promising approach. However it is not in used in humans yet.
ERYTHROPOIETIN FOR NEUROPROTECTION IN VERY PRETERM INFANTS

Jean-Claude Fauchere

Background
Premature birth, cerebral intraventricular hemorrhage and hypoxic ischemic encephalopathy remain major risk factors for delayed psychomotor development, for cognitive deficits and cerebral palsy. Inflammation, excitotoxicity or oxidative stress can impact on brain development.
To date, there are few clinically established interventions to ameliorate brain injury after fetal or perinatal compromise in very premature infants. Recombinant human erythropoietin (rhEpo) has been evaluated as being one of the most promising substances for postnatal neuroprotection in newborn infants. The Epo/EpoR system in the brain becomes stimulated in response to hypoxic-ischemic injury and subsequently acts on early and late tissue healing. Numerous in vitro and in vivo experiments demonstrated the anti-inflammatory, anti-excitotoxic, anti-oxidant and anti-apoptotic effects of Epo on neurons. rhEpo promotes neurogenesis and angiogenesis, which are essential for repair processes after brain injury and development of compensatory mechanisms for proper neurodevelopment. Finally, retrospectively performed analysis of clinical data from preterm infants treated with rhEpo for the anemia of prematurity showed a robust improvement of neurodevelopmental outcome.
Some clinical trials initiated for neuroprotection in very premature neonates were either placed on hold by the FDA due to safety concerns and later restarted with or without modified dosing schedules.

Objective
High dose recombinant human erythropoietin (rhEpo) has been suggested to reduce perinatal brain injury and to improve long-term neurodevelopmental outcome in very preterm infants, but concerns about safety have been raised. We therefore investigated whether high dose rhEpo given shortly after birth to very preterm infants is safe in terms of short-term outcome. The primary hypothesis of this trial is that high-dose rhEpo improves the Bayley’s mental developmental index of infants born very preterm at 24 months of age compared to placebo.

Study design
Randomized, double masked phase II trial. Preterm infants (gestational age 26 0/7 to 31 6/7 weeks) were given rhEpo (n₁ = 229; 3,000 U/kg body weight) or NaCl 0.9% (nₑ = 214) intravenously at 3, 12-18 and 36-42 hours after birth.

Results
There were no relevant differences between both groups regarding short-term outcomes such as mortality, retinopathy of prematurity, intraventricular hemorrhage, sepsis, necrotizing enterocolitis and bronchopulmonary dysplasia. At day 7-10, we found significantly higher hematocrit values, reticulocyte and white blood cell counts, and a lower platelet count in the rhEpo group.

Conclusion
Early high-dose rhEpo administration to very premature infants is safe and causes no excess in mortality or major adverse events.
FOUR-CHAMBER VIEW: OBSTRUCTIVE LESIONS (HYPOPLASTIC LEFT HEART SYNDROME, HYPOPLASTIC RIGHT HEART SYNDROME, AND OTHERS)

Queralt Ferrer Menduiña

Hypoplastic left heart syndrome (HLHS) is a clinically useful description of a constellation of cardiac malformations, all characterized by underdevelopment or absence of the left ventricle, but the clinical features of HLHS include varying degrees of hypoplasia of the left ventricle, mitral and aortic valve stenosis or atresia, and hypoplastic arch and coarctation. It is not uncommon to find more than one obstructive left-sided anomaly at the same time and some of them might be progressive during foetal and post-natal life, conditioning long-term survival of these patients. Prenatal counselling of HLHS is difficult as the clinical outcome depends on the precise anatomical lesions, therefore the postnatal implications can be difficult to predict.

During the last decade, prenatal interventional therapy has emerged as an option for some of these lesions and might improve the postnatal survival of these patients, but its clinical implications are still to be elucidated and therefore referral to a high level expertise centre is a must in this type of cardiac malformations.

Hypoplastic right heart syndrome (HRHS), even though it is less frequent, it can be easily misdiagnosed during foetal life due to its different physiology. As in left-sided lesions, right obstructions (pulmonary or tricuspid stenosis or atresia) can be progressive and some anatomic features are associated with different perinatal outcomes. Fetal interventional therapy is also a possible option in pulmonary stenosis or atresia.

There is a specific group of lesions that include any type of single ventricle, but without aortic obstruction that have a very different outcome. This kind of malformations will have lower surgical risk and better long-time survival than those with HLSH, with better quality of life.

Although discrepancy of ventricular size can be normal at the 3th trimester, is very important to assure that it is not due to an obstructive lesion of the ductus arteriosus, the foramen ovale or pulmonary stenosis that has not been detected previously.

All these lesions will have an abnormal foetal echocardiographic 4C view. Therefore it is really important to rule out any of these diseases with a prenatal accurate diagnosis, because they are associated with very different surgical treatment and long-time survival. During First trimester scan diagnosis of some of these lesions might not be well-defined, then prenatal counselling should be delayed.
DEVELOPMENT OF THE BRAIN IN THE FIRST TRIMESTER OF PREGNANCY: A MULTI-MODAL STUDY

Stamatian Florin

Introduction: Understanding brain morphogenesis gives insights into the mechanisms of congenital anomalies development. The aim of this descriptive study is to assess the morphology of the developing brain in the first trimester of pregnancy by using a multi-modal approach: anatomical examination, 3D high-frequency vaginal ultrasound and micro-MRI.

Materials and Methods: The material used in this study consists of embryos and fetuses in the first trimester of pregnancy. For in vitro studies, 8 embryos ranging from 6 to 10 gestational weeks and 12 fetuses ranging from 11 to 14 gestational weeks were used. The subjects belong to the collection of the Department of Anatomy and Embryology, University of Medicine and Pharmacy Cluj-Napoca, Romania. They were anatomically examined under direct light and by transillumination when immersed in formalin solution 9%. Magnetic resonance analysis was performed using a Bruker Biospec 7.04 Tesla scanner. Post-scanning processing of magnetic resonance images and 3D reconstructions were performed by employing ParaVision® software. Then, the fetuses were dissected in order to examine the brains. For in vivo studies, a total of 18 singleton non-malformed embryos and fetuses at 9-13 weeks of gestation were studied. The subjects were examined with a Voluson E10, BT 15 ultrasound scanner (GE Healthcare, Zipf, Austria), using a high-frequency 6-12 MHz/256-element 3D/4D transvaginal transducer. The 3D sonography including the 3D HDlive rendering mode and Silhouette® mode was performed routinely as the subjects were scanned. The Omni view® software was used for digitally slicing the selected volumes.

Results: We describe the morphological characteristics of the developing brain of the embryos and fetuses. The 3D transvaginal ultrasound using the HDlive rendering mode and Silhouette® mode provides accurate images of small-sized structures of the developing brain, such as the ganglionic eminences. Accurate details of the developing brain assessed by micro-MRI are reported. Some structures like the red nucleus and nucleus accumbens are imaged at an early gestational age than previously reported in literature.

Conclusions: Studies of embryology are still needed for a complete assessment of the developing brain. 3D sonography using a high-frequency vaginal ultrasound transducer is a feasible method for imaging the embryonic brain with an acceptable quality for clinical studies. Micro-MRI offers to embryologists an alternative to the classical histological techniques. Each morphological method has its advantages and disadvantages. The three methods used in this study are complementary.
SPANISH SOCIETY OF NEONATAL NURSES (SEEN), A CHANCE TO SHARE AND GROW

Miguel García Fernández

The Spanish society of neonatal nursing is a nonprofit organization dedicated to fostering the development of Neonatal Nursing organization. Among its objectives are the following:

- Create links between the different professionals dedicated to newborn and family care.
- Ensure career advancement for all partners.
- Organizing all kinds of social, cultural and scientific activities related to the activities of the SEEN and sponsor the ones organized by members.
- Implement the creation of a body of knowledge through the creation of committees and commissions, constituted to deal with particular aspects of Neonatal Nursing.
- To promote recognition of the specialty of Neonatal Nursing in the workplace both as an academic.

Since 2004 SEEN has organized five national congresses of neonatal nursing and participated as a partner in many more, becoming a meeting point of reference for nurses dedicated to care for the newborn and his family.

From this position SEEN aims to become a facilitator of development, not only as discipline but also the individual neonatal nurses, promoting research networks, providing assistance to scientific activities and collaborating in training and academic activities.

By the close ties we have with national and international organizations we aim to become a platform to facilitate the international projection of the Spanish neonatal nurses.
PRESSURE ULCER RISK ASSESSMENT SCALES FOR NEONATAL HOSPITALIZED POPULATION. ADAPTING THE NEONATAL SKIN RISK ASSESSMENT SCALE TO THE SPANISH HEALTH CONTEXT. ARE USEFUL IN NEONATES?

Pablo García-Molina

Introduction
Epidemiological studies conducted to date in hospitalized infants are scarce. In Spain, neonatal units PU prevalence moves from 50% in intensive care units (NICU) and 12.5% in inpatient units. All health organizations promote and enhance patient safety through the PU prevention. To achieve this, it is necessary to provide health professionals with validated tools adapted to the neonatal age for evaluating the risk of the hospitalized population. In this way health care professionals can efficiently manage preventive resources and develop plans of care focused on the newborn. Until the present there were not validated scale specifically for infants in Spain. Therefore, the main objective of our research was to adapt to the Spanish context the original scale NSRAS and evaluate the validity and reliability of the Spanish version.

Method
The study was divided into three phases. In the first phase the transcultural adaptation of the original NSRAS scale was performed using the method of “translation and back-translation”. Subsequently, a group of experts performed the content validity by IVC. The adapted version of the scale was evaluated by two phases of analytical observational multicenter study, neonatal units in 10 public hospitals in the Spanish National Health System. Interobserver and intraobserver reliability and construct validity in the second phase was evaluated. In a third phase the predictive capacity and the cutoff of the NSRAS Spanish version was evaluated.

Results
At the first stage, the content validity obtained a “IVC value” 0.926 [95% CI 0.777 to 0.978]. During the second phase, the evaluation sample was 336 neonates. Internal consistency showed a Cronbach’s alpha of 0.794. And the intraobserver reliability was 0.932 and interobserver reliability was 0.969.
In the third phase the sample was 268 neonates. Multivariate analysis of the relationship between risk factors, preventive measures and the presence of UPP showed that three variables were significant: the NSRAS score, length of stay and use of NIV.
In scoring 17, the NSRAS scale showed a sensitivity of 91.18%, a specificity of 76.5%, NPV of 36.05% and a PPV of 98.35%. The area under the ROC curve was 0.8384 in scoring 17.

Conclusions
The Spanish version of the NSRAS scale is a valid and reliable tool to measure the risk of UPP in the neonatal population hospitalized in the Spanish context. Infants hospitalized with a score equal or less than 17 are at risk develop PUs.
Accurate assessment of birthweight and fetal growth is a central requirement for good perinatal care. A series of studies in different maternity populations have found striking similarities in the way fetal growth varies with maternal and pregnancy related characteristics. This has led to the development of the customised ‘gestation related optimal weight’ (GROW) standard which can predict each fetus’ individual growth potential, thereby enhancing our ability to differentiate between physiological and pathological smallness.

Recent work has focused on comparing the customised GROW standard with the one-size-fits-all approach advocated by the Intergrowth (IG) Project group. Two analyses were undertaken in an English regional database of 148,276 deliveries which included 798 perinatal deaths [1]. A fetal weight standard based on the Intergrowth growth curves for HC, BPD, AC and FL was compared to the customised GROW fetal weight standard. Comparison of the fetuses identified as SGA by either method showed that all but 5% of fetuses small by IG were also small by GROW, and these had no increased risk of perinatal death. In contrast, GROW identified an additional 56% of SGA fetuses which were considered not SGA by IG, and these fetuses had a significantly increased risk of perinatal death compared to non-SGA fetuses (OR 2.0, CI 1.6-2.5). A second analysis in the same database, comparing IG and GROW birthweight standard [1] showed similar results, with nearly half of SGA babies at increased risk of perinatal death not identified by the Intergrowth standard.

The Figure illustrates the perinatal mortality risk for SGA babies according GROW and IG standards.

The customised GROW standard provides a useful research and audit tool for the study of risk factors for fetal growth, and a clinical standard for antenatal surveillance which has been shown to improve the detection of fetal growth restriction while reducing the need for unnecessary investigations. An increasing number of country specific coefficients are being derived from suitable databases, thereby constructing an internationally applicable, individually adjustable standard for fetal growth.

**PREVENTION OF STILLBIRTHS THROUGH IMPROVED ANTENATAL RECOGNITION OF IUGR**

Jason Gardosi

Stillbirths represent a challenge for clinical services as well as public health. Most deaths used to be categorized as ‘unexplained’ and were considered, by implication, unavoidable. This is a probable reason as to why stillbirth rates have remained essentially unchanged in England for the last 20 years. However independent case reviews have found that the majority of normally formed fetal deaths were potentially avoidable, and often had unrecognized intrauterine growth restriction (IUGR). In many such cases there was evidence of substandard care and a failure to recognize and act on risk factors. Large population based cohort studies found that that while babies with IUGR had a seven fold increased risk of stillbirth, the risk can be substantially reduced by antenatal detection by ultrasound and Doppler, followed by timely delivery of the babies at risk [1]. We initiated a regional, then national initiative of clinical training and adoption of standardized, evidence based protocols for screening and surveillance. The programme, by now including over two thirds of all hospitals in the UK, has led to significant increases in antenatal detection rates of IUGR, which in turn resulted in a year on year reduction in stillbirths to their lowest ever levels. The figure shows UK Office of National Statistics (ONS) stillbirth rates for England since the commencement of the programme in 2009, with comparison to the preceding 10 year average.

Amniotic fluid (AF) analysis is used to assess the likelihood of intra-amniotic infection and inflammation in preterm PROM. This is useful for clinical management, allowing to balance the benefits of prolonging gestation to reduce prematurity against the risks of intra-amniotic infection and/or inflammation.

Tests to assess intra-amniotic infection and inflammation traditionally include AF culture, Gram stain, white cell count and glucose determination. However their sensitivity is not always adequate for the diagnosis of intra-amniotic infection and inflammation. Determination of Interterleukin-6 (IL-6) and metalloproteinase-8 (MMP-8) appears to be adequate for the recognition of intra-amniotic inflammation, but the results of these tests are not readily available for clinical decisions.

Recently a broad-range polymerase chain reaction coupled with mass spectrometry (PCR/ESI-MS) has been used for early detection of microorganisms and viruses in the AF of patients with preterm PROM. PCR/ESI-MS was able to identify microbial invasion of the amniotic cavity in 8 hours and the increase in the detection of microorganisms compared to cultures was 50%.1

A MMP-8 rapid test has been introduced into clinical practice for identification of intra-amniotic infection and/or inflammation and in the assessment of the likelihood of adverse pregnancy outcome (short latency, chorioamnionitis, significant neonatal morbidity) in patients with preterm PROM. The test can be performed in 15 minutes, the sensitivity and specificity in the identification of intra-amniotic infection and/or inflammation are 90% and 80% respectively.2

Additionally, a rapid bedside assessment of IL-6 has shown to be useful for the prediction of microbial invasion of the amniotic cavity (MIAC) and intra-amniotic inflammation in pregnancies complicated by preterm PROM.3,4

In conclusion, rapid tests in the setting of preterm PROM represent a promising tool for timely intervention in order to reduce the risks of perinatal complications.

References

**NON-INVASIVE VENTILATION FOR THE TREATMENT OF APNOEA OF PREMATURITY**

Camilla Gizzi

Apnoea of prematurity (AOP) is a common problem in preterm infants, and desaturations and bradycardias, considered as mainly elicited by AOP, are associated with longer-term neurodevelopmental problems. Standard therapies for treating AOP are nasal continuous positive airway pressure (NCPAP) and methylxanthines. For infants who do not respond to this combined strategy, nasal intermittent positive pressure ventilation (NIPPV) has been proposed as an alternative to NCPAP. Synchronised NIPPV (SNIPPV) can be even more effective, as synchronisation of mechanical breaths with spontaneous ones may offer some favourable effects on ventilation. Delivering the peak inspiratory pressure immediately after the start of a respiratory effort, when the glottis is open, allows pressure to be effectively transmitted to the lungs with little or no deviation through the oesophagus to the stomach, thus obtaining the double advantage of increasing tidal volume and reducing the risk of gastrointestinal side effects. Several studies have found that synchronization of mechanical breaths during nasal ventilation increases tidal and minute volumes while decreasing respiratory effort. Moreover, thoracoabdominal motion asynchrony and flow resistance through the nasal prongs are decreased in neonates on SNIPPV, with improved stability of the chest wall and pulmonary mechanics. Until present, two devices have been commonly used to trigger the ventilator during NIV in preterm infants: the abdominal capsule, and the flow sensor. Recently, a device using a diaphragmatic electromyogram has been introduced in neonatology, however few data are available on clinical outcomes. The abdominal capsule, although quite effective, has some disadvantages due to its high sensitivity to the infant's spontaneous movements and to the considerable skill required for correct placement. Studies reporting on abdominal capsule-SNIPPV for AOP showed contrasting findings. Conversely, airflow trigger detection is a recognised and easy means for synchronising. Moreover, it offers an advantage when preterm infants employ breathing strategies with inversion of the usual sequence, that is, diaphragmatic contraction commences in advance of glottic opening, occurring in up to 60% of spontaneous breaths. A clinical study showed that, for infants suffering from AOP, flow-SNIPPV therapy is associated with an overall reduction in the combined incidence of adverse events, desaturations and bradycardias of about 40% compared to NIPPV and NCPAP, and also that it results in a 50% decrease in the incidence of central apnoeas.
PREVENTION OF PREMATURE IN TWINS WITH ARABIN CERCLAGE PESSARY

Orion Gliozheni

Objective: The purpose of this study was to evaluate the effectiveness of Arabin cerclage pessary in twin pregnancies.

Background: Although advances in recent years, prematurity in twins and its complications especially in severe prematurity remains a problem in modern obstetrics. Evidences from randomized studies have shown that bed rest, classic cerclage, tocolytics and progesterone do not improve the prematurity rate in twins.

Methods: In this cohort randomized study were included 218 twin pregnancies in the period Feb. 2010 – Feb. 2015. The patients were divided randomly in two groups: 109 in the group of Arabin cerclage pessary and 109 in the group of expectant management. The randomization was done at 18 to 24 weeks of gestation, regardless of parity, chorionicity, or cervical length. We excluded cases with uterine malformations, placenta praevia, fetal abnormalities, twin-to-twin transfusion, painful regular uterine contractions, ruptured membranes, severe fetal growth restriction or death of one of the fetuses. The outcomes measured were: gestational age at delivery, fetal birth-weight, Apgar at 5-10 minutes, day-stay at NICU, RDS morbidity, early neonatal outcome, and maternal complications. A questionnaire evaluation within the treatment group was performed for every patient, scoring complaints of descensus, discharge, pain at insertion or removal and whether patients would chose this treatment again.

Results: Among the outcomes analyzed at the group of twins with pessary cerclage compared with the group of twins without pessary, we found a significant difference (p<0.05) at the pessary group concerning: longer gestational age at delivery, larger fetal birth-weight, shorter day-stay at NICU, better neonatal outcome, reduced admission days for preterm labor and no major maternal complications attributable to the pessary. In general, all patients treated and delivered at our hospital had a positive opinion of the treatment.

Conclusion: Insertion of a vaginal pessary in twin pregnancies is a simple, non-invasive technique and may be a cost-effective preventive treatment for SPB in twins. Pessaries may be useful in women at risk for preterm delivery and seem to be without significant risks. Other prospective, randomized studies are needed in the future to address these issues.
CERVICAL PESSARY TO PREVENT PRETERM BIRTH IN WOMEN WITH A SHORT CERVIX PREGNANT WITH TWINS: A MULTICENTER RANDOMIZED CONTROLLED TRIAL (PECEP-TWINS)

Maria Goya

Background
Spontaneous preterm birth (SPB) is the leading cause of perinatal morbidity and mortality. A Dutch study using cervical pessary in the prevention of SPB in twin pregnancies, with promising results in women with a short cervix, was published last year. We propose the use of a cervical pessary for preventing SPB in twin pregnancies of mothers with a short cervix.

Methods
The PECEP-Twins Trial was conducted in 5 hospitals in Spain. Cervical length (CL) was measured in 2,287 women; 137 pregnant women with a CL ≤ 25 mm (of 154 detected with a short cervix) were randomly assigned to receive a cervical pessary or expectant management (1:1 ratio). The primary outcome was SPB before 34 weeks of gestation. Neonatal morbidity and mortality were also evaluated. This study is registered as ClinicalTrials.gov NCT01242410.

Results
SPB before 34 weeks of gestation was significantly less frequent in the pessary group than in the expectant management group (11/68 (16.2%) vs. 26/66 (39.4%); OR: 0.30; 95% confidence interval: 0.29 to 0.71). Pessary use was associated with a significant reduction in the rate of birth weight <2500 g (p=0.01). No significant differences were observed in composite neonatal morbidity outcome (8/136 (5.9%) vs. 12/130 (9.1%); OR: 0.30; 95% confidence interval: 0.07 to 1.02) or neonatal mortality (none) between the groups. No serious adverse effects associated with the use of a cervical pessary were observed.

Conclusions
In our population, the insertion of a cervical pessary reduced the SPB rate in women with a short cervix carrying twins.
MATERNAL SERUM BIOMARKERS FOR ASSESSMENT OF PREECLAMPSIA:
GLYCOSYLATED FIBRONECTIN AS A POINT-OF-CARE BIOMARKER

Michael Gravett

Objective:
Hypertensive disorders, including preeclampsia, are the 2nd leading cause of maternal mortality worldwide. Unfortunately, clinical manifestations of preeclampsia occur late in the course of disease. Robust biomarkers are needed for screening and diagnosis of preeclampsia to mitigate adverse outcomes, especially in high burden, low resource setting. We assessed the association of glycosylated fibronectin (GlyFn), an early marker of endothelial injury, with preeclampsia and its performance in a point-of-care (POC) test in comparison to other conventional biomarkers as a screening and diagnostic test for the prediction and diagnosis of preeclampsia.

Study design:
Retrospective case control study utilizing stored serum from a Finnish cohort. GlyFn, placental growth factor (PlGF), and soluble vascular endothelial growth factor receptor 1 (sFlt1) levels were determined by immunoassay from 107 pregnant women. In all, 45 were normotensive and 62 were diagnosed with preeclampsia. The ability of GlyFn to assess preeclampsia status and relationships between GlyFn and maternal characteristics and pregnancy outcomes were analyzed and compared to a simple lateral flow point of care test.

Results:
GlyFn serum levels in the first trimester were significantly higher in women with preeclampsia (P < .01) and remained higher throughout pregnancy (P < .01). GlyFn, sFlt1, PlGF, and the sFlt1/PlGF ratio were significantly associated (P < .01) with preeclampsia status, and the classification performance of these analytes represented by area under the receiver operating characteristic curve was 0.99, 0.96, 0.94, and 0.98, respectively, with 95% confidence intervals of 0.98-1.00, 0.89-1.00, 0.86-1.00, and 0.94-1.00, respectively. Increased GlyFn levels were significantly associated with gestational age at delivery (P < .01), blood pressure (P = .04), and small-for-gestational-age neonates. Repeated-measures analysis of the difference in weekly GlyFn change in the third trimester demonstrated that mild preeclampsia was associated with a weekly change of 81.7 μg/mL (SE 94.1) vs 195.2 μg/mL (SE 88.2) for severe preeclampsia. The GlyFn POC demonstrated similar performance to a plate assay with an area under the receiver operating characteristic curve of 0.93 and 95% confidence interval of 0.85-1.00.

Conclusion:
GlyFn is a robust biomarker for monitoring of preeclampsia in both a standard and POC format, supporting its utility in diverse settings in the appropriate management and triage of patients with preeclampsia.
LUNG FUNCTION OF PRETERM INFANTS BEFORE AND AFTER VIRAL INFECTIONS

Anne Greenough

Respiratory syncytial virus (RSV) infection in previously healthy infants is associated with lung function abnormalities at follow-up including elevated thoracic gas volume and airway resistance at one year of age, airways obstruction in children and lower forced expiratory volume over one second in young adults. We have demonstrated amongst prematurely born infants, those who had at least one proven RSV LRTI had higher airways resistance (Raw), more days of wheeze and bronchodilator requirement. Regression analysis also identified that human metapneumovirus LRTI was associated with elevated Raw at follow-up (1). Several studies, however, have shown that infants who develop symptomatic lower respiratory tract infections (LRTIs) have diminished premorbid lung function. In one study (2), term-born infants who developed bronchiolitis in the first year after birth, compared with those who did not, had a trend to a lower maximal flow at functional residual capacity, that is, before they developed bronchiolitis. Amongst infants born before 32 weeks of gestation, those who subsequently developed an RSV LRTI had a significantly higher resistance of the respiratory system (Rrs) prior to developing the LRTI (3). Amongst infants with a wide range of gestational ages (range 23–36 weeks) those admitted to hospital because of an RSV or another viral LRTIs had higher Rrs results (4). It may then be that RSV LRTIs occur in those destined to have reduced lung function at follow up because of poorer premorbid lung function. Indeed, term born infants had reduced lung function soon after birth before they had had viral bronchiolitis and had similar levels of reduced lung function at 11 years of age (5). In contrast, amongst 70 prospectively followed infants, median gestational age 34 (range, 24–35) weeks, although there were no significant differences in lung function at 36 weeks PMA between those who did and did not develop LRTIs, at one year the viral LRTI compared to the no LRTI group had a higher mean Raw (6). Those results suggest that viral LRTIs in prematurely born infants do adversely affect their lung function at follow up.

REFERENCES
**FIRST TRIMESTER ULTRASOUND (SONOGRAPHY)**

Anupam Gupta

Since last 3 decades, Major improvement in the ultrasound assessment of early pregnancy came up with the introduction of transvaginal ultrasound. Embryonic and early foetal ultrasound is becoming a routine diagnostic modality for early pregnancy. Modern high-frequency ultrasound transducers make it possible to obtain detailed images of the early conceptus and its organs, and helps in early diagnosis of foetal anomaly. High-frequency transvaginal transducers improve the image quality to an extent that detailed description of the embryonic morphology became possible with in-depth anatomical studies of the brain compartments, the spine, the heart, the stomach, the midgut herniation and the limbs. There are three main characteristics that mark the early human conceptus: its small size, its rapidly changing anatomical appearance and its uniform development and constant growth. Today, detection of embryonic and foetal structural abnormalities in the first trimester is increasingly being reported. One has to distinguish between diagnosis during the early period until about 10 weeks when the embryo or early foetus is small and transvaginal ultrasound is applied, and diagnosis during the late period at the nuchal translucency screening, usually carried out using transabdominal ultrasound. Three-dimensional ultrasonography in obstetrics has evolved in the last years, and nowadays it is a methodology that greatly helps prenatal diagnosis. Through its rendering mode it allows the careful evaluation of foetal face and limbs, and in multiplanar mode it allows the assessment of the anatomy through the many possible planes. In the first trimester of gestation, three-dimensional ultrasonography permits the detailed evaluation of embryonic development. Its main advantages over two-dimensional ultrasonography are shorter examination time and the possibility of storage of the volumes for later processing and analysis.

Ultrasound is essentially used for assessing gestational age, current viability and maternal wellbeing. Ultrasound is a valuable diagnostic tool in assessing the following indications like - Unsure of Dates, Vaginal Bleeding, Pelvic Pain, to exclude an ectopic pregnancy, Threatened Miscarriage etc.
PREDICTION OF PRETERM DELIVERY IN PATIENTS IN PRETERM LABOR

Marija Hadji Lega

Objective
Preterm labor and delivery is a multifactorial entity that has serious medical, health-related, economical and personal implications. Its worldwide incidence ranges from around 5%-15%, depending on the population. The worldwide rates of preterm birth have increased in the past couple of decades in spite of the efforts to alleviate the problems associated with preterm delivery and the medical advances made. Preterm deliveries and associated complications account for over 75% of the neonatal mortality rates and for around half of the neurological sequelae in newborn children. Even though there have been detailed reports concerning the patophysiology of preterm delivery leading to the identification of many of the associated risk factors, preterm labor and delivery is still difficult to predict.

Materials and methods
The study was conducted as a prospective study at the University Clinic of Gynecology and Obstetrics, Skopje Macedonia. The study included 58 women with singleton pregnancies with a menstrual age between 24 and 34+6 gestational weeks, admitted at the Clinic with a diagnosis of preterm labor.

Aim
The primary aim was to evaluate the most important biochemical markers (fFN, ph-IGFBP-1, IL-6, IL-2R, TNF-α), ultrasonographically measured cervical length, as well as different combinations of markers in the prediction of preterm birth within 14 days of testing in women with symptoms of preterm labor. The study also evaluated the maternal risk factors, the demographic and socio-economic characteristics of pregnant women at risk of preterm labor in Macedonia. We also made an effort to describe the most successful prediction model that foresees preterm labor within 14 days of testing in symptomatic pregnant women.

Results
The best statistical model for predicting preterm labor in our study was to use a combination of the actim partus test, a positive fFN test, cervical length less then 21.5mm, levels of IL-6 higher than 1305 pg/mL in the cervico-vaginal secretion, serum levels of CRP higher than 6.1mg/L which was excellent at identifying the patients that were to deliver within 14 days of admittance.

Conclusion
However, the study is only the beginning of this type of research in our population. Further research is required in terms of the evaluation of cost-benefit of using such test to prevent subsequent unnecessary interventions in the low-risk group, as well as achieve the benefits from such intervention in the high-risk groups of patients.
ANATOMY OF THE HEART AND THE GREAT VESSELS

Mauricio Herrera

This presentation reviews the anatomy of the fetal heart and the great vessels with focus in the real anatomic correlation, the unique anatomic patterns, the impact in the fetal echocardiography and in the prenatal diagnosis of the congenital heart disease. With the real anatomic correlation reviewing all the landmarks and the correlation in the fetal echocardiography, and the applications in the congenital heart disease. One of the main problems in the congenital heart disease is the low rate in the prenatal diagnosis (35%), the most important tool is the knowledge and understanding of the normal heart anatomy and the anatomy of the congenital heart disease and the appearance in the fetal echocardiography. A new concept in the fetal echocardiography is the anatomical determinants of the congenital heart disease, and these include the abdominal, heart and thoracic determinants involved in the fetal heart malformations. Also include the virtual dissection of the fetal heart, where all the delegates will experiment the sensation of the anatomical travel around of the fetal heart.
ANOMALIES OF THE PLACENTA AND UMBILICAL CORD IN TWIN GESTATIONS

Corinne Hubinont

Twin gestations incidence has increased over the last decades, mainly due to the older maternal age at childbearing and the use of assisted reproductive technology treatments. Compared with singletons, twins are at higher risk of structural fetal defects, aneuploidies and placental anomalies. Among placenta and cord abnormalities found in twins, some are non specific such as complete hydatiform mole, placenta previa, placenta abruption, placental vascular lesions, velamentous cord insertion, vasa previa and single umbilical artery. Other pathological conditions are unique to twinning and mainly associated with monochorionicity. Placental anastomoses unbalance play a major role in twin’s morbidity as they are responsible for twin to twin transfusion syndrome and the associated forms (twin anemia polycythemia sequence, twin oligo -polyhydramnios sequence), involved in discordant growth and intrauterine fetal death. Cord vessels number and insertion anomalies are associated with an increased morbidity, specially in monoamniotic twins. Intertwin septum may play a role in the pregnancy prognosis, mainly in the presence of septostomy in monochorionic diamniotic pregnancies.

The aim of this presentation is to review the diagnostic tools for these specific and non specific placental and cord anomalies, mainly ultrasound and postnatal placental analysis. An accurate prenatal diagnosis by ultrasound has a direct impact on twins perinatal morbidity and mortality as well as short- and long-term morbidity. Post-natal macroscopic and microscopic placenta and umbilical cord assessment in twins is essential for confirming antenatal anomalies diagnosis and also for improving twin pregnancy pathogenesis knowledges.
SCREENING FOR CONGENITAL ANOMALIES IN THE FIRST TRIMESTER

Tamara Illescas

First-trimester ultrasound brings us a great opportunity for the evaluation of the patient-specific risk for different conditions. The combined screening for aneuploidies uses age-related maternal risk, nuchal translucency (NT) and biochemical parameters to obtain a detection rate over 90% for a FPR <5%. The new techniques for the detection of cfDNA in maternal blood will be eventually included, probably in a contingent protocol, to complement the screening of chromosomopaties.

Regarding the study of anatomy, a sagittal view of the whole fetus and different cross-sectional views of the head, thorax and abdomen are mandatory for the detection of certain malformations that must be never missed: cephalocele, acrania, holoprosencephaly, exomphalos, gastroschisis and megacystis.

A mid-sagittal view of the fetal head serves to measure the NT and to evaluate the nasal bone and the facial profile. Several midline structures of the CNS can be identified (thalamus, midbrain, brain stem, cisterna magna); the inability to image the fourth ventricle (intracranial translucency) has been reported as an ultrasound marker for the early diagnosis of open spina bifida.

One of the main contributors to a thickened NT in the presence of a normal karyotype is a fetal cardiac defect; a fetal echocardiography is then indicated and it can be accomplished in the late first trimester. An enlarged NT increases the risk for other adverse outcomes, the larger the NT, the higher the risk: skeletal dysplasia, diaphragmatic hernia, different syndromes, fetal death and macrosomia.

In multiple pregnancies, chorionicity and amnionicity should be established in the first weeks. None of the potential markers for monochorionic-pregnancy-related complications have proven to accurately identify the high-risk cases thus close follow-up is still indicated throughout pregnancy.

Assessment of risk for other complications of pregnancy (preterm birth, preeclampsia and IUGR) is also amenable to first-trimester ultrasound, although the evaluation should not be restricted to early pregnancy. At present, cervical length seems to be a better predictor for prematurity when evaluated during the second trimester. Preeclampsia and IUGR are often late events of multifactorial origin therefore some cases are difficult to be predicted at the beginning of pregnancy.

The advantages of first-trimester detection of chromosomopaties and fetal malformations are undeniable. Regarding other adverse outcomes, though, there are still some controversies (best algorithms for each condition, prevention and treatment interventions, false positive cases, late-onset events) to be discussed before we can state that early detection is a synonym for better outcomes.
FETAL SURGERY AND MEDICAL THERAPY FOR CONGENITAL DIAPHRAGMATIC HERNIA

Deprest Jan

In EU-27, 2100 babies with congenital diaphragmatic hernia (CDH) are born annually. CDH may be isolated or associated with other structural anomalies, the latter with poor prognosis. The defect allows viscera to herniate through the defect into the chest, competing for space with the developing lungs. At birth, pulmonary hypoplasia leads to respiratory insufficiency and persistent pulmonary hypertension that is lethal in up to 30% of patients. When isolated, survival chances can be predicted by antenatal measurement of lung size and liver herniation. Chromosomal microarrays and exome sequencing contribute to understanding genetic factors underlying isolated CDH. Prenatal intervention aims at stimulating lung development, clinically achieved by percutaneous fetal endoscopic tracheal occlusion (FETO) under local anesthesia. The Tracheal Occlusion To Accelerate Lung growth trial (www.totaltrial.eu) is an international randomized trial investigating the role of fetal therapy for severe and moderate pulmonary hypoplasia. Experimental fetal surgery in severe cases results at best in a survival rate of 50-60%, due to insufficient lung growth, persistent pulmonary hypertension or prematurity induced by the procedure. For non-survivors alternative strategies are required. Survivors undergo anatomical repair, but large diaphragmatic defects are closed using a patch. Currently used materials are less than ideal, mainly because of recurrence and chest deformation. To overcome the above limitations, alternative medical (pharmacologic or cell therapy) that are more potent and less invasive are needed. A more functional postnatal repair may be possible when using novel scaffolds or engineered constructs. We see a prominent place for autologous amniotic fluid derived stem cells in this, which could be prenatally harvested following appropriate patient selection by non-invasive imaging.
LOW-RISK PREGNANCY

Samuel Karchmer

Delivery, whether on a hospital or outside, has been recently discussed. However the choice assumes that complications of labor and delivery could be predicted and accurately identifies low-risk pregnancies.

In many countries of the world, maternity care is provided with a multi-disciplinary team involving an anesthesiologist, obstetricians, neonatologists, and midwives, but there are places where only a small percent of the populations have this kind on attention.

The term “low-risk pregnancy” is widely accepted in clinical practice, it has become an integrated part of the vocabulary in health policies and medicine, mainly in our specialty, and it refers to a pregnancy with a decreased risk of poor outcome for both mother and fetus.

Determining the appropriate site of care for any type of medical attention assumes a successful match of patient risk-to-facility capabilities and resources. In obstetrics, predicting patients who will need additional resources beyond “routine” obstetric and neonatal care is difficult because a patient with a low-risk pregnancy could had several complications and severe hemorrhage or other life-threatening complications like eclampsia and be in need of specialized support in a third care level facility. It is well known that women without risk factors and their newborns may experience unexpected complications during delivery or postpartum.

Sometimes, patients with high-risk pregnancies have better results than patients with a low-risk pregnancies because the risk is minimized.

The purpose of this paper is to reflect on the impact of labeling a patient as having a “low-risk pregnancy” and determining appropriate sites of care for all pregnant women to get a successful delivery.

There are several studies about the complications among patients with “low-risk pregnancies” and without identified prenatal risk factors. Also there are reports with near of 30% of the patients identified as a low-risk pregnancy with at least an adverse outcome that would require non-routine obstetric or neonatal care during delivery or postpartum period. On the other hand, 30% of patients that have a “low-risk pregnancy” profile in early pregnancy are referred to a hospital during the third trimester of their pregnancy, and 20% of women are referred while giving birth. Also, there are publications that shown and incidence of emergency cesarean section of 7-9%, among these 68% were performed because of failure-to-progress and 30% for suspected fetal distress.

.... So, our question should be: “Does the low-risk pregnancy” really exist?
FETAL AND NEONATAL PROGRAMMING AND THE IMPORTANCE OF MATERNAL NUTRITION

Berthold Koletzko

Many characteristics of an individual persist from early childhood to old age, which is usually explained by genetic determination of phenotypic characteristics. Evidence has accumulated that demonstrates marked environmental influences during sensitive time periods of early developmental plasticity on the development of the phenotype. An important influencing factor is early nutrition during the first about 1000 days of life (270 days of pregnancy and 2 x 365 days of the first two postnatal years). During this sensitive time window, nutrition modulates cytogenesis, organogenesis, metabolic and endocrine responses, pre- and postnatal growth trajectories, epigenetic regulation of gene expression, and hence induce programming effects on long-term health and disease risks until old age (www.project-earlynutrition.eu). Three identified key mechanisms in early programming include “fuel mediated ‘in utero’ programming”, indicating that intrauterine excessive supply of fuels (glucose and fatty acids) induces increased fetal growth and neonatal adiposity as well as increased later obesity; “accelerated postnatal growth” indicates a link between high weight gain in early childhood and an increased risk of later obesity and other adverse outcomes; and “mismatch programming” reflects a developmental mismatch between sub-optimal prenatal conditions with low birthweight followed by an obesogenic childhood environment with high weight gain, which leads to a very high risk of obesity and related co-morbidities. Before and during pregnancy, a balanced diet and regular physical activity have short as well as long-term positive effects on health and well-being, amongst others on the risk of obesity and its related disorders in later life. Rapid growth and development of the unborn child puts a high demand on the fetal nutrient supply. Women who pay special attention to eating nutrient-dense foods before and during pregnancy are able to create optimal conditions in the womb for the development of their children. Metabolic and weight status of the mother before conception, a healthy balanced diet rich in micronutrients such as folate, vitamin D, iodine, iron, as well omega-3 DHA, and the prevention of excessive weight gain during pregnancy, contribute markedly to the health of the unborn child. At the same time, an oversupply of energy and a high gestational weight gain should be avoided, and gestational diabetes should be screened for and treated if detected. In conclusion, the quality of substrate supply before and after birth has powerful long-term programming effects on health, well-being and performance, with very large effect sizes.
FETAL AND NEONATAL PROGRAMMING AND THE IMPORTANCE OF MATERNAL NUTRITION

Berthold Koletzko

Many characteristics of an individual persist from early childhood to old age, which is usually explained by genetic determination of phenotypic characteristics. Evidence has accumulated that demonstrates marked environmental influences during sensitive time periods of early developmental plasticity on the development of the phenotype. An important influencing factor is early nutrition during the first about 1000 days of life (270 days of pregnancy and 2 x 365 days of the first two postnatal years). During this sensitive time window, nutrition modulates cytogenesis, organogenesis, metabolic and endocrine responses, pre- and postnatal growth trajectories, epigenetic regulation of gene expression, and hence induce programming effects on long-term health and disease risks until old age (www.project-earlynutrition.eu). Three identified key mechanisms in early programming include “fuel mediated ‘in utero’ programming”, indicating that intrauterine excessive supply of fuels (glucose and fatty acids) induces increased fetal growth and neonatal adiposity as well as increased later obesity; “accelerated postnatal growth” indicates a link between high weight gain in early childhood and an increased risk of later obesity and other adverse outcomes; and “mismatch programming” reflects a developmental mismatch between sub-optimal prenatal conditions with low birthweight followed by an obesogenic childhood environment with high weight gain, which leads to a very high risk of obesity and related co-morbidities. Before and during pregnancy, a balanced diet and regular physical activity have short as well as long-term positive effects on health and wellbeing, amongst others on the risk of obesity and its related disorders in later life. Rapid growth and development of the unborn child puts a high demand on the fetal nutrient supply. Women who pay special attention to eating nutrient-dense foods before and during pregnancy are able to create optimal conditions in the womb for the development of their children. Metabolic and weight status of the mother before conception, a healthy balanced diet rich in micronutrients such as folate, vitamin D, iodine, iron, as well omega-3 DHA, and the prevention of excessive weight gain during pregnancy, contribute markedly to the health of the unborn child. At the same time, an oversupply of energy and a high gestational weight gain should be avoided, and gestational diabetes should be screened for and treated if detected. In conclusion, the quality of substrate supply before and after birth has powerful long-term programming effects on health, well-being and performance, with very large effect sizes.

Acknowledgments: The work of the authors is financially supported in part by the Commission of the European Communities (FP7/2007-13, EarlyNutrition Project, www.project-earlynutrition.eu) and the European Research Council (Advanced Grant n° 3226059). This abstract does not necessarily reflect the views of the Commission and in no way anticipates the future policy in this area. Further support has been provided by the German Federal Ministry of Education and Research and the German Research Council.
THE ODÓN DEVICE: A NEW APPROACH

Hugo Krupitzki

The following presentation describes our preliminary experience with the Odón device, a new low cost instrument for fetal delivery when complications during the second stage of labour arise. The Odón device, made of a polyethylene-like film, is designed for easy application, and its use requires minimal training. In comparison with currently available instruments for operative vaginal delivery, the device has specific features that could reduce the risk of fetal-maternal injury.
To assess the safety and feasibility of the Odón device in assisting the vaginal delivery of singleton term pregnancies during the second stage of labour, the World Health Organization implemented a phase 1 study in Argentina.
The prospective study enrolled 48 pregnant women at CEMIC University Hospital, Buenos Aires, Argentina. The device was applied with full dilation, ruptured membranes, anterior presentation, +2 station and normal fetal electronic heart rate. Safety was assessed by examining short and long term maternal morbidity; feasibility, in terms of ease of application and successful delivery.
The Odón device is designed to minimize trauma to the mother and the fetus. It may also protect the fetus from intrapartum infection and has potential for application by mid-level providers in low resource settings. These features combined, make it a potentially revolutionary development in obstetrics.
IMAGING OF FETAL NEUROBEHAVIORAL

Asim Kurjak

One of the greatest challenges of obstetrical ultrasonography is the better understanding of fetal neurological function. Neurological problems such as cerebral palsy are poorly understood and often falsely attributed to intrapartum events, while for the majority of cerebral palsy cases it has been proven that the causative pathway starts long before delivery. Several attempts have been made in order to define normal and abnormal fetal neurological function and to develop a method of assessment of the integrity of the fetal nervous system, but still without satisfactory sensitivity.

Fetal behavioral patterns are directly reflecting developmental and maturational processes of fetal central nervous system. It has been suggested that the assessment of fetal behavior during different periods of gestation may provide valuable information about normal and abnormal brain development, and contribute to the early diagnosis of various structural or functional neurological abnormalities. The introduction of three and four dimensional ultrasound (3D & 4D) allowed real time assessment of fetal behavior. Details of the fetal face, and especially movements of mouth, eyes (facial expressions) and fingers have been made possible with the introduction of 4D ultrasound. KANET is the first method that attempted to use 4D ultrasound in order to assess and combine parameters of fetal behavior and form a scoring system that would assess the fetus in a comprehensive and systematic approach, in the same way that neonatologists perform a neurological assessment in newborns during the first days of their life, in order to determine their neurological status. KANET appears to be able to identify functional characteristics of the fetus that predict normal and abnormal neurological development and hopefully future results of the prospective multicentric studies that are taking place at the moment in the next few years it will provide more information on fetal neurology. Such information will be of great value in counseling mothers of high risk pregnancies, like for example in cases with previous child with cerebral palsy and also provide valuable evidence for cases of litigation.
Prenatal Evaluation of Neurologic Function: The KANET Test

Asim Kurjak

Fetal behavior refers to the fetal activities observed or recorded with ultrasonographic equipment. Behavior can be spontaneous, generated by the fetus itself, or elicited in response to external stimulus such as vibroacoustic stimulation. Analysis of the fetal dynamics in comparison with morphological studies has led to the conclusion that fetal behavioral patterns directly reflect developmental and maturational processes of the fetal central nervous system (CNS). In addition, there is a carryover effect of movements from prenatal to postnatal life. There were no movements observed in fetal life that were not present in neonatal life. Furthermore, prenatal-neonatal continuity exists even in subtle, fine movements such as facial mimics. Altered quality of fetal movements might reveal the structural or functional impairment of the fetal central nervous system. Improvement of four dimensional (4D) technology enabled introduction of Kurjak Antenatal Neurological Test (KANET), scoring test for the assessment of the fetal behavior. Our preliminary results have confirmed the usefulness of this test in fetal behavior assessment. The KANET test has potential to detect and discriminate normal from borderline and abnormal fetal behavior in normal and in high-risk pregnancies, which means that it could become a valuable diagnostic tool for fetal neurological assessment. Over 100 fetuses from pregnancies with threatened preterm labor have been studied using KANET in our multicentric program. Recently study with the largest number of fetuses (620 fetuses) where prenatal KANET test has been applied was published. Among the fetuses with abnormal KANET score, most frequently presented were fetuses from the threatened preterm delivery group. Preterm labor accounts for 75% of perinatal mortality and over 50% of perinatal morbidity. Although preterm survives, they are at increased risk of neurodevelopmental impairment. It has been shown that fetal behavior differs in preterm than term infants. Further, fetal behavior differs in neurologically compromised compared to normal fetuses. There are developmental differences between fetuses threatening to deliver early and other high risk fetuses. Preterm infants are at higher risk for cerebral palsy due to prematurity, intrauterine growth restriction, infection or multiple pregnancy. Pediatricians know that they need to wait until the age of 6 months postnatally to diagnose a severe CP and at least 24 months or even longer for a minor non-disabling CP. KANET test and behavioral assessment give new hope in the attempt of early diagnosis of cerebral palsy and provide identification of fetuses at neurological risk from pregnancies with threatened preterm labor.
MANAGEMENT OF PLACENTA ACCRETA AFTER PREVIOUS CESAREAN SECTION

Mark Kurtser

We researched medical documents of 138 patients with placenta accreta, in combination with an uterine scar after previous cesarean section (CC) from 1999 to 2014 years. Placenta accreta was diagnosed during pregnancy by ultrasonography of the lower uterine segment, NMRI. Patients’ age was from 28 up to 42 years. 65 of 138 (47,1 %) patients were undergone one prior CC. Primary cesarean section was scheduled for 66 patients from 138 (47,8 %).

Pregnant were divided into two groups: Group 1- 43 (31,2%) patients, delivered using a transverse lower segment hysterectomy incision, Group 2 - 95 (68,8%) patients which were undergone midline laparotomy and corporal cesarean section. 56 of 95 (58,9%) patients were performed an uterine artery embolization (UAE); 24 (25,3%) - a prophylactic balloon occlusion of the internal iliac arteries (BOIA), 15 (15,8%) – without angiosurgery methods.

The majority of patients (33) were carried out metroplasty, and reproductive function has been preserved. Average volume of blood loss in Group 1 was 3698 ± 1120 ml, Hysterectomy was required in 10 (23,3%) patients.

Average amount blood loss in patients with UAE was 2 100 ± 910 ml, in group with BOIA - 1 329 ± 920 ml.

For all the parturients from Group 2 uterus incision was sutured without removing the placenta. Then we performed UAE or BOIA. The next step for the majority of patients - excision of the uterine hernia, removal of the placenta and plastic of the lower uterine segment. Reproductive function of all pationes in Group 2 has been preserved.
EVALUATION OF THE CENTRAL NERVOUS SYSTEM USING AN AUTOMATIC APPROACH

Ja-Young Kwon

Central nervous system (CNS) anomalies constitute about 10% of anomalies found in perinatal autopsy cases, and neural tube defect (NTD) is most frequent CNS anomaly with its prevalence being 1-2% per 1000 births. Complying with the guidelines for performing basic examination of the fetal brain using ultrasound (US) may increase the detection rate of fetal CNS anomalies and promote correct referral to tertiary care centers for further diagnosis and counseling. Basic examination of fetal CNS includes confirmation of structures (qualitative) and measurement of structures (quantitative) relevant to anatomic integrity.

Two-dimensional (2D) scanning is an efficient technique for fetal neurosonography, only in the hands of operator knowledgeable with appropriate planes and landmarks, able to mentally reconstruct the three-dimensional (3D) anatomy from the real-time 2D information in all three axes including coronal planes. In this context, use of 3D ultrasound in fetal brain examination has been proposed as feasible technique as it allows you to save volume data and retrieve to generate multiple planes of section supported by visually reconstructed 3D anatomy.

Nonetheless, obtaining correct plane sections using 3D volume data is operator-dependent, as it requires skill on volume acquisition and manipulation. And performing 3D US lacking necessary skills, one would find it much cumbersome and time-consuming than 2D. With the advancement of technology, converting manual process of 3D volume into automated program has been promising in various area of fetal US such as nuchal translucency, long bone, or cardiac evaluation.

Recently, a commercially available automated program installed in the US equipment automatically reconstructs multiple plane sections and measurements within seconds of single volume sweep of fetal head. This automated approach may add potential benefits to fetal 3D US of CNS including: 1) possibility of standardization of CNS basic exams, 2) reduced volume process time with 3) increased reproducibility. In this lecture, we will introduce how automated program can be applied in the examination of fetal CNS.
INDIVIDUALIZED GROWTH ASSESSMENT

Wesley Lee

Population-based reference ranges provide an important means for identifying size abnormalities although they do have some limitations because the growth potential of an individual fetus is not considered. Interpretation of fetal biometry, based on percentiles, poses additional challenges secondary to the biological variability in such standards that is inherent in the development of cross-sectional reference ranges from large groups of fetuses. A common problem arises when an EFW for a fetus from a specific group is interpreted using weight percentiles derived from an entirely different reference population. This can lead to confusion as to whether or not the fetus has any ultrasound evidence for an intrauterine growth abnormality. Individualized growth assessment (IGA) can be used to evaluate changes in various fetal size parameters (including EFW) over time (t) by comparing current and expected growth. Actual measurements are compared to 3rd TM size predictions, derived from 2nd trimester Rossavik size models, that have been previously established for an individual fetus (e.g. each fetus is its own control). Rossavik models are used to summarize growth characteristics of 1D, 2D, and 3D size parameters (P) by only changing coefficient values (c, k, and s) that are hypothesized to hold biological significance. Coefficient c represents control mechanisms that specify fetal growth and can be estimated from the calculated linear slope between two or more scans during an assumed time of normal second trimester growth (empirical measure of growth potential). Coefficient s represents an unknown control system that regulates the growth process at the end of pregnancy. Coefficient k reflects the anatomic characteristics of the measured parameter. The model can predict 3rd trimester size trajectories in normally growing fetuses and provides a way by which abnormal growth can be detected and evaluated in newborns as well. Neonatal evaluation compares an actual birth parameter measurement with a value predicted from 2nd trimester Rossavik growth model. Individualized Growth Assessment Program (iGAP), is a web-based application that quickly generates expected 3rd trimester growth trajectories for a single size parameter or set of parameters, using each fetus as its own control. The software graphically summarizes composite growth for several parameters over time. During this session, the basic features and utility of iGAP software will be demonstrated for a personalized assessment of fetal growth and neonatal growth outcome.
FAMILY CENTERED CARE, THE NORTHERN COUNTRIES APPROACH

Liisa Lehtonen

Modern neonatal care should support parenting from the beginning of neonatal hospital care by allowing the parents to be the primary caregivers for their infants even if the infant needs medical care. The traditional hospital care culture in neonatal intensive care units has largely ignored the needs of the parents and the need of a newborn to have his/her parents present.

Many hospitals in Nordic countries have developed their care cultures to better promote parent-infant emotional and physical closeness and to empower parents in their role as primary caregivers. Goal-oriented programs have been developed to enhance implementation of family centered care in everyday practice. The Close Collaboration with Parents Training Program aims to change the attitude of the staff who, in their turn, find the context-specific new practices which best support parents and parenting in their unit. The foundation of the program is to sensitize the doctors and nurses to the behavioural cues and individual characteristics of the infants, and to the uniqueness of each family. Then, the staff members learn to involve the parents as equal partners in negotiations about infant care. Parents become more empowered and contribute to the infant’s care on many levels. They bring sensitivity and continuity in the infant care and they inform the staff about the development of their infant and potential concerns in the infant condition. Mutually respective partnership can be reached instead of traditional hierarchical attitudes.

Even if many features of family centered care can be reached in a traditional architecture, the state-of-art hospital design provides parents facilities to stay close to their infant throughout the day and night. During the last 10 years, such hospitals have been built in the Nordic countries. In addition to the basic facilities for sleeping, eating and hygiene, the parents find privacy as an essential feature enabling them to stay for a prolonged time with their infant. Single family rooms increase parent-infant closeness and interaction thereby supporting infant growth and development, and development of healthy attachment relationship.
**N-CAP AND HHFNC IN THE MANAGEMENT OF RDS OF PRETERM INFANTS: AN UPDATE**

Gianluca Lista

Many preterm infants breathe at birth, but they frequently need a respiratory support to facilitate the fetal-neonatal transition and to achieve and maintain an adequate lung volume. For this target, the neonatologists have to choose the best respiratory support to deliver a continuous distending pressure (CDP) to obtain an adequate lung volume from the delivery room preferably supporting the spontaneous effort of the baby, reducing the risk of lung injury.

In literature, above all in the recent years, there are many studies published on different modalities of non-invasive respiratory support (N-CPAP, bi-level N-CPAP, N-SIPPV/N-SIMV, HHFNC, etc) to deliver a CDP.

The most recent European RDS guidelines underline the importance to initiate CPAP and caffeine for extremely preterm infants as soon as possible and to consider tracheal intubation plus mechanical ventilation (MV) for depressed infants or when other method of respiratory support failed. The AAP also confirmed that early initiation of CPAP with subsequent selective surfactant administration in extremely preterm infants with RDS results in lower occurrence of BPD and death. In fact some recent meta-analysis indicate that avoiding tracheal intubation and early mechanical ventilation (MV) reduces the incidence of death and BPD in preterm infants < 32 wks'GA.

Nevertheless, nasal injury can occur and it is related to the length of time CPAP is used. Recently, also for pediatric patients, the Heated Humidified High Flow Nasal Cannula (HHFNC) has been used for preterm infants with respiratory failure because its potential advantages: in fact it is well-tolerated with less nasal injury, it is easy to apply and allows a good nursing and parental care. HHFNC actually seems to be a valid alternative in very preterm infants after extubation. Actually there are not in literature consistent RCTs on HHFNC in preterm infants (especially for very premature babies below 1 Kg and < 27 wks'GA) and therefore at this time there is not sufficient evidence to conclude that HHFNC as “first intention” could have an effect both on short-term (e.g. less need of MV in the acute phase of RDS) and long-term outcome (e.g. death or BPD). Further well-designed RCTs are needed.
WHY IS FAMILY CENTERED CARE THE MODEL OF THE NICUS FUTURE - A PATIENTS VIEW

Silke Mader

The best long-term development of the preterm infant should be the primary objective in neonatology. Development-support covers a variety of strategies in addition to medical care, to protect and to promote the development of the baby. This part of newborn care is of increasing importance because many babies born long before their due date, although being very small and vulnerable to the world, survive today. Although most of these children go along well in life, many of them do not realize their real potential. They can have a variety of problems, not always serious, but yet serious enough to need special support in their schooling. Developmental care aims to minimize the risk of such problems. To reduce these risk factors is not only important for the baby and its family – this will reduce high financial, economic and social costs for the whole society in Europe and beyond. Preterm babies are not rare - this matters because one baby in ten is born premature - worldwide! Newborn care is practiced in various intensive care units in quite a different way - and this applies also to developmental care. However, there are some key principles that are widely used: Primarily, the idea of a “family-centered care” which means nothing more than to emphasize the vital role played by parents for their children. Even, if baby’s need technical and medical support at the highest level, parents are the most important people for the baby’s life.

Silke Mader, Co-founder and chairwoman of the European Foundation for the Care of Newborn Infants knows from her own experiences that a family needs much more than medical care and support - the entire family needs to be in the centre of interest. Parents need to be empowered in their parental role from their first day in the NICU. The most important point from the beginning is communication with parents in a respectful and understandable way, accepting their autonomy, helping them with education and guidance to find their parental role. For sure, not all parents are easy to handle, but these parents are in a traumatic situation and some of them stay in the unit for months. Family centred care also means to provide support and help for the many times neglected needs of the siblings. Preterm birth has many side effects and often traumatizes the whole family.
Combining Forces in Maternal and Newborn Health – A European Example in Preterm Birth

Silke Mader

Depending where in Europe a woman becomes pregnant, the level of care received will vary. Some care practices fall far short of promoting and protecting the right to a healthy start in life. Appropriate treatment and care as well as social support are often lacking from the very start of a pregnancy until after the traumatic experience of preterm birth. Faced with the non-existence of support of any kind, the absence of public and political awareness and lacking information and education for expecting parents, parents and healthcare professionals, decided to make a difference together and finally give one of Europe’s most vulnerable and still overlooked patient groups a voice: In 2008, two parents and a neonatologist founded EFCNI.

After seven years of existence, EFCNI has grown to a renowned organization, representing the interests of preterm and newborn infants and their families. EFCNI gathers together parents and healthcare experts from different disciplines with the common goal of improving long-term health of preterm and newborn children by ensuring the best possible prevention, treatment, care and support.

EFCNI collaborates with scientific and professional societies and is involved in many research programmes and studies. It also acts as parent representative in the boards of different societies. EFCNI published two major policy reports and started with EU-wide campaigns to bring awareness for the topic prevention and preterm birth as well as the demands of parents and experts to the attention of European policy makers and to the wider public. The most famous and from EFCNI founded campaigns are “World Prematurity Day” and “Socks for Life”. EFCNI’s latest project, the development of “European Standards of Care for Newborn Health” is supported by over 50 health professional societies, parent organisations and third parties and is a further milestone to ensure better and more harmonised treatment and care in Europe to enable the best start in life for all infants.
Preterm labor is a pathological condition with multiple etiologies. The problem Preterm delivery, with its collateral effects on neonatal mortality, short- and long-term infant morbidity and astronomical healthcare costs. In spite of advances in obstetric care, the rate of prematurity has not decreased over the past 40 years and in developed countries there has been an increase, possibly as a result of assisted reproductive technology (ART) programs. To some extent symbiotic relationship between neonatologists, obstetricians and sonologists, has improved outcomes of babies by improvements in neonatal care, obstetric interventions applied to reduce the risk of preterm birth, use of antenatal steroids for accelerating lung maturation, reducing non-medically indicated inductions by fine tuning of timing by doppler and fetal surveillance along with using magsulf for neuroprotection. Prenatal ultrasound has also made major contributions to the reduction of infant disability, not only through the detection of fetal anomalies and selective termination of pregnancy but also through improved prediction and monitoring of IUGR. The realization that shortening and effacement of the cervix is the final pathway common to many if not most cases of spontaneous PTB, following routine measurement of cervical length from 19 to 24 weeks gestation and administration of progesterone to women with a short cervix will now redefine antenatal care. Transvaginal ultrasound (TVUCL) for cervical assessment is one of the best if not the best of available technique for PTB prediction. TVUCL< 25mm between 16 and 24 weeks—most reliable threshold for an increased risk of PTB. A transvaginal scan in the second trimester in singleton pregnancies along with per speculum examination to rule out bacterial vaginosis, carried out between 19 and 24 weeks to measure cervical length is the best method with which to identify a group of women (approximately 2% of the pregnant population) who would benefit from prophylactic progesterone treatment to prevent spontaneous PTB. Progesterone vaginal pessary every night from 20 to 34 weeks reduces preterm delivery rate by 25%. Measurement of cervical length every 2 weeks between 14 and 24 weeks and cervical cerclage if the cervix becomes less than 25 mm reduces preterm delivery rate by 25%. Vaginal progesterone prophylaxis has no reported side effects attributable to the drug and treatment compliance is high (> 90%). Universal cervical-length screening and vaginal progesterone prevents early preterm births, reduces neonatal morbidity and is cost saving: doing nothing is no longer an option.
F.I.G.O. GOOD PRACTICE ADVICES ON ISSUES IN MATERNAL–FETAL MEDICINE

Narendra Malhotra

F.I.G.O. working group on “Fetal Medicine” felt that it is necessary to prepare Good practice clinical advices rather than strict guidelines.

Eight such good practice advices are being presented:

1. Screening for chromosomal abnormalities and non invasive prenatal diagnosis and testing.
2. Periconceptional folic acid for the prevention of neural tube defects.
3. Cervical length and progesterone for the prediction and prevention of preterm birth.
4. FIGO Best Practice Advices on “Magnesium sulphate use in Obstetrics”.
5. Magnesium Sulphate use in fetal neuroprotection.
6. FIGO Best Practice Advices on “ultrasound examination in pregnancy”.
7. FIGO Best Practice Advices on Thyroid disease in Pregnancy.
8. FIGO Best Practice Advices on “Hyperglycemia in Pregnancy”.

DISCLAIMER:
Please note that these advices should not be considered as standards of care or legal standards in clinical practice.

Note: All these are available on F.I.G.O. website.
**THE RELATIONSHIP BETWEEN NUTRITION AND NEONATAL INFECTION**

Paolo Manzoni

Preterm neonates in NICU are at risk of intestinal disturbances with proliferation of a pathogenic microflora, because treatment with antibiotics, TPN, or nursing in incubators may delay or impair the intestinal colonization process. Preterms thus acquire commensals such as bifidobacteria more slowly and are likely to acquire gut pathogenic colonization from the NICU.

Owing to this, the digestive tract is regarded as the most important reservoir for colonisation by all kinds of pathogens and subsequent sepsis in preterms. In this view, optimal nutrition, and provision of specific nutrients, can be seen as a tool to prevent the development of infections in neonates. Among all the nutrients that have been assessed for their impact on infections, lactoferrin and probiotics have accumulated a growing evidence over the last years.

Probiotics can restore normality of gut microbiota, and prevent its disturbances in humans including neonates. Mice studies showed that selected probiotic strains reduce both enteric colonization and systemic infections by E.Coli and fungi. Such strains may act at several levels simultaneously: exclusion of pathogens by competition, prevention of adhesion, reduction of their ability to colonise the mucosa through enhanced IgA responses, changes in mucosal permeability increasing the barrier effect, and immunomodulation with modification of local and systemic immune responses to fungal and bacterial toxins or products.

To date, only few clinical trials have reported the outcomes of preterm neonates given probiotics: these studies consistently show beneficial effects of some probiotic mixtures in preventing fungal colonization, improving feeding tolerance by enhancing gastrointestinal maturity and function, and reducing the incidence of NEC.

Lactoferrin is a mammalian milk glycoprotein involved in innate immune host defences, and can reduce the incidence of late-onset sepsis in VLBW infants (Manzoni, JAMA 2009) and of NEC in animal models. The bovine isoform is nearly homologous to the human one. Lactoferrin targets all pathogens, has bifidogenic properties, and enhance maturation of the nascent gut.

In a recent RCT, bovine LF produced a 65% decrease in any-cause Late-onset sepsis, regardless of the pathogen, and a significant decrease in all-stages NEC (Manzoni, EHD 2014). The effect of Lactoferrin on prevention of NEC was amplified –as expected- by the concomitant addition of the probiotic Lactobacillus RhamnosusGG, that is synergistic with LF. As no adverse effects or intolerances to treatment have been reported to date, the role of LF in the management of infections and NEC in NICU looks very promising and worthy of future, larger-sized trials to confirm these findings.
THE ASSOCIATION OF MATERNAL OBESITY AND PREGNANCY RELATED DEATHS

Federico G. Mariona

The maternal mortality ratio (MMR) is a reflection of a country’s dedication to health care. It measures women’s healthcare. The current MMR in the USA is 16.0 /100,000 births, an upwards trend initiated almost 30 years ago. Obesity is defined as a body mass index (BMI) ≥ 30 Kg/m². It is considered a worldwide public health concern of epidemic proportions. Maternal obesity affects 28.9 % of pregnant women in the USA. Pre-pregnancy obesity reaches 24.3%. Our objective is to report the association between maternal obesity and pregnancy related deaths (PRD) in the state of Michigan, rated the tenth fattest state in the US (2013). PRD is defined by the Centers for Disease Control and Prevention as “the death of a woman during the pregnancy or within one year from the end of the pregnancy caused by a pregnancy complication or a chain of events initiated by pregnancy or the aggravation of an unrelated condition by the physiologic effects of pregnancy”. This definition differs from that of the World Health Organization (WHO) that reports maternal deaths during pregnancy and within 42 days after its end. The Michigan Maternal Mortality Survey multidisciplinary committee has been active in the state for 50 years; it produces enhanced analysis of maternal death cases voluntarily reported to the state. This is a retrospective secondary analysis of a selected limited cohort reviewed by the committee. The data includes 2004 to 2006 using linked birth-deaths certificates. 205 pregnancy associated (PA) deaths occurred in 384,765 live births. 59 deaths (28.7%) were classified as PRD (ratio 15.33/100,000). Within this group, on 36 (61%) the maternal BMI ranged from 30 to 73 Kg/m² (average BMI 34 Kg/m²). 23 patients were non-obese (38%). BMI data was missing in 2 % of cases. The maternal age ranged from 15 to 37 years old. 54% of obese women were Black American, 42% were Caucasian. 4.87% of PRD occurred 42 days after the end of the pregnancy. Gestational age at the time of maternal death ranged from 10 to 41 weeks. The direct relationship between increasing maternal BMI and pregnancy morbidities has been repeatedly reported. This report demonstrates that PRD occur significantly more often in obese than in non-obese women. Physicians, public health officials and policy makers must work together to educate the population to achieve ideal body weight prior to conception and limit gestational weight gaining.
THE HIGH RISK FETUS WITH CCHD AND PLANNING FOR DELIVERY

Gerard Martin

Congenital Heart Disease (CHD) is the most common birth defect, impacting nearly 1/100 Live Births. Approximately 40% of defects will require intervention in the first year of life. A number of conditions are at risk for compromise at delivery or in the neonatal period and may have survival rates less than 50%. These infants can be predicted based upon their anatomical condition or findings from fetal echocardiography. Utilizing a Level of Care Protocol, decisions to deliver the child at the local hospital (Level 1), or hospital with tertiary care NICU (Level 2), or hospital with tertiary CHD care “on standby” (Level 3), or hospital with tertiary CHD “on ready” (Level 4) can be made and improve safety of the transitional period. Utilizing this decision tree we have improved survival of “at risk” infants with CCHD to over 80%.
GENETIC SCREENING FOR BIRTH DEFECTS

Manjeet Mehta

Birth defects, which occur in nearly one in 20 pregnancies, range in severity from minor anatomic abnormalities to extensive genetic disorders or mental retardation. Genetic conditions are a major cause for morbidity and mortality, but are often under-diagnosed.

Screening for genetic diseases that may affect offspring depends upon the racial or ethnic background of the couple, their family, medical history, and associated conditions. Various racial and ethnic groups demonstrate an increased prevalence of specific diseases, and couples of these backgrounds have their carrier status screened accordingly, if there is a family history of the disorder or if they belong to an at-risk racial or ethnic group.

Newborn screening is the practice of testing every newborn for certain harmful or potentially fatal disorders that aren’t otherwise apparent at birth. Newborn screening tests help to identify potentially treatable or manageable congenital disorders within days of birth. Early intervention to treat these disorders can eliminate or reduce symptoms that might otherwise cause a lifetime of disability. Life-threatening health problems, mental retardation, and serious lifelong disabilities can be avoided or minimized if a condition is quickly identified and treated.

Among pediatric genetic conditions, Down’s syndrome, major birth defects and mental retardation are pretty well known. However, there are several other genetic conditions which appear to be invisible until later in life. Many diseases impair normal life and pose life threatening complications. In such diseases,, diagnosis at an early stage & early intervention can provide a healthier life. A predictive genetic screen reduces the impact of genetic conditions on those who may be affected and their families. A Newborn Genetic Panel would include disorders that have an early onset during childhood, are severe, yet treatable, and sometimes completely curable by timely intervention.

Testing for Inborn Errors of Metabolism is being done at several centers by chromatography method. However, there are several conditions which could be only tested on DNA. These are later onset, may not be picked up at birth, and an early intervention could save the infant from severe implications. List of such conditions include: Wilson Disease, Cystic Fibrosis, Beta Thalassemia, Sickle Cell Disease, Cardiomyopathy, Long QT Syndrome, Hereditary Hemochromatosis, Epilepsy, Wilms Tumor, amongst others.

The talk would highlight importance of genetic DNA testing to screen newborns for several disorders that, unless detected and treated early, can cause physical problems, developmental delay, and in some cases, death.
AGING OF THE CERVIX

Micaela Menárguez

Physiologic factors causing a disturbed mucus symptom are usually seen at the extremes of the child-bearing years. According to Odeblad’s studies, cervical crypts, at this age, are mostly S cryps while there are just a few G cryps. That’s means that most of agents against infections are not present in the mucus. This could be one of the reasons why sexual transmitted infection diseases are frequent in adolescents before 18 with an activ sexual life.

The menstrual cycle is often irregular in pre-menopause due to an increase in the incidence of anovulation or of delayed ovulation.

The cervix undergoes a natural process of aging. At puberty S cryps are very numerous but with increasing age, L cryps replace the S cryps. (Pregnancy stimulates the production of S cryps and rejuvenates the cervix by two to three years). In pre-menopause the decrease in number of S cryps results in a decrease in the number of days of the more-fertile mucus. The contraceptive medication has also an “ageing” efect on the cryps, according to Odeblad’s studies.

References:
5. Odeblad E; ‘Aging of the cervix’.
FERTILITY AWARENESS AS A HUMAN VALUE

Micaela Menárguez

Human sexuality is the set of physical, psychological and intellectual characteristics that make the human being revealed as male or female. Human sexuality has four facets, whose integration enables the sexual maturation of adolescents and youth. These are: 1) Emotional facet, which means tenderness, smile and gestures. 2) Cognitive facet, which is conversation, friendship, admiración... 3) Placer, which is the vital spring which encourages sexual fulfillment and 4) The procreation, which is the main objective of nature to do man and fertile woman.

When sexuality is an expression of love, and therefore, the gift of the whole person, privacy has characteristics that are not present in other circumstances. Body language expresses then, that when I give my skin, not only give you my skin but also my life. And with my body I give myself and hope to receive yours. Privacy then has qualities that improve a person, and dignified, making the vehicle body a sublime expression of love of the person. Those qualities are: 1) Gearing to another, respecting the importance of different sexual response times. 2) Generosity, taking into account sex, the good of others and not oneself. 3) Time, as the expression of love through sexuality requires time and dedication; 4) And patience, as the sexual Patience is the virtue that enables us to expect the best possible time for intimacy, but for various reasons then have to be postponed.

Knowledge of human fertility, along with the complicated mechanisms of sexual response, especially in women, makes it possible that there is sexual harmony between a man and a woman who love each other.
MORPHOLOGICAL CHARACTERIZATION OF DIFFERENT CERVICAL HUMAN MUCUS TYPES. A STUDY BY LIGHT AND SCANNING ELECTRON MICROSCOPY

Micaela Menárguez

This study has been done with light microscopy and scanning electron microscopy of human cervical mucus.

Objective. The morphological characterization of the different mucus types.

Methodology. The samples taken from the bulk of the cervix and the different secretory zones from the cervical mucosa. The samples were spread out on slides and dried on air. The phenomenon of “ferning” occurs in these samples. They were also studied with SEM, from the bulk and from the different secretory zone, which were spread out on coverslips and fixed with glutaraldehyde (2,5%).

Results. Allowed us to see the presence of different mucus types, called L, S, P and G in the samples from the bulk and from the different mucus secretory zones of the crypts, with both dried and fixed technics.

Conclusions. The human cervical mucus, from the bulk, seems to be a heterogeneous entity. It contained different types of secretions, whose percentages varied along the cycle. They showed different types of crystallization, different ultrastructure, related probably to the arrangement of the glycoprotein network, and they were produced in different secretory zones, from the crypts, in the cervix.

IMAGING OF THE FETAL FACE: STATE OF THE ART

Eberhard Merz

Introduction: Conventional ultrasound technology can provide only two-dimensional sectional views of the fetal face. In fetuses with an unfavourable position individual sectional planes of the face cannot be demonstrated with 2D ultrasound and fetuses with complex face anomalies require an evaluation in multiple planes.

Despite the fact that an experienced examiner can readily piece together two-dimensional planes to create a three-dimensional mental image of the fetal face, the parents cannot be expected to form an accurate three-dimensional picture in their minds.

Material and Methods: High quality 3D/4D imaging of the fetal face requires an ultrasound equipment with a transvaginal and transabdominal 3D/4D transducer. Once the fetal profile is demonstrated with 2D ultrasound, volume acquisition is activated and a volume of the fetal face is stored in the memory of the ultrasound system.

Results: 3D ultrasonography is a reliable tool in the demonstration of normal and abnormal fetal anatomy. The simultaneous display of all three orthogonal planes allows a precise control of every fetal plane such as the facial profile, even in severe oligohydramnios. When one plane is rotated or shifted, corresponding changes are displayed at once in the two other planes. This provides an ideal basis for a further detailed survey. The translucency mode provides a complete survey view of the fetal skull, similar to the appearance of an X-ray film. The three-dimensional surface view of the fetal head allows a precise depiction of surface anomalies such as facial dysplasia, cleft lip/palate and cyclops. HDlive technology offers even more photo-realistic images of the region of interest due to a moveable virtual light source with different shadowing effects and an advanced skin rendering technique. The alternate use of the different rendering modes enables the examiner to visualize the region of interest in that mode that is best for the demonstration or exclusion of a fetal defect. Rendering of an animation sequence gives an excellent view to the fetal face from different angles. With 4D ultrasound the movements of the fetus can be visualized three-dimensionally in real time.

Summary: Compared with conventional 2D ultrasound, 3D/4D ultrasonography provides the operator with much more visual possibilities to identify facial abnormalities of the fetus.
ANATOMY AND ANOMALIES OF THE FETAL CORPUS CALLOSUM

Eberhard Merz

Introduction: 3D ultrasonography enables the exact demonstration of the corpus callosum as a hypoechoic structure starting from 17/18 weeks of gestation. Growth charts and tables are useful in the detection of corpus callosum anomalies.

Material and methods: All prenatal scans were performed using E8 General Electric equipment (Zipf, Austria), with a 5-8 MHz 3-D transabdominal and 5-9 MHz 3-D transvaginal transducer. Growth charts and tables were established for the following parameters: curved corpus callosum length (CCL-C), inner-inner corpus callosum length (CCL-II), outer-outer corpus callosum length (CCL-OO), rostrum height (rostrum-H), genu height (genu-H), body height (body-H) and splenium height (spleminum-H).

In all cases of corpus callosum underdevelopment length and height of the present segments of the corpus callosum were measured and compared with the normal growth charts. In corpus callosum agenesis direct and indirect signs of the malformation were observed. All corpus callosum anomalies were controlled for associated anomalies.

Results: All corpus callosum parameters show a non-linear growth. During the second trimester the corpus callosum shows an increase in height (= thickness) and a progressive flexion, while in the third trimester a flattening can be observed.

35 fetuses with pathological corpus callosum could be diagnosed with 3D ultrasound between the years 2009 and 2013. The gestational age at the time of diagnoses ranged from 18 to 38 weeks of gestation. 14 cases showed agenesis, 12 cases partial agenesis, 5 cases hypoplasia, one case hyperplasia, 2 cases a combination of partial hypo- and hyperplasia, and one case a lipoma of the corpus callosum. In corpus callosum underdevelopments, the most affected parts were the body and the splenium. Associated anomalies were present in 29 of 35 cases of corpus callosum pathologies.

Conclusion: With 3-D ultrasound and the established reference ranges of the seven fetal corpus callosum parameters structural abnormalities of the corpus callosum can be detected precisely. Nevertheless counseling of the parents remains a major problem in all cases of corpus callosum anomalies, because a precise prognosis is not predictable for the different corpus callosum defects.
During last three decades the rate of multiple pregnancies increased dramatically as more than two times. On the millennium border the extensive increase of the rate of high order multiples identified the introduction of restrictive measures to limit the number of transferred embryos in ART cycles. In consequence of these measures the need for multifetal pregnancy reductions decreased significantly. However, the average frequency of multiple pregnancies in the develop countries population still exceeds 2% and in specialized perinatal centers as our, the frequency of deliveries in multiple pregnancy reaches 5%. Implementation of the concept of “turning the pyramid of perinatal care” in multiple pregnancies is crucially important.

Modern prenatal diagnosis in the first trimester of pregnancy is a complex of clinical, ultrasound, biochemical and high-tech genetic methods those enables to detect fetal congenital and hereditary abnormalities and pregnancy complications with very high probability. However, in multiple pregnancies and in high order multiples in particularly, the limitations of each method of prenatal diagnosis are significant.

Prenatal care in high order multiple pregnancy with MFPR is a mirror allows to assess the clinical effectiveness and economic feasibility of applying each of the possible methods of diagnosis, depending on the technical equipment and availability and accessibility, routing of patients, organizational structure and the financial capacity of the health system.

More than three hundred multiple pregnancies underwent MFPR. The basis of perinatal care is still the ultrasound diagnosis at appropriate level. Determination of type of chorionicity and amnionicity, identification and exclusion of markers of chromosomal pathology (NT, nasal bone, blood flow in the tricuspid valve and ductus venosus) and also the identification and exclusion of anatomical abnormalities as a result prevented chromosomal and significant structural abnormality among neonates been born. This result was achieved when invasive prenatal diagnosis (CVS) carried out only in cases when markers of fetal chromosomal pathology were identified.

During last years noninvasive testing broke into investigation on prenatal diagnosis. Several studies have shown that in singleton pregnancies NIPT by massively parallel sequencing could provide high level of sensitivity and specificity in detection of trisomies 13, 18 and 21. But in multiple pregnancy there are additional limitations as needs of not only chorionicity but zigoity assessment, estimation of appropriate lower limit of fetal DNA fractions for aneuploidy detection to minimize a risk of false negative results, and the influence of the method of conception on cfDNA testing should not be ignored.
CLINICAL AND ETHICAL ISSUES ABOUT MULTIFETAL PREGNANCIES

Giovanni Monni

Multiple pregnancies are associated to higher both maternal, fetal and neonatal risks such as miscarriage, preterm birth, stillbirth, neonatal mortality, low birth weight, antepartum haemorrhage, chorioamnionitis, etc. Pre-treatment counseling and accurate information about risks and complications is mandatory for couples undergoing Assisted Reproductive Techniques. The selective feticide (also known as embryo reduction, selective reduction, multifetal reduction) is normally performed to reduce the high order multiples (HOM) to twins. The procedure has generally positive outcome, although not exactly the same as when the twin pregnancy is spontaneous. Selective feticide before viability in HOM does not involve the killing of a fetal patient and is therefore consistent with professionally responsible obstetric and perinatal practice. The current tendency is towards performing the reduction later in the pregnancy (at 12-13 weeks rather than at 10-12 weeks): the risk of fetal loss does not substantially increase and there is the possibility to do the conventional first-trimester fetal scan screening by Nuchal Translucency, Nasal Bone, Ductus Venosus, Mitral Regurgitation and eventually suggest to the patient a prior chorionic villus sampling. However, not all medical centres are able to perform chorionic villous sampling, especially in pregnancies with ≥ 3 fetuses. Also, the risk of not being able to distinguish the aneuploid fetus can lead to additional complications. We can render the selection of the fetuses more targeted by searching for aneuploidy markers and conducting a preliminary study of the fetal anomalies. The overall loss rate of selective feticide procedures in multiples is about 5% but it does improve with the larger expertise of the operator and the increased resolution of the ultrasound equipment. There is a direct correlation between pregnancy loss and the starting number of fetuses, with a rate of 15.4% for sextuplets or above. We have performed ART in our centre at Microcitemico Hospital, Cagliari since 1994 and so far we have had a large number of triplets reduced to twins as well as several HOM (> 3 fetuses) (52 pregnancies, 259 fetuses) achieved mainly by intrauterine insemination (IUI). The patients with HOM pregnancies were mainly referred to us from other Italian centers in order to perform selective feticide.
NON-INVASIVE VENTILATION: TECHNIQUES AND PHYSIOLOGICAL EFFECTS

Corrado Moretti

Avoiding mechanical ventilation is thought to be a critical goal, and different modes of non-invasive respiratory support may reduce the intubation rate: nasal continuous positive airway pressure (NCPAP), nasal intermittent positive pressure ventilation (NIPPV) and its more advantageous form, synchronized nasal intermittent positive pressure ventilation (SNIPPV). SNIPPV was initially performed using a capsule placed on the baby’s abdomen. Actually the abdominal capsule, although highly sensitive, has several disadvantages. First, positioning the capsule requires considerable skill. For example, when the capsule is positioned too close to the rib margin of an infant with respiratory distress, subcostal retractions can cause asynchrony because the abdomen expands during expiration rather than inspiration. Secondly, movement is often misinterpreted as breathing and when preterm infants are breathing faster the capsule response is less consistent. Under these circumstances the neonate’s respiratory conditions can deteriorate because of asynchrony.

To overcome these disadvantages, our team developed a flow-sensor expressly for nasal ventilation. With this device we studied the physiological effects of SNIPPV in 11 VLBW infants after extubation, comparing them with NCPAP. During SNIPPV, TcPCO₂ and the infant’s mean respiratory rate were significantly lower than during NCPAP, while Vt and Ve were significantly greater. Also a significant reduction of Pe was recorded during SNIPPV as a result of the unloading provided by the ventilator. The mean trigger response time was 65 ± 12 ms and the ventilator triggered successfully on more than 90% of the infant’s breaths. In the following years several papers have confirmed that, compared to NCPAP, SNIPPV is able to reduce the patient’s work of breathing and chest wall distortion. More recently some of our results have also been confirmed by Chang et al. and Owen et al. The first studied the effects of nasal ventilation in clinically stable preterm infants and concluded that synchronization reduces the breathing effort of the patient and results in better infant-ventilator interaction than non-synchronized nasal ventilation. The second, studying the effects of NIPPV on spontaneous breathing in preterm infants, concluded that, only when pressure peaks occur during spontaneous inspiration, does tidal volume increase, suggesting that synchronization is beneficial. These favorable effects are probably due to the fact that the mean Paw is higher during SNIPPV than during NCPAP, and the pressure waves are effectively transmitted to the lungs because mechanical inflations are timed with spontaneous efforts, when the glottis is open.
STRATEGIES TO PREVENT INVASIVE MECHANICAL VENTILATION

Corrado Moretti

NCPAP was the earliest form of non-invasive respiratory support to be used in infants with respiratory failure. Its use as primary mode of respiratory support has become standard practice in order to avoid invasive mechanical ventilation (MV) and to facilitate weaning from the ventilator but, despite its considerable efficacy, this technique cannot always prevent intubation or extubation failure. The failure rate of NCPAP is inversely correlated to the gestational age of the newborn and the more immature infants are those at higher risk of developing complications associated with invasive MV. NCPAP combined with early surfactant replacement therapy, administered by intubation and rapid extubation (intubation-surfactant extubation, INSURE) or more recently by less invasive techniques (LISA), has been introduced as a primary mode of respiratory support in premature infants with RDS with varying degrees of success, depending on the patient’s gestational age and the severity of the radiological stage of RDS and FiO₂ at surfactant administration.

NIPPV or nasal intermittent mandatory ventilation (NIMV) are more effective forms of respiratory support that provide CPAP plus superimposed ventilator mandatory breaths and are identified as SNIPPV/SNIMV when the ventilator pressure waves are synchronized with the spontaneous efforts of the patient. These techniques are being used increasingly in preterm infants with respiratory failure in order to decrease further the percentage of patients who are treated with invasive MV or who fail extubation.

Our group recently conducted a study using flow-SNIPPV as the primary mode of ventilatory support in < 32 weeks’ gestation preterm infants with RDS. The aim of the trial was to evaluate whether SNIPPV, used immediately after INSURE technique, was effective in further reducing the incidence of MV compared to conventional INSURE/NCPAP treatment. We had statistically significant results: 11 out of 31 (35.5%) infants in the NCPAP group and 2 out of 33 (6.1%) infants in the SNIPPV group failed the INSURE approach and underwent MV. Fewer infants in the INSURE/SNIPPV group needed a second dose of surfactant, a high caffeine maintenance dose, or pharmacological treatment for PDA. Differences in O₂ dependency at 28 days and at 36 weeks of postmenstrual age were at the limits of statistical significance for SNIPPV treated infants. We concluded that SNIPPV use, combined with surfactant, seems to be a promising strategy for treatment of infants in the acute phase of RDS without using invasive mechanical ventilation.
FETAL MORBIDITY IN DIABESITY

Daniel Muresan

Diabetes and obesity represent today an almost epidemic condition in developed countries. Many pregnant women present one or two of these conditions, and due to their common pathologic pathways they are now known as Diabesity.

The evolution of pregnancies in these conditions is altered by complications developing from the embryonic period, during the second and third trimester, in the neonatal period and as some recent papers suggest also metabolic and developmental problems in childhood and adult life.

During the first trimester the main risk in diabetes is the occurrence of malformations, that have a 3-4 OR and is dependent of the metabolic balance before and during the embryonic period. The obesity prior to pregnancy has also an increased risk for malformations. In these conditions early ultrasound scan at 11-14 weeks is mandatory, especially when the HbA1C is augmented. In obesity transvaginal scan can be very helpful.

In obese patients there are metabolic modification which are similar with those of patients with gestational diabetes mellitus, and there is a strong correlation between obesity and diabetes in pregnancy. There is also a small systemic inflammatory reaction and an endothelial dysfunction.

During the second and the third trimester structural and functional problems in patients with diabetes and/or obesity are more frequent than in normal pregnancies. The morphologic ultrasound scan at 19-22 weeks must be perform with a special emphasis on the fetal heart.

The fetal growth is altered in diabetes by the occurrence of asymmetrical macrosomia that is dependent of the pre-pregnancy BMI, of the higher gestational weight gain and of the maternal glycemic control. These factors can act alone or in combinations. The main pathways are increased peripheral insulin resistance in the pregnant woman and the fetal hyperinsulinism. Serial ultrasound scan can identify these anomalies from 26-28 weeks onwards. The association of preeclampsia is frequent in these pregnancies and can determine a late placental insufficiency and fetal distress in a normal or even a macrosomic fetus. The utilization of Doppler examination is mandatory.

The cardiac structure and function of fetuses in diabetic pregnancies is modified. A systolic dysfunction may by present due to hypertrophic cardiomyopathy.

The perinatal morbidity is increased due to the complications of the delivery of a macrosomic fetus and to the complications of the neonatal period.

The long-term outcome of these fetuses is affected by the risk of developing obesity, cardiovascular disease and type II diabetes.
DEVELOPMENTAL ASPECTS OF DRASIC CHANGES OF LIPOPROTEIN METABOLISM IN NEONATAL INFANTS

Nobuhiko Nagano

Introduction
In neonatal infants, lipid is one of the most important nutritional components that are related to the development of central nervous system. Also, late preterm infants (LPIs; 34-37 gestational weeks at birth) have higher risk for several morbidities than do term infants (TIs). It has been suggested that a cholesterol and fatty acid supply may improve their outcomes. We investigated the lipoprotein subclass profile in LPIs to evaluate their early postnatal lipid metabolism as the first research. On the other hand, low birth weight was associated with the risk of cardiometabolic diseases in adult age. Insulin-like growth factor-1 (IGF-1) has a crucial role in fetal growth and also associates with cardiometabolic risks in adults. Therefore, we elucidated the association between IGF-1 level and serum lipids in cord blood of preterm infants as the second research.

Methods
Eighty-one infants (25LPIs, 56TIs) were included in the first research. Cholesterol (C) and triglyceride (TG) concentrations in 12 lipoprotein subclasses were measured at birth and at 1 month using HPLC. Forty-one preterm infants, including 10 small for gestational age infants (SGA; birth weight <10th percentile) were included in the second research. IGF-1 levels and serum lipids were measured at birth using HPLC.

Result
In LPIs, the cord blood exhibited higher cholesterol concentrations in medium and large subclasses of very low-density lipoprotein (VLDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) compared to the value in TIs. During the first month of life, LPIs had greater increases in cholesterol concentrations of medium and large subclasses of VLDL than TIs, whereas postnatal increases in cholesterol concentrations of medium and large subclasses of LDL and HDL were smaller. TG concentrations were not different in each VLDL subclass at birth and at 1 month. SGA infants had lower IGF-1, total cholesterol (TC), LDLC and HDLC levels, and higher VLDLTG levels than appropriate for gestational age infants. Multiple regression analyses demonstrated that IGF-1 was an independent predictor of TC, HDLC and TG levels after the gestational age and birth weight were taken into account.

Conclusion
In LPIs, cord blood lipoprotein subclass profiles and the early postnatal change exhibited different, especially in cholesterol concentrations. Also, in preterm SGA infants, cord blood lipids profile altered with the concomitant decrease in IGF-1 level.
EFFICACY OF ANTIMOAGULATION THERAPY IN EARLY ONSET PREECLAMPSIA

Masao Nakabayashi

Objection:
A. In this study, heparin or antithrombin (AT) was given to severe early onset preeclamptic women (onset before 32 weeks of gestation) with fetal growth restriction (FGR), and the efficacies in maternal and fetal findings were compared.
B. Bases on the clinical findings of efficacies of AT to severe preeclampsia (PE), in vivo experiments were performed using the cultured trophoblastic cells or decidua cells. The effects of AT or thrombin on the cell surface thrombomodulin (TM) antigen and the production of prostaglandin I2 (PGI2) were analyzed.

Materials and Methods:
In 29 cases of severe early onset PE women were divided in two groups. In 14 cases, 1500u/day of AT concentrate plus 5000 u/day of heparin was administered for 7 days (AT group) and in 15 cases, 5000 u/day of heparin was given for 7 days (heparin group). Maternal symptoms, coagulation markers, and fetal findings were inspected. Estimated fetal weight was calculated by ultrasonographic measurement.

Results:
1. Levels of plasma AT were significantly lower (P<0.05) and the thrombin-AT complex (TAT) were significantly higher (P<0.05) in the severe PE, that means severe PE patients were in hypercoagulable states. The amniotic PAI-1 levels were significantly higher (P<0.01) in the severe PE. These results demonstrate the imbalance of coagulation and fibrinolysis in severe PE.
2. After the anticoagulation therapy, the mean systolic blood pressure decreased significantly (P<0.01) and the estimated fetal weight gain was significantly higher (P<0.05) in the AT group. In the heparin group, no change was recognized.
3. In vivo experiments showed that AT increased the TM antigen on the cell surface, and also increased prostaglandin I2 (PGI2) production by cultured trophoblastic cells. On the other hand, thrombin decreased the TM antigen in cultured cells, and increased the production of PAI-1 by decidual cells.

Conclusions:
AT replacement therapy is useful for improving maternal hypertension and fetal findings in severe PE with FGR through the increased of TM and PGI2 production in both maternal and placental circulation. It was clarified that AT and thrombin had the effects to regulate the TM on the cell surface, which is known as the key factor to suppress the coagulation system.
DUTCH HOME DELIVERY EXPERIENCE ON CCHD SCREENING

Ilona Narayen

BACKGROUND: Pulse oximetry (PO) screening for critical congenital heart defects (CCHD) has proved to be accurate and cost-effective, and is increasingly implemented worldwide. It is unknown whether PO screening is feasible in settings with home births and very early discharge. We assessed this in the Netherlands, where there is a high home birth rate and early discharge after delivery in hospital, by using an adapted protocol.

METHODS: PO screening was performed in the Leiden region, both in hospitals and by community midwives at home or at the policlinic. Measurements were taken ≥ one hour after birth and on day two or three, fitting the visit scheme of community midwives. Primary outcome was the percentage of screened infants with obtained parental consent. The time point of screening, oxygen saturation (SpO₂), false positive (FP) screenings, CCHD and other detected pathology were registered.

FINDINGS: in a one-year period 3625 eligible infants were born. Parents of 419 infants were not approached for consent and 44 refused the screening. PO screening was performed in 3059/3090 (99%) infants with obtained parental consent. Median (IQR) time points of the first and second screening were 1·8 (1·3-2·8) hours and 37 (27-47) hours after birth. In 394 infants the first screening was performed within one hour after birth; the median pre- and post-ductal SpO₂ were 99% (98-100%) and 99% (97-100%). No CCHD was detected. The FP rate was 1.0% overall and 0.6% in the first hours after birth. After referral, significant pathology was found in 62% of the FP screenings.

INTERPRETATION: PO screening for CCHD is feasible after home births and very early discharge from hospital. Important neonatal pathology was detected at an early stage, potentially increasing the safety of home births and early discharge policy.
NON-INVASIVE PRENATAL SCREENING FOR ANEUPLOIDY

Mary Norton

Noninvasive prenatal screening using cell free DNA (cfDNA) takes advantage of small segments of DNA of placental origin that are present in the maternal circulation. Since the clinical introduction of this test, the field of prenatal diagnosis has changed drastically. Far fewer diagnostic procedures are being performed, as more patients are choosing to have screening given the high sensitivity and specificity. With widespread utilization of this technology, many interesting aspects of the biology of cell free DNA, of placental as well as maternal origin, have become apparent. The fetal fraction (FF), or relative proportion of cell free DNA that is of placental, as opposed to maternal origin, varies tremendously between pregnancies. Emerging data are investigating the significance of these variations, and how these might reflect placental development. The FF has been inconsistently found to be associated with perinatal outcomes such preeclampsia, preterm birth, and fetal growth restriction. Low FF can be seen with maternal obesity, and appears to be due to higher levels of cfDNA of maternal origin, rather than lower absolute quantities of placental DNA. FF is also associated with aneuploidy, with a slightly higher FF seen in trisomy 21 and lower FF seen with trisomies 13 and 18, and with triploidy. Why some pregnancies are associated with very high FF, and which maternal or fetal characteristics might be responsible for these large differences, warrants further investigation. Because sequencing of maternal cfDNA includes maternal as well as placental sequences, in some cases maternal variations and pathologies will be uncovered. Maternal mosaicism, particularly for sex chromosomal aneuploidy, as well as maternal malignancies, have been identified following cfDNA screening in pregnancy. The population significance of these diagnoses, as well as the most appropriate evaluation of women with a false positive result felt not to reflect a chromosomally abnormal fetus, remains an important area of investigation.
ENDOCERVICAL CELLS PRODUCERS OF ENZYMATIC GRANULLES

E. Odeblad

OBJECTIVE. To identify Z-enzyme releasing endocervical cells (Z-cells).

METHOD. 1. Aspire cervical secretion with a pipette. 2. Extend secretion on a microscope slide. 3. Let it air dry at room temperature for an hour, so water evaporates. 4. Study under optical microscope.

RESULTS.
Location: Upper part of the cervical neck (cervical isthmus).
Characteristics: They produce abundant enzyme granules and they do not have mucosa secretion. Their action begins five days before ovulation and stops two days after: maximum from day -2 to day 0 (ovulation). The highest levels are detected 3-4 hours postcoitus.
Functions: To create a mucolytic effect which favours sperm ascent. The enzyme in Zgranules combines with P2 secretion, which acts as transporter.
Hypothesis: They might inactivate spermatozoids non suitable for fertilization.

CLINICAL CASES: Case 1. Pre-ovulation (day –3). Z-cells with secretion type L and S2 are shown. Their round morphology can be seen among the scattered crystals of the sample.
Case 2. Pre-ovulation. Identifies Z-cells, showing their size in relation with an epithelial cell.

BIBLIOGRAPHY
HUMAN STEM CELL THERAPIES FOR BRONCHOPULMONARY DYSPLASIA

Won Soon Park

Bronchopulmonary dysplasia (BPD), a chronic lung disease affecting very preterm infants, still remains a major cause of mortality and long-term morbidities despite recent improvements in neonatal intensive care medicine. Although any effective treatment or preventive strategy for BPD has not been developed yet, recent stem cell research results seem to support the assumption that stem cell therapy could be a promising and novel therapeutic modality for attenuating BPD severity. In this lecture, recent advances in the stem cell research for treating BPD will be summarized. In particular, the preclinical translational research data about the therapeutic efficacy, optimal cell type, timing, route, dosage, therapeutic potency marker, and safety of stem cell therapy in protecting against BPD that are essential for clinical translation will be focused. In addition, the successful phase I clinical trial results of human umbilical cord blood derived mesenchymal stem cell therapies for BPD, and 2 year follow up data of these infants will also be discussed.
THERAPEUTIC HYPOTHERMIA IN NEWBORNS WITH LAMINAR FLOW UNIT

José María Pérez Rodríguez

We have managed twenty eight newborns with diagnosis of the Hypoxic Ischemic Encephalopathy, our inclusion criteria were:1- six hour or less of the life; 2- thirty five weeks or more of the gestational age; 3- apgar 1'<3; 4- pH < 7.1; 5- informed consent signed. We managed 11(39.2%) from moderate Sarnat score and 17(60.7%) serious Sarnat score. These newborns 20 (71.4%) were male and 8 (28.5%) female and they were treated with total body hypothermia with Neonatal laminar flow unit1 Our outcomes were mortality 8 newborns (29.6%), 14 newborns with seizures (51.85%), early sepsis 15 newborns (51.8%), late sepsis 3 newborns (10.7%), pulmonary hypertension 4 newborns (14.2%), NEC 3 newborns (10.7%), hyperglycemia 2 newborns (7.1%), cerebral palsy 3 newborns (11.11%). Our outcomes were similiar trials from Jacobs2 at alls and Tagin at alls3; our incidence of the cerebral palsy was lower than both trials2,3.

References
NUTRITION STRATEGY IN PRETERM INFANTS: HUMAN MILK FORTIFICATION

Jean-Charles Picaud

Human milk (HM) has a positive impact on health of preterm infants by reducing the prevalence of necrotizing enterocolitis, late-onset sepsis and by supporting neurocognitive development. However, unfortified HM does not provide preterm infants with sufficient amounts of nutrients (protein, minerals, sodium, zinc,...) to obtain a postnatal growth at least equivalent to fetal growth. Even using HM from mothers who delivered preterm, as the protein content of preterm HM is only slightly higher than term HM, and only during the first month of lactation.

Standardized fortification relies on the addition of a multicomponent fortifiers starting after few days of life when 50 to 100 ml/kg.d of enteral feeding is well tolerated. Preterm infants fed fortified HM grow better than when HM is not fortified, but slower than infants fed a preterm formula.

In some infants fed HM, standardized fortification may be inappropriate because nutrients’ intake may be insufficient or nutrients’ needs could be particularly high. It is now well-known that protein and lipid contents of HM is variable and may be low. On the other hand, nutrient’s need may be high in infants with severe intrauterine growth retardation, or with diseases like bronchopulmonary dysplasia. Henriksen et al reported that a significant proportion of preterm infants are growth retardated at discharge (Henriksen 2009).

The insufficient nutrient content may be compensated by an appropriate fortification of HM. Optimization of HM fortification relies on the use of high quality standard fortification completed by an individualized fortification. Evaluation of optimal standard fortification relies on the evaluation the safety (osmolality, digestive and metabolic tolerance) and efficacy (protein and energy intakes, growth. Individualized fortification is either “targeted” or “adjustable”. The first one requires the analysis of HM and then a fortification adapted to reach the targeted nutrients’ intake. The definition of the target nutrient’s content relies on an assumption about nutrient’s requirement. Adaptation of fortification is performed by using protein (Polberger 1989) and/or energy: lipids (De Halleux 2007) and/or carbohydrates (Rochow 2013). The second one relies on periodic determinations of serum urea assessment as a marker of the individual metabolic response to standardized fortification. Additional protein fortification is proposed (Arsanoglu 2006). The only randomized controlled trial about individualized fortification has been performed by Arslanoglu et al in very low birth weight infants (Arslanoglu 2006). These authors and reported a significant positive effect on weight gain and head circumference growth. In our unit, we observed that a third of extremely low birth weight infants needed additional protein fortification to reach a sufficient weight gain (20 g/kg.d). That additional protein fortification improved significantly short term weight, length and head circumference growth. By improving protein to energy ratio in infants fed adjustable fortification of HM, we observed that body composition at discharge can be improved, with increased fat free mass. Recent study suggested a relationship of fat-free mass to speed of brain processing in preterm infants Diminished linear growth and FFM gains could be markers of future cognitive deficit in VLBW preterm infants (Pfister 2014).

Therefore nutritional care of preterm infants, and especially in HM-fed infants, has beneficial short-term (postnatal growth) and long-term (cognitive development) effects.

References


DISORDERS OF BRAIN PROLIFERATION, MIGRATION, AND CORTICAL ORGANIZATION

Ritsuko Pooh

The prevalence of neurological deficit has not decreased despite major improvements in clinical care in antenatal/neonatal period as well as intrapartum period. In about 70 percent of cases, neurological deficit results from events occurring before birth that can disrupt normal development of the brain. The antepartum risk factors should include fetal brain maldevelopment and intrauterine brain injuries, which are unclassifiable into congenital brain anomalies and may exist unconspicuously during pregnancy and even after birth. Especially, neuronal migration disorder, proliferation disorder, cortical malorganization and acquired brain damage in utero should be responsible for postnatal neurological impairment. Imaging technologies including 3D ultrasound have been remarkably improved and contributed to prenatal evaluation of fetal central nervous system (CNS) development and assessment of CNS abnormalities in utero. In this presentation, objective and precise imaging diagnoses of fetal CNS including brain developmental disorders and acquired brain damages. Migration takes place in the first and early-second trimesters and phenotype of migration in the cortex appears after 28 weeks of gestation.

It has been believed that migration disorder such as lissencephaly or pachygyria cannot be detected before 28 weeks. However, detailed observation of the fetal brain structure by transvaginal sonography via anterior fontanelle as an ultrasound window has clarified detailed brain development and revealed neuronal developmental disorder such as migration disorder from early-second trimester by demonstrating Sylvian fissure development and cortical development.

Furthermore, 3D bidirectional power Doppler angiography has depicted fine cerebral vessels of medullary veins which may relate with brain development and/or timing of insult as well as with postnatal neurological prognosis. From 16 weeks, medullary veins grow rapidly from pial veins towards the lateral ventricular wall. Those vascular development in the cerebral hemispheres may be strongly related to brain perfusion accompanying with brain development of migration or proliferation. Therefore, observation of fetal brain vascular development during pregnancy will be important for predicting postnatal neurological development.

It is promising to clarify the developmental mechanism of CNS damages with advanced ultrasound diagnostic techniques in the near future. Postnatal unexplained neurological deficits may strongly relate with intrauterine brain development therefore fetal neurology has great responsibility and an important role in perinatal medicine.
ANATOMY OF THE CENTRAL NERVOUS SYSTEM WITH 2D, 3D, AND SILHOUETTE ULTRASOUND

Ritsuko Pooh

Transvaginal sonography of the fetal brain opened a new field in medicine, “neurosonography”. Furthermore, three-dimensional (3D) ultrasound is one of the most attractive modality in a field of fetal ultrasound imaging. Combination of both transvaginal sonography and 3D ultrasound may be a great diagnostic tool for evaluation of three-dimensional structure of fetal CNS. Recent advanced 3D ultrasound equipments have several useful functions.

3D ultrasound demonstrates the surface anatomy of the brain and brain-related organs. Bony structural imaging of the calvaria and vertebrae are useful in cases of craniosynostosis and spina bifida. In multiplanar imaging of the brain structure, it is possible to demonstrate not only the sagittal and coronal sections but also the axial section of the brain, which cannot be demonstrated by transfontanelle approach with a conventional 2D transvaginal sonography. Parallel slicing provides a tomographic visualization of internal morphology similar to MR imaging producing tomographic ultrasound images and demonstrate a series of parallel cutting slices on a single screen as well as MRI does. Thick slice imaging of the intracranial structure and simultaneous volume contrast imaging (VCI) of the same plane or vertical plane of conventional 2D image are often convenient to observe the gyral formation and inside lateral ventricles. The premature brain image obtained by use of VCI clearly demonstrates anatomical CNS structure. Volume extracted image is demonstrated and volume calculation data is shown. Volume analysis by 3D ultrasound provides exceedingly informative imaging data, an intelligible evaluation of the brain structure in total, and longitudinal and objective assessment of enlarged ventricles and intracranial occupying lesions. Recent 3D angiostructural image by high-frequent transvaginal neuroscan has become furthermore sophisticated. Most recent up-to-date application of 3D ultrasound is HDlive Silhouette/flow imaging. By HDlive silhouette mode, an inner cystic structure with fluid collection can be depicted through the outer surface structure of the head and it can be appropriately named as ‘see-through fashion’. The advantages of this ‘see-through fashion’ imaging are comprehensive orientation and persuasive localization of inner morphological structure as well as of fetal angio-structure inside CNS.

Fetal neuroimaging with advanced 3D technology is easy, non-invasive, and reproducible methods producing not only comprehensible but also objective imaging data.
RAPID DIAGNOSIS OF NEONATAL SEPSIS USING MOLECULAR TECHNIQUES

Octavio Ramilo

Neonatal sepsis represents a major cause of mortality and morbidity in young infants worldwide. In recent years the implementation of new treatment strategies for “maternal fever” and chorioamnionitis has reduced the incidence of early onset neonatal sepsis, but has not eliminated this condition, or reduced the incidence of late onset sepsis. The gold standard to establish the diagnosis of sepsis requires the isolation of the causative agent—traditionally bacterial pathogens—by blood culture. Standard bacterial blood cultures, however, have important limitations including the 24-48 hours time to positivity; the percentage of false positive results; as well as false negative results, explained in part by the small blood volume available for testing and the administration of maternal antibiotics. Thus, there is a clear need for novel, more sensitive and precise assays, with shorter turn-around time.

Implementation of molecular PCR-based assays has been very successful and has revealed an important role for viral pathogens as etiologic agents of “neonatal sepsis” and “neonatal fever”. Enteroviruses and herpes simplex viruses are well recognized as significant pathogens early in life. More recently, parechoviruses, post-natally recognized cytomegalovirus, and respiratory viruses have been clearly associated with neonatal infections and sepsis in both infants hospitalized in the neonatal unit and in those presenting to the Emergency Department (ED) from home. Despite these advances, identification of bacterial pathogens (and Candida) remains suboptimal, as PCR assays are not sufficiently sensitive to detect the low amounts of bacterial pathogens present in the small blood volumes routinely tested. An exception is the cerebrospinal fluid (CSF) samples, which in cases of meningitis contain sufficient bacterial loads that can be successfully detected by PCR assays. Because of the limitations of the current pathogen-based assays, alternative strategies have focused on measuring the host response by quantitation of inflammatory markers such as C-reactive protein (CRP), procalcitonin, and cytokines such as IL-6, IL-1 and TNF. These inflammatory makers have advantages, as they are easy to perform, their relatively low cost, and have rapid turn-around time, but have limitations in their analytical performance. One alternative approach being investigated is to comprehensively examine the host immune response. The premise is that each pathogen induces a unique host transcriptional response that can be measured using microarray-based assays. Although this approach is still in an early phase of investigation, the initial results using small blood samples from young infants evaluated for “possible sepsis” in the ED are quite promising.
Non-invasive ventilation is used in preterm infants as a primary support to avoid invasive Mechanical Ventilation (iMV) and also, if intubation is required, to remove endotracheal tube as soon as possible in order to decrease ventilator induced lung injury. Different devices and different strategies had been studied in Clinical trials.

- nCPAP from delivery combined with early surfactant administration avoiding iMV is a standard of care in preterm infants. (Sweet, Carnielli et al. 2013, Committee on, Newborn et al. 2014) Although successful in a large proportion of infants, nCPAP is not always effective in avoiding intubation (Dargaville, Aiyappan et al. 2013).
- Nasal Intermittent Positive Pressure ventilation applied as a primary support and for extubation decrease intubation rates compared to nCPAP (Li, Long et al. 2014) (Lemyre, Davis et al. 2014).
- Synchronized-NIPPV (SNIPPV) seems to increase effectiveness of NIPPV by delivering the Positive pressure during spontaneous inspiration, ensuring glottis patency and pressure transmission (Chang, Claure et al. 2011, Owen, Morley et al. 2011, Gizzi, Montecchia et al. 2015).
- A Bi-level device was the non-invasive device used mainly in a large multicentre randomized trial finding no differences in intubation and BPD rates compared to nCPAP. (Kirpalani, Millar et al. 2013).
- High-flow nasal cannula for RDS and for extubation in preterm infants needs to be evaluated in randomized clinical trials. (Wilkinson, Andersen et al. 2011).

Our Institution applies flow-Synchronized NIPPV in preterm infants as a second line treatment, it means when nCPAP has already failed or for extubation in ventilator dependent infants. Success rates (avoiding iMV in the next 3 days) are 60,7% in nCPAP failure patients and 88,2% when used for extubation.

**Long-term respiratory outcomes.**

- Despite the reduction found in iMV use no clear difference has been found in BPD rates. Studies in which NIPPV is applied in high risk patients (lower GA who requires surfactant replacement) shows lower BDP incidence with NIPPV use compared to nCPAP (Bhandari, Finer et al. 2009, Ramanathan, Sekar et al. 2012).

**Conclusion.**

Non-invasive respiratory support should be the standard treatment for respiratory support in preterm infants. nCPAP is effective in a high proportion of infants, so SNIPPV could be reserved for more immature infants with more severe RDS, especially for those who require surfactant replacement and also for elective extubation in high-risk patients. Technological improvements in these devices, especially in terms of Synchronization will probably improve beneficial results. Larger clinical trial of SNIPPV use in this high-risk population is required.
**IMMEDIATE POSTNATAL SUPPORT IN EXTREMELY PRETERM NEONATES AT EDGE OF VIABILITY**

Enrique Salguero García

Birth of a healthy term newborn, is a physiological process that represents the start of life as a physically separate being. It signifies a transitional phase that every neonate undergoes, thus leaving the highly protected intrauterine environment to independent existence. Majority of the neonates adapt to this process smoothly without needing our intervention.

This natural process when it comes to a premature birth, is conditioned by the presence of pathological conditions which determine the end of pregnancy, leading the birth of a newborn who is not only under such circumstances but he also has to face the anatomical and functional immaturity of his biological systems which leads to a pathological condition whose severity increases while decreasing gestational age.

Furthermore, this situation will necessarily require our immediate intervention after the birth in order to initiate measures of stabilization and live support which includes keeping body temperature, gentle ventilation and judicious use of oxygen, etc.

We use the term "limit of viability" to describe the time of birth of that neonates that born alive before the 25 complete weeks of gestation.

The limit of viability expresses the probability of survival of a extremely preterm newborn, depending of his gestational age and other perinatal and socioeconomic factors, such as:

- Birth weight.
- Gender of neonate.
- Use of prenatal corticosteroids.
- Simple or multiple gestation.
- Country and place of birth.
- Perinatal pathological circumstances like chorioamnionitis, gestosis,etc.
- Intrauterine growth retardation.

In other words, the limit of viability is the line below which the infant is too immature to have any reasonable chance for survival without severe deficits and will die despite any resuscitation attempt.

It’s worth emphasizing, the value of our intervention at first minutes of life. There are several procedures such as the application of early intermittent or continuous positive airway pressure, the oxygen administration with FiO₂ control, the maintenance of body temperature, the oxygen saturation measured by preductal pulse oximetry, and other controversial procedures such as delayed umbilical cord clamping and/or milking and the sustained lung inflation which are discussed later that have a significant impact on outcomes of these extremely vulnerable infants.

We must not forget that the final prognosis of these newborns, begins to decide at the prenatal period, being that we can act before the birth with measures like tocolytics, antibiotics, magnesium sulphate, prenatal corticosteroids and finally with a adequate coordination of the obstetric and neonatal teams and whenever the situation allows, with the consensus of parents in order to the decision making, implementing active support or adequacy of therapeutic effort and comfort care as occur in the gestations and births at the edge of viability.
ADVANCES IN FETAL NEUROPHYSIOLOGY

Aida Salihagic Kadic

The development of diagnostic strategies to prevent and reduce the burden of perinatal brain damage has become one of the most important tasks of modern perinatal medicine. The development of any such strategy requires the understanding of normal neurodevelopmental processes and their influence on the fetal functional and behavioral patterns, detectable by modern diagnostic methods. Major developmental events, such as the establishment of neural connections in different regions of the brain, are accompanied by the occurrence of new patterns of fetal activities or by the transformation of existing patterns. Progression in behavioral complexity begins with spontaneous fetal movements and culminates with presumed preferences for the sound of mother’s voice, reflecting maturational events that take place in the brainstem, followed by forebrain structures. Furthermore, the fetus needs stimulating matrix of movements, sounds, vibrations and other stimuli for normal neurodevelopment and the development of other organs and organ systems. For instance, by performing of various movements, the fetus stimulates the development of the central nervous system, muscles, lungs, retina and gastrointestinal tract. The fetus also needs stress-free environment for the normal development of brain and other organs, as well as for normal somatic growth. Studies carried out using four-dimensional (4D) sonography have shown the fascinating diversity of fetal functions and activities as well as that fetal movement and behavioral patterns are valuable indicators of the functional and structural brain development. A new prenatal neurologic scoring test, based on evaluation of fetal spontaneous motor activity by 4D ultrasound, has been produced. This test, named KANET (the Kurjak Antenatal Neurodevelopmental Test) has potential in recognizing fetal pathologic and borderline behavior in high-risk pregnancies and in prediction normal and abnormal neurologic development. We would be a step closer to prevention of perinatal brain damage by predicting neurological development of the fetus.
THE CURRENT STATUS OF DIAGNOSIS OF PLACENTA ACCRETA

Azen Salim

Introduction.
Placenta accreta or morbidly adherent placenta is a term to describe placental villi adheres to the myometrium. Using ultrasound, the all changes of the invasiveness of the placenta into myometrium could be defined such as loss of retroplacental clear zone, presence of lacunae, changes of uterine serosa –bladder interface. As better technology of ultrasound is available, we try to focus the interface of suspected placenta accreta site using 3D High Definition Power Doppler.

Objectives.
To diagnose placenta accreta using 3D high definition power Doppler.

Methods.
From November 2013 until May 2015, 12 patients suspected having placenta accreta were recruited and informed consent were given. Using Voluson of E8 and E10 (GE Healthcare Ultrasound, Milwaukee, WI,USA) ultrasound machines. Transabdominal probes RAB 4-8D Curvilinear and eM6C were used. Ultrasound appearance of placenta accreta by 2D were collected and at the site suspected of invasiveness of the placenta into myometrium were studied using 3D high definition power Doppler.
The definite diagnosis was based on the outcome after delivery by caesaren section.

Results.
Compare the two kind of machines, E10 with eM6C showed very clear vessels of the placenta inside of the myometrium(100%), E8 with RAB 4-8D probe got 80% of the cases.

Conclusions.
New electric 3D transabdominal probe performance in power Doppler study prove better result than the mechanical 3D transabdominal one.
ERLY STAGES OF THE EVOLUTION OF PERINATAL MEDICINE

Erich Saling

Since its beginning, obstetrical medicine had been predominantly mother-oriented for a very long time, and nearly nothing was known about the condition and health state of the fetus. The most impressive evolutionary event in our field was the great change to the combined concept which began in the 1960s, when for the first time also the unborn became accessible to applied routine medicine. This unique development was started by obstetricians, and in the following years we came close together with open-minded pediatricians and colleagues from other interested disciplines and created powerful interdisciplinary cooperation. In 1967, we coined the term ”Perinatal Medicine”. In view of all this new progress, in 1968 we recommended a reform of clinical structures. The first Latin American Center of Perinatology was founded in 1970 in Montevideo. In the USA, there are “Maternal Fetal Units” since 1972.

Up to the end of the 1960s, in applied routine medicine four main sub-fields had developed:

• Assessment of fetal heart activity, mostly the frequency. Important pioneers in this field were Caldeyro-Barcia, Hon, and Hammacher.
• The first direct approach to the fetus in form of sampling and analyzing fetal blood from the presenting part (at first in 1960 by us).
• Examination of amniotic fluid mainly by amniocentesis and later by amnioscopy (the latter in 1962 by us).
• Application of ultrasonography. Father of its widespread use in obstetrics is Ian Donald, later pioneers were Brown, Thompson, Campbell and Hansmann. Doppler was first used in obstetrics in 1964 by Callagan.

The main points of the evolution of clinical structures and “official” aspects of Perinatal Medicine were:

• In 1967 the foundation of the first national Society of Perinatal Medicine, the German, as well as the first national congress in Berlin.
• In 1968 the first international Congress of Perinatal Medicine, the European, with the foundation of the European Association of Perinatal Medicine”, both in Berlin.
• After 1968 a great number of national and international societies have been founded, one of particular importance was “The Fetus as a Patient” in 1984.
• In 1991 the first Worldwide Congress of Perinatal Medicine took place in Tokyo, followed by the Foundation of The World Association of Perinatal Medicine.

Keywords: History of Perinatal Medicine, Fetus as a patient, Intrauterine medicine, Official foundation of Perinatal Medicine.
FAMILY- CENTERED CARE, THE PARENTS´ VIEW

María Jesús Sánchez Moreno

Family-centered care is an approach to health care and decision-making among family members and health care professionals that acknowledges the essential role of the family as a fundamental element of care in the infant’s life. It is based on participation, collaboration and information sharing of all the health care givers, family members as well as professionals, that leads to improved mutual satisfaction. It is essential that a clear communication and trusting relationship exists between the family and the health care team. Family-centered care has demonstrated beneficial effects for the infant, family and health professionals. It has been shown to reduce the length of hospital stay, short-term morbidity and improve the long-term development of the infant. It increases the professional and family satisfaction. Better information and collaborative processes are evidence of improved clinical decision-making. In addition, it has a positive influence on well-being in families, enhancing the attachment between the infant and the family. The outcomes are improved when family members are integrated as care givers and decision makers. In conclusion, family centered-care should be taken into account for the standard practices and guidelines in hospitals.
SKIN CARE ON NEWBORN IN CRITICAL SITUATION: ECMO AND HYPOTHERMIA

Gloria Sanz Prades

The topic of this lecture is something that is ours, a very studied issue and that brings us back to the basics of our profession and our art of caring: The skin care.
This time we will focus on skin care in the newborn in very specific situations and at the same time delicately.
They are working conditions that combine basic care and Hi-technology:
The skin care in patients ECMO therapy and hypothermia therapy.
WHERE ARE THE LIMITS OF VIABILITY?

Ola Didrik Saugstad

The so-called limit of viability of premature infants have been dramatically lowered during the last decades. In spite of that some have advocated absolute lower limits for initiating treatment. For instance in the Netherlands for many years preterm infants < 25 weeks gestation were not treated. Such absolute limits are, however probably in conflict with the UN Convention on the Rights of the Child from 1989 signed by almost all countries of the world. Each child has the right to be assessed individually regarding the level of treatment offered.

One reason that absolute limits are not acceptable is that gestational age is only a proxy for prognosis. Gender, weight, race, antenatal care, and antenatal steroids are only some of the prognostic factors. In addition, determination of gestational age is not absolute. Further, in the delivery room there are no indicators that reliably indicate prognosis. For these reasons and because there has been an immense progress regarding survival of the most immature newborn babies many centers treat actively preterm infants born after 22 and 23 weeks. Several studies indicate that this gestational age at the time being represents the physiological limit of viability.

Recent studies also indicate that a proactive attitude gives better results than a passive wait and see approach.

There is therefore a strong trend worldwide to offer intensive care to newborns with lower the gestational age than some years ago. This active attitude has contributed to the extremely good results achieved in newborn medicine, however it creates ethical challenges as well.
PREGNANCY WITH ADVANCED MATERNAL AND PATERNAL AGE

J. G. Schenker

Delayed child-bearing, which has increased greatly in recent decades. Many women are unaware of the success rates or limitations of assisted reproductive technology and of the increased medical risks of delayed child-bearing, including multiple births, preterm delivery, stillbirth, and Caesarean section. It is reasonable to expect in the next decade that the options to preserve oocytes and oocytes donation programs child-bearing at advanced maternal age will expand.

Increasing male age is related with decreasing percentages of progressively motile sperm and morphologically normal sperm, but not obviously with the rates of fertilization, good quality embryo, implantation, Father’s age increase miscarriage, malformations, risks of autism, schizophrenia, and bipolar troubles in children. Possible biological mechanisms include de novo aberration and mutations or epigenetic alterations associated with male aging.

Care providers need to be aware of these complications and adjust obstetrical management protocols to ensure optimal maternal and perinatal outcomes.
THE ODÓN DEVICE: A NEW APPROACH

Javier Alfonso Schvartzman

The following presentation describes our preliminary experience with the Odón device, a new low cost instrument for fetal delivery when complications during the second stage of labour arise. The Odón device, made of a polyethylene-like film, is designed for easy application, and its use requires minimal training.

In comparison with currently available instruments for operative vaginal delivery, the device has specific features that could reduce the risk of fetal-maternal injury.

To assess the safety and feasibility of the Odón device in assisting the vaginal delivery of singleton term pregnancies during the second stage of labour, the World Health Organization implemented a phase 1 study in Buenos Aires, Argentina.

The prospective study enrolled 48 pregnant women at CEMIC University Hospital. The device was applied with full dilation, ruptured membranes, anterior presentation, +2 station, and normal fetal electronic heart rate. Safety was assessed by examining short and long term maternal morbidity; feasibility, in terms of ease of application and successful delivery.

The Odón device is designed to minimize trauma to the mother and the fetus. It may also protect the fetus from intrapartum infection and has potential for application by mid-level providers in low resource settings. These features combined, make it a potentially revolutionary development in obstetrics.
FETAL INFLAMMATORY RESPONSE AND POSSIBLE CONSEQUENCES FOR THE VERY IMMATURE PRETERM INFANT

Christian P. Speer

Chorioamnionitis is a major risk factor for spontaneous preterm birth, especially at earlier gestational ages, and it contributes to prematurity-associated mortality and morbidity. A gestation-independent effect of chorioamnionitis on neonatal outcome is much more difficult to assess, and the influence of chorioamnionitis on neonatal outcome has become less evident with advances in neonatal care. Shortcomings of many clinical studies have been their retrospective character and a lack of power to identify gestational age or other factors which confound or modify detected associations between chorioamnionitis and outcome parameters. Besides, there is great variability in inclusion criteria between studies and in the way chorioamnionitis has been defined. Nevertheless, clinical chorioamnionitis was shown to be associated with an increased risk for neonatal sepsis and respiratory distress syndrome (RDS). However, a short-term beneficial effect on incidence and severity of RDS could be demonstrated for histological chorioamnionitis, and the molecular mechanisms of inflammation on the maturation of the surfactant system have been identified by now. This maturational effect on the lung seems to be accompanied by a susceptibility of the organ for further postnatal injury which predisposes for bronchopulmonary dysplasia. Increased concentrations of proinflammatory cytokines in human amniotic fluid and fetal cord blood, indicating a systemic inflammatory response during chorioamnionitis, are independent risk factors of BPD. A pronounced infiltration of inflammatory cells, an increased expression of cytokines and markers of endothelial activation as well as a large number of apoptotic airway cells have been observed in lung tissues of human fetuses with funisitis that have been exposed to chorioamnionitis. In addition, the presence of proteomic biomarkers characteristic of inflammation in the amniotic fluid was associated with an increased fetal inflammatory response at birth. Chorioamnionitis is also associated with cystic periventricular leukomalacia and cerebral palsy in preterm infants, but its association with noncystic white matter disease is not clear yet. In conclusion, chorioamnionitis has a profound impact on neonatal outcome.
NEUROBEHAVIOR OF THE FETUS AND NEONATE: TO WHAT EXTENT ARE THEY DIFFERENT OR SIMILAR?

Milan Stanojevic

Background: The development of the brain is unique and continuing process throughout the gestation and after birth, it is expected that there is also continuity of fetal and neonatal behavior which is functional indicator of developmental processes of the brain.

Aim: is to present assessment tools of neurobehavior in fetal and neonatal period and their significance for prediction of neurodevelopmental outcome.

Patients and Methods. While two dimensional ultrasound (2D US) is used only for the assessment of fetal startles and general movements, introduction of Kurjak Antenatal Neurodevelopmental Test (KANET) by four dimensional ultrasound (4D US) enabled assessment of not only movements but also some signs used in postnatal neurological assessment like cranial sutures, head circumference and finger movements of the hand for the detection of neurological thumb (adducted thumb in the clenched feast). Overall impression on general movement (GM) called by Prechtl “Gestalt perception” is also a part of KANET assessment. Postnatal application of Amiel Tison Neurological Assessment at Term (ATNAT) and GMs are approved methods for clinical postnatal assessment. Although there is a continuity of neurobehavioral continuity from prenatal to postnatal period, important obstacle to compare prenatal and postnatal assessment tools are different environments in fetal and postnatal life.

Conclusions. It is still questionable whether prenatal assessment of neurobehavior using KANET and postnatal assessment of neurobehavior by application of postnatal assessment tools could improve our ability for early detection of brain impairment.
SHOULD PATIENTS WITH PRETERM PROM BE INDUCED?

Ali Sungkar

Preterm labor is a global problem which is a complex disease with high rate morbidity and mortality, also has long term consequences for the baby and the family. The well-known morbidities related to preterm labor are respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, retinopathy of prematurity, anemia of prematurity.

In developing country, management of preterm labor is limited by poor health system, low education level of the mother, poor financial support, lack of facility and trained health personnel, and demography barrier. This limitation leads to high morbidity and mortality of preterm birth, especially in developing country. It is important to reduce rate of preterm birth by preventing the event. Interventions to reduce the morbidity and mortality related to preterm birth can be classified as primary (directed to all women before or during pregnancy to prevent and reduce risk), secondary (aimed at eliminating or reducing risk in women with known risk factors), or tertiary (initiated after the parturition process has begun, with a goal of preventing delivery or improving outcomes for preterm infants). Corticosteroid is given in treatment of preterm birth to increase fetal surfactant and accelerate lung maturation. Corticosteroid is proved to reduce neonatal death, respiratory distress syndrome (RDS), necrotizing enterocolitis, cerebrovascular haemorrhage and neonatal hospital length of stay. Refer patient using Kangaroo mother care to secondary level hospital, and deliver the baby without sign of infection is another strategy to prevent infection and early onset neonatal sepsis.
TYPES OF CERVICAL SECRETION UNDER OPTICAL AND ELECTRONIC MICROSCOPY: TRANSMISSION AND SCANNING

Helvia Temprano

Introduction.
Crystallization is one of the biophysical parameters of cervical secretion. Odeblad classifies this types of secretion: Type E (L and S), G; and P (fertility peak).

Aims
1. To identify the types using optical and electronic microscopes. 2. Analise the elements of crystals by X-Ray

Area of study
Women attending in the Obstetrics and Gynaecology Service of the University Hospital of A Coruña, Spain.

Material

Methodology
The cervix is visualized by a speculum The cervical secretion is suctioned with a syringe. The quantity, aspect and elasticity are reflected on a mucogram.

For OM study: the sample is settled on a microscope slide, spreading it out in a radial dispersion, according to Odeblad´s technique, and letting it air dry. On identify every type of secretion through its own crystallographic pattern. To establish the level of fertility, 10 fields at 10x. are evaluated, measuring the percentages of the different secretion present.

TEM study: the sample is spread on 0.3x 0.3mm circle shaped grids, covered by a photographic film and supported on Watman paper, letting it air dry at room temperature. We using a MET Zeiss - 109, at 50 Kv.

SEM study: the sample is spread out on 2.5 x 2.5 cm. and 0.1 cm. thick carbon disks, letting it air dry at room temperature, and metallized with carbon thread in a Sputter SCD004. To identify the elements an X-Ray energy dispersion (EDS) analysis was conducted with eXL-LINK equipment. Since X-Rays don’t analyse carbon, data belong only to the sample.

Results
OM. 2543 photos.
TEM. 374 photos It gives more precise information about the internal crystallization of ferns.
SEM. 132 photos. The elements were identified: sodium, magnesium, sulphur, chloride, calcium, potassium and phosphorus.

We find levels of K (18.88%) in periovulation. These levels decrease (10-11%) during the second phase of infertility and are irrelevant in lactation. The S type rises (>15%) in premenstrual samples.

Conclusions
1. OM idenifie the types of cervical secretion and measuring the fertility degree of the sample.
2. TEM gives precise information about crystalline typography.
3. SEM allows identifying the crystalline composition of the sustratum.
4. Natural analysis of the sample using the three techniques
MATERNAL LACTATION, MIXED AND ARTIFICIAL. RETURN TO FERTILITY

Helvia Temprano

The ultimate natural nutrition for a newly born is maternal breast milk. Lactation amenorrhea has been attributed to an imperfect balance between the hypothalamus-pituitary function and gonadotropin secretion. The lactation amenorrhea period depends on suckling.

1. Maternal Lactation.

During the first 3 months. Dr. Rötzer’s rules: 1. Intervals between feedings < 6 hours (day and night) 2. The baby is suckling 100 minutes a day. 3. At least 5 feeds a day 4. Exclusively breast milk. Pregnancy rate = 0.

From 3 to 6 months. If any of Dr. Rötzer’s conditions stops before the 12th week, the Lactation Amenorrhea Method (LAM) should be used. Pregnancy rates below 2%.

Billings Method. Women can learn to recognise their Basic Infertility Pattern (BIP) by registering, during 2 weeks, their daily self-observations on cervical mucus. The clue is the invariability of the pattern. Records should start 3 weeks after childbirth, registering also the number of feedings a day. If secretion starts to appear after a period without secretion, fertility might be returning.

Symptothermal Method. Daily record of mucus patterns plus basal body temperature. For women in exclusive breastfeeding situations, taking the temperature after 3 months. Due to the complexity of tracking body basal temperature during lactation, the guidance of an instructor/counselor is imperative.

2. Combined/Mixed Lactation. When breast milk is combined with juices or other complementary foods, the infertility period might come to an end.

3. Artificial lactation. In 5% of the cases, there is ovulation before the first post-partum menstruation. After the first menstruation, fertility is back.

A study conducted at the Obstetrics and Gynaecology Service of the University Hospital in La Coruña, studied 122 weeks of lactation (exclusive and mixed) and 33 cycles: 3 in combined lactation, 30 in post-lactation, belonging to 6 women. It included the study of 53 cervical secretion samples: 23 form women in breast milk lactation, 15 in combined and 15 in post lactation.

Results: 1. During breast lactation BIP was Dry/no secretion. 2. In mixed lactation we frequently found a mucus type IBP, eventually fertile, which indicates the return to fertility 3. With less than 6 feeds a day, menstruation appears. 4. Studying cervical secretion under optical microscope is useful to establish the fertility rate of the sample.
MALE VIEW NFP

Fernando Trullols

For man practicing NFP is one attractive opportunity to promote communication between spouses on the subject of sex. The training received in the course of learning, receiving partner, provides a broad overview of the biological, anatomical and physiological differences between men and women, promoting such knowledge with mutual respect and dialogue about their intimate relationships with the challenge of conquest and reconquest daily, so stimulating for many couples.

The study of the most common sexual dysfunctions, indicates that inhibition of sexual desire is the most common disease, monitoring of NFP gives us a preventive element of that dysfunction, by providing a rich and rewarding sex for both.

Man addition to these circumstances, experienced in the practice of NFP, is involved in the cooperative aspect that these methods require. Their collaboration in the recording and monitoring of standards to postpone or try to get a pregnancy opens the door to a greater understanding.

NFP is in conclusion, a good opportunity to promote “travel frequently boyfriends”, that is, to live a lifestyle that will help us not fall into the routine in our married life, one of the most powerful enemies of marital cohabitation.
INFERTILITY. PREGNANCY RATES IN PRIMARY HEALTH CARE

Isabel Valdés

Introduction
Currently, achieving gestation in pregnancy seeking couples is a priority of Health Care Systems. Teaching Health Education and training women and couples in the knowledgeable use of Biological Indicators of Fertility, is an efficient way of achieving pregnancies in primary attention clinical environments.

Objectives
To evaluate the efficiency of the use of fertility indicators to achieve pregnancies, in primary health care clinics.

Method
We have established the Success Rate in achieving pregnancy by directed coitus and as a percentage of live births per gestation after training and use of Biological Fertility Indicators, in different groups of women/couples (n=224).

Our study also aimed to identify the profile of women/couples attending this type of clinic (time seeking pregnancy, recruitment source, previous and/or associated pathology, previous sterility studies, etc.) and the success rate in each group.

Finally, we mapped the nursing and counselling protocol required for this type of clinic, the costs, and estimated user satisfaction with a randomly selected group of users.

Results
93 pregnancies were achieved in the 224 couples studied: 41.5% success rate (CI 95% 34.8-48.2). Information on live births was obtained from 221 couples, with 90 childbirths (40.7% IC 95% 34.0-47.4). The profile of the women/couples attending the primary health care clinic was summarized in three groups. 1st group: women/couples with pre-conception counselling. (n=64, 28.6% of the total, gestations achieved: 42.2%). 2nd group: women/couples identified as having difficulty to achieve wanted pregnancy, with infertility/sterility not studied previously in specialized units.. (n=143, 63.8%, gestations achieved: 44.1%). 3rd group: Women/Couples who had been subject of previous infertility/sterility studies in Specialized Attention, without reaching pregnancy, and in which Assisted Reproduction Techniques were not successful, or who did not want to use such techniques, but alternatively choose to be trained in Fertility Awareness through biological indicators. (n=17, 7.6%, gestations achieved: 17.6%).

Global cost of the procedure estimated in 30,93 €.- per user, with a high degree of user satisfaction.

This study is part of PhD Thesis. Rey Juan Carlos University. Madrid 2012.
FROM SEEN TO COINN. GLOBAL PROJECTION OF THE SPANISH NURSE FROM THE HOSPITAL SETTING

Raquel Valera Monsalve

A baby born under 37 – 40 weeks of gestation has a profile of care given, regardless of the country where he or she has born, regardless of the characteristics of the health system of his or her country or the educational system for nurses. These parents need emotional support, empowerment for the care of their child from the moment he or she is born and until they go home with their little baby.

So, why should there be differences in the quality of care for these families? Of course, always saving the cultural characteristics of each society. This is what they have in mind, those nurses who altruistically choose to join in regional, national or international partnerships.

What is the impact of an international association on the career development of a neonatal nurse? Why do we need a central force to organize the pool of knowledge of neonatal nurses? What kind of collaboration and coordination is necessary to ensure that we provide neonatal nurses working worldwide in the same line, with the same protocols regardless of the country they work in?

Our international level, COINN, is unifying neonatal nurses globally. Creating evidence for developing neonatal care and profession, from clinical and educational neonatal care to leadership and policy issues.

Which is the projection of a Spanish nurse worldwide? How are we connected?

We’ve gone from working strictly in our hospital (we all used to think we were doing better than anyone else) to have access to procedures anywhere in the world. Access to global knowledge. Joining COINN, from SEEN, we contribute to a worldwide network that follows different lines of work, like nursing education, neonatal care standards, policy changes, research to provide evidence for work and the worldwide recognition of neonatal nursing as a specialization, with specific training in universities all around the world.

We pretend to build new roads, new paths to care and education through evidence based projects and research.
Microarray Analysis and Genome-Wide Sequencing in Congenital Anomalies and Fetal Death

Ignatia B. Van Den Veyver

Prenatal genetic testing is offered to prospective parents to provide information about the health of their fetus and to identify or address an increased risk for chromosomal abnormalities or other genetic conditions, such as single-gene mutations underlying de novo or inherited Mendelian disorders. This information benefits identification of the cause of fetal structural abnormalities detected by prenatal imaging and better assessment of prognosis. With the development of genome-wide technologies, first chromosomal microarray analysis, and more recently diagnostic whole exome sequencing (WES) and whole genome sequencing, our ability to detect clinically significant genetic abnormalities has increased significantly. However, these new genetic tests can also uncover incidental secondary findings and variants of uncertain significance (VUS), which can complicate the genetic counseling. Chromosomal microarray is now becoming more integrated into prenatal care and has the ability to detect clinically significant abnormalities in 1-1.7% of pregnancies and in 6-7% of those affected with ultrasound-detected fetal structural abnormalities, but also VUS in about 1%. The use of diagnostic WES for prenatal diagnosis is currently still very limited but it is anticipated to increase in the near future. Limited early data suggest that pathogenic variants can be detected in up to 30% of prenatal WES. We have observed an increasing number of patients within the reproductive and prenatal genetics clinic, who are referred for genetic counseling related to a diagnostic WES result in a family member that has implications for a current or planned pregnancy, or who are referred for consideration of diagnostic fetal WES for an ongoing pregnancy complicated by fetal abnormalities. While guidelines are becoming available on how to integrate diagnostic WES in patient care and which findings to report, they often exclude the prenatal setting because of its unique set of challenging considerations. These challenges include more limited knowledge of the clinical impact of de novo genetic variants detected in an ongoing pregnancy, the limitations with defining clinically recognizable phenotypes at the time of testing, and the different decision-making processes that will ensue from testing. In this presentation, I will review the use of these genome-wide diagnostic technologies for the diagnostic work-up of congenital anomalies in ongoing pregnancies and after fetal demise, and discuss the associated challenges unique to prenatal care.
OPTIMAL TARGET OXYGEN SATURATION IN THE PERIVIABLE NEONATE

Maximo Vento

Fetal life evolves in a hypoxic environment relative to the extra uterine one. After preterm birth two main factors are going to condition postnatal adaptation, lung immaturity and an inefficient antioxidant defense system. Preterm infants frequently will need positive pressure ventilation in the delivery room to overcome respiratory insufficiency. Gas admixture used to ventilate preterm infants has usually an elevated FiO₂ (>21%) leading to the generation of a burst of oxygen free radicals which will not only cause direct damage to the lung but also trigger an inflammatory cascade in other organs (brain, liver, etc.).

To avoid deleterious consequences of oxygen supplementation during postnatal stabilization a nomogram was put forward merging databases from Australia and Spain. This nomogram was made up with data from babies not needing resuscitation at birth. However, the nomogram is highly representative of term and late preterm infants but not for VLBW or ELBW. A recent meta-analysis has shown that it is feasible and less injurious to start ventilation of very preterm infants with an iFiO₂ ≈ 21%-30%, and thereafter titrate oxygen according to SpO₂ readings. The target is to stabilize the baby in SpO₂’s around 90% at 10-15 min after birth.

Another issue is to establish limits of saturation until 36 weeks of postmenstrual age. A series of multicenter, randomized, controlled trials have pursued to establish the optimal SpO₂ range for preterm babies during oxygen supplementation (NEOPROM). Meta-analysis of these studies that recruited 5000 babies in two arms (85%-89% vs. 91% to 95%) have shown that babies kept in the lower saturation arm had less mortality and NEC, while babies in the upper saturation range had higher incidence of ROP. However, other studies show that mortality in the lower saturation group could be reduced by enhancing control over hypoxic episodes (COT study, Canada). Notwithstanding, recommendations tend to consider the 90% to 95% saturation range as the most convenient. When preterm infants reach 34-36 weeks of postmenstrual age, the upper limit of SpO₂ should be perhaps increased to avoid retinal vessel proliferation or to permit an adequate growth of babies with chronic lung disease needing oxygen supplementation. Studies in this field are highly needed.

References:
PREVENTION OF CONGENITAL ANOMALIES THROUGH PERICONCEPTIONAL MICRONUTRIENT SUPPLEMENTATION: THE BIRTH OF A NEW CONCEPT

Attila Vereczkey

Adequate nutritional habits during the periconceptional period are now proven to be of crucial importance for optimal pregnancy outcomes. Particularly maternal vitamin deficiencies during the periconceptional period often increase children’s risk of adverse birth outcomes, e.g. congenital abnormalities.

The Hungarian interventional trials have already proven the efficiency of folic acid in preventing neural tube defects, one of the most common and severe malformation of the nervous system. Folic acid has been demonstrated to prevent 90% of neural tube defects when administered in the form of a multivitamin preparation, and 70% prevention of the malformation when applied alone during the periconceptional period. The application of folic acid in the same manner was able to prevent a large proportion of congenital cardiovascular abnormalities as well.

Even though these findings represented the breakthrough in the prevention of congenital malformations, the method of periconceptional folic acid supplementation is still not consistently used in medical practice indicating the need for continuous HCP and patient education. The possible routes of periconceptional folate intake would be the following: (i) dietary intake; (ii) periconceptional medication such as folate containing supplements; (iii) food fortification; (iv) combination of oral contraceptives with folate. Recently the use of folic acid has been extended to late-pregnancy, particularly to the third trimester as well, in which case it has been shown to decrease the rate of preterm births.

In summary, folate applied before and during pregnancy may significantly contribute to the reduction of the occurrence of factors influencing offspring morbidity and mortality, thus playing important role in children’s long-term health as well.
TREATMENT AND PREVENTION OF PREECLAMPSIA WITH LOW MOLECULAR WEIGHT HEPARIN, STATINS, PLACENTAL GROWTH FACTOR, ANTITHROMBIN III FOR THE PREVENTION OF PREECLAMPSIA AND FETAL DEATH

Liliana Susana Voto

Preeclampsia is a complex multifactorial disease. Placental oxidative stress, a result of deficient spiral artery remodeling, plays an important role in the pathophysiology of preeclampsia. Antiangiogenic factors secreted from malperfused placenta are instrumental in mediating maternal endothelial dysfunction and consequent symptoms of preeclampsia. The mechanism is likely to involve increased ET-1 secretion and reduced NO bioavailability.

Therapeutic interventions so far remain only experimental and there is no established remedy for the treatment of preeclampsia. The therapeutic potential of antioxidants, ER chaperones, NO and H2S donors, and statins (3-hydroxy-3 methyl-glutaryl coenzyme-A reductase inhibitors) are under study. These compounds display pleitropic antioxidant, anti-inflammatory, and pro-angiogenic effects in animal and in vitro studies.

Due to pathophysiologic similarities between cardiovascular disease and preeclampsia there is an interest in studying this kind of medication during pregnancy to prevent and/or treat preeclampsia. Epidemiological data collected to date suggest that statins are not major teratogens. The world’s first randomised placebo-controlled trial, StAmP (Statins to Ameliorate Early Onset Pre-eclampsia) for the use of statins in early-onset preeclampsia is underway and its outcome will inform obstetricians how safe is the use of statins in pregnancy.

Other potential approaches for preventing preeclampsia through amelioration of oxidative stress include the use of supplements in the preconceptual period, selenium supplements, antiperoxynitrite strategies. Onda studies show that proton pump inhibitors, potently decrease sFlt-1/sEng release, switch on anti-oxidant defenses and quench endothelial dysfunction. Widely prescribed for gastric reflux during pregnancy, they represent an exciting novel candidate therapeutic to treat/prevent severe preeclampsia.

There are meta-analyses in the literature that strongly suggest that low-molecular-weight heparin reduces the risk of recurrent placenta-mediated complications. The project is called AFFIRM: An individual patient data meta-analysis of low-molecular-weight heparin For prevention of placenta-mediated pregnancy complications.

According to Rodger and co, “the goal of the proposed individual patient data meta-analysis is a thorough estimation of treatment effects in patients with prior individual placenta-mediated pregnancy complications and exploration of which complications are specifically prevented by low-molecular-weight heparin”.

Further studies are needed to enlighten these promising studies for future preventive treatments of preeclampsia.
MATERNAL STRESS: FETAL AND NEONATAL IMPACT PROF. LILIANA S. VOTO MD PHD

Liliana Susana Voto

Much discussion has been held about when life starts, which is valid not only from the ethical, philosophical or religious but also from the biological point of view. Procreation is such a natural fact that, for many years, researchers had not considered the fact that from the gametes that come from two different persons with different lives to the embryo from the very moment of implantation, all the events of that intrauterine life leave in that future child-adult an unchangeable indelible imprint. Epidemiologic, clinical and experimental data indicate that the experiences of the first moments of development, both before and after birth, play a decisive role in the appearance of chronic diseases: coronary and ischemic diseases, diabetes, osteoporosis, metabolic diseases, among others.

How can we explain all these changes? We all have an inherited genetic condition (genome), but not all that is written in that genetic code will be expressed: the environment, both intra and extra-uterine, will modulate the expression of those genes allowing for a healthy environment or, otherwise, if the environment is adverse, will leave an imprint for future health problems.

The events registered during pregnancy and especially those close to birth, will leave those imprints that will be independent from the experiences of adult life.

Malnutrition in the newborn is common, not only due to an inadequate nutrition but also as a result of maternal diseases such as hypertension, metabolic diseases like diabetes, autoimmune diseases that prevent normal intrauterine fetal growth. All these diseases bring about a neonate with serious malnutrition.

Now, what will happen with those children in the future? They may belong to a middle class family with parents that provide an early stimulation and adequate nutrition to recover the weight lost in the intrauterine life or, otherwise, they leave the assistance centers by decision of their parents who, due to different reasons, but especially due to lack of education or economic resources do not take care of those children with the special care they request. As a consequence, these children lose the possibility of developing their intellectual potential as brain interconnections are formed in the early stages of extra-uterine development and, therefore, will be in a disadvantageous condition to face their daily adult life.
SICKKIDS INTERNATIONAL - BUILDING CAPACITY AND SUSTAINABILITY

Hilary Whyte

The eight Millennium Development Goals which ranged from halving extreme poverty rates to halting the spread of HIV/AIDS and providing universal primary education, formed a blueprint for the entire world to focus their efforts on the world’s poorest countries. Canada like many other countries looked at the part they could play in these lofty goals. Specific to health care, academic institutions such as SickKids, targeted programs in global health for development. Fund raising efforts resulted in educational programs specific to developing countries. We also launched a new strategic program called SickKids International in 2006 aimed at building capacity and sustainability for health care programs in other countries whilst supporting the SickKids vision: Healthier Children, a Better World. Our SickKids mission as leaders in child health, to partner locally and globally, to improve the health of children through the integration of care, research and education, is an important part of what we do at SickKids International.

Through our ‘Business Advisory Services’ portfolio, we provide tailored services in these areas of care, education, and research. We assist other organizations in assessing their current paediatric healthcare practices through our ‘Needs Assessment Service’ and then work to develop innovative, sustainable strategies that facilitate the organization to achieve excellence in child health care. Our ‘International Education Services’ customize the education and delivery to meet the specific needs of the hospital staff as well as the local environment in which they must operate. This is not a ‘cookie cutter’ approach but rather a careful collaborative approach to ensure we cater to the specific needs of our partnerships in countries as diverse as China, Europe and Qatar or Saudi Arabia. Our commitment to build a self sustaining health care facility whether providing primary, secondary or tertiary care will result in fully competent and skilled health care professionals and management teams.

Separate from our advisory services, our SickKids International Patient Program works to help physicians caring for infants and children with highly specialized needs which cannot be managed locally in their home country. Through consultation, provision of second opinions and treatment as ambulatory or inpatients, a limited number of complex care patients are cared for at SickKids Hospital. We also support the work of the International Program by providing avenues to train allied health professionals and subspecialty physicians. Every year over 100 international doctors come for ‘fellowships’ in one of our 255 programs and 11 centers of excellence.
PREGNANCY AFTER SOLID ORGAN TRANSPLANTATION (KIDNEY/LIVER)

Miroslaw Wielgos

Organ transplantation has evolved from medical experiment to generally accepted treatment of choice of end stage organ failure. Nowadays kidney and liver are the leading transplanted solid organs worldwide. Excellent long term result of transplantation are associated with the increasing number of pregnancies noted in female recipients. The data of the course of pregnancy after transplantation are still limited and all pregnancies in graft recipient are considered high risk.

A total number of 116 deliveries in solid organ transplanted women (63 liver recipients and 53 kidney recipients) were recorded in I Dept of Obstetrics and Gynecology Medical University of Warsaw, Poland. Maternal, neonatal and graft outcomes of 81 deliveries from years 2005-2013 (complete data) were retrospectively analyzed and compared between the groups of kidney and liver recipients. The period from transplantation to conception varied from 2 months to 15 years (mean 57.97 months SD 40.28). Pre-pregnancy hypertension was more often observed in pregnant kidney recipients (73%) compared to women after liver transplantation (9%, p=0.000). The rate of preeclampsia was also significantly higher in kidney transplanted women (56.6% vs 11.4%, p=0.01). Premature labor (86.5% vs 43.2%), low-birth weight neonates (45.9% vs 22.7%) and small for gestational age neonates (40.5% vs 6.8%) occurred more frequently in kidney posttransplant pregnancies. Labors < 34 wks were noted in 13.5% and 9.1% of kidney and liver recipients respectively. The incidence of late preterm labors (35-37 wks) associated with pregnancy complications was much higher and reached 71.1% for kidney and 43.2% for liver posttransplant pregnancies. The rate of cesarean sections was also high (75.3%), however lower in liver recipients. 5 cases (6.2%)of malformations in newborns were reported in the study group. No case of acute graft rejection was observed.

Kidney recipients are at much higher risk of pregnancy complications and poor neonatal outcome compared to liver recipients mainly as a result of coexisting diseases. Posttransplant pregnancies seem no to be associated with significantly increased risk of graft-loss or congenital malformations of the newborns.
CONCEPTUAL EXAMINATION: GUIDELINES PROPOSED BY PROFESSIONAL SOCIETIES

Lami Yeo

Congenital heart disease (CHD) has an estimated incidence of 4-13 per 1000 live births. The identification of CHD prior to birth is important, since it is the most prevalent organ-specific birth defect, and is the leading cause of infant morbidity and mortality from congenital malformations. In addition, for infants diagnosed prenatally with specific CHD types, there is an improved preoperative condition, pre-surgical mortality rate, survival after surgery, and long-term neurocognitive function and outcome. Yet, structural cardiac anomalies are among the abnormalities which are most frequently missed by prenatal sonography. Due to various factors, the prenatal detection of CHD remains challenging, with studies reporting low sensitivity even when more than 90% of women in the population undergo sonographic examination. The purpose of fetal cardiac examination using ultrasound is to maximize the detection of CHD. Therefore, various professional societies have established guidelines for both sonographic screening examinations of the fetal heart, as well as the performance of fetal echocardiography.
SPATIOTEMPORAL IMAGE CORRELATION (STIC) OF THE FETAL HEART: ACQUIRING STIC VOLUMES, EVALUATION OF ADEQUACY, AND EXAMINATION OF THE STIC VOLUME

Lami Yeo

Four-dimensional (4D) sonography with spatiotemporal image correlation (STIC) technology allows the acquisition of a fetal cardiac volume dataset, and displays a cine loop of a complete single cardiac cycle in motion. It is considered an indirect motion-gated offline scanning mode. Once STIC has been activated, the array within the transducer housing begins an automatic single sweep over the predetermined volume, or region of interest. The STIC volume display is comprised of thousands of two-dimensional images acquired through the area of interest during this single automated sweep. Since STIC was first described more than 10 years ago, studies have demonstrated that volume acquisition can be incorporated into the daily practice of centers. Importantly, a solid body of evidence indicates that 4D sonography with STIC facilitates examination of the fetal heart through visualization of standard cardiac diagnostic planes, thus reducing operator dependency. STIC has also been proposed for the prenatal evaluation and diagnosis of congenital heart disease. However, the effective performance of fetal cardiac examination using STIC technology requires several elements, including volume acquisition, evaluation of its adequacy, and examination of the STIC volume dataset. As a result, various algorithms based upon STIC technology have been developed to aid users in interrogating volume datasets in a systematic and efficient manner to display cardiac views. Novel automated and semi-automated algorithms using software applied to fetal cardiac volume datasets have also been developed.
PRESENTATION OF 5 CASES OF CONGENITAL HEART DISEASE: JUST IMAGES

Lami Yeo

The incidence of congenital heart disease (CHD) is estimated to be 4-13 per 1000 live births. For specific CHD types, when infants have been diagnosed prenatally there is an improved preoperative condition, pre-surgical mortality rate, survival after surgery, and long-term neurocognitive function and outcome. However, structural cardiac anomalies are among the abnormalities which are most frequently missed by prenatal sonography. Despite almost universal access to sonographic screening during pregnancy, the prenatal detection of CHD remains low. Anatomical defects of the fetal heart remain difficult to diagnose due to the complex structure of the organ, its small size, and the high level of expertise required when performing a thorough examination. Thus, efforts should be directed towards improving the sensitivity of CHD on prenatal ultrasound. One such approach is to provide targeted education and training for sonologists. In this session, we will review prenatal sonographic images of cases with congenital heart disease.
AORTIC ARCH ANOMALIES (COARCTATION OF THE AORTA AND MORE)

Lami Yeo

Coarctation of the aorta is a common cardiac anomaly, and is found in approximately 5% of newborns with congenital heart disease. It is characterized by narrowing of the distal aortic arch, typically located at the isthmic region between the left subclavian artery and ductus arteriosus. Both chromosomal and extracardiac abnormalities are common features of coarctation of the aorta. Notably, this type of congenital heart disease is one of the most difficult conditions to diagnose during fetal life, primarily due to the patency of the ductus arteriosus before birth. The presence of coarctation of the aorta may be suspected on fetal cardiac examination by observing ventricular size discrepancy and/or asymmetry of the great vessels. However, some fetuses with prenatally suspected coarctation of aorta prove to be normal after birth. Interruption of the aortic arch is rare, occurring in approximately 1% of congenital heart defects. It is characterized by complete separation of the ascending and descending aorta. A right-sided aortic arch is diagnosed when the transverse aortic arch is located to the right of the trachea in a transverse view of the fetal chest. While a right-sided aortic arch can be isolated, it may also be part of a complex cardiac malformation. In double aortic arch, the aortic arch splits into both a right and left arch, which encircles the trachea and esophagus. Both arches then join together to form the descending aorta. This session will review the prenatal sonographic features of aortic arch anomalies.
WHAT IS THE VALUE OF PERINATAL DOPPLER: CEREBROPLACENTAL RATIO?

Ivica Zalud

This review aims to provide an update on the present and potential clinical applications of Doppler ultrasound in perinatal medicine including most recent evidence of cerebroplacental ratio (CPR) importance in the evaluation of fetal well being. Umbilical artery Doppler plays an important role in the management of intrauterine growth restriction (IUGR) and preeclampsia and aids in twin-to-twin transfusion syndrome management. Middle cerebral artery Doppler reliably detects fetal anemia and may be useful in the assessment of IUGR and fetal well being as well. CPR should be considered as an assessment tool in fetuses undergoing third trimester ultrasound examination, irrespective of the findings of the individual umbilical artery and MCA measurements. In addition, CPR is also an earlier predictor of adverse outcome than biophysical profile, umbilical artery or MCA Doppler. 3D power Doppler allows better small vessel visualization that is not affected by angle of insonation and has been used to diagnose placental and cord abnormalities. Greater sensitivity of 3D Doppler ultrasound to macro- and microvascular flow has provided improved anatomic and physiologic assessment throughout pregnancy. The rapid development of these new ultrasound techniques will continue to enlarge the scope of clinical applications in placental studies. As clinical experience with these new technologies increase and as the technology improves further, it is reasonable to expect that 3D Doppler and 4D ultrasound will be complementary addition to well established traditional Doppler ultrasound imaging.
Growth restriction, whether it occurs \textit{in utero} (intrauterine growth restriction) or postnatally, leads to a deficit in lean body mass. Recovery of the deficit in lean body mass, i.e., catch-up growth, is associated with long-term benefits in cognition, but may also be associated with long-term adverse effects on cardiovascular and metabolic health. While it is true that all infants who are small as a result of growth restriction have the potential for catch-up growth, infants who are born small because they are intrinsically small do not have that potential. Since catch-up growth involves recovery of a deficit in lean body mass, it requires increased retention of protein, which in turn requires an increased intake of protein. Using the factorial approach, nutrient requirements for catch-up growth have been estimated. It is presumed that only catch-up of lean body mass is required for benefits in cognition to accrue, whereas recovery of fat mass is optional.

The maintenance nutritional needs (no catch-up growth) of the SGA infant are moderately different from those of the normally grown infant. Energy needs are somewhat increased due to a higher resting metabolic rate per unit of body mass whereas protein needs are somewhat diminished due to slower fractional growth. Contrasting with these modest changes in the absence of catch-up growth, with catch-up growth nutrient needs are greatly increased. Even with relatively slow catch-up growth (50\% recovery in 4 weeks), needs for protein are greatly increased. With faster catch-up growth, the needs for protein are greatly increased. Since energy needs are only modestly increased, the protein/energy ratio of nutrient needs is appreciably increased with catch-up growth. These high protein needs are difficult to meet with the usual feedings for preterm infants, unless special measures are taken to increase the protein content, i.e., to increase the protein/energy ratio. Without the requisite protein intake, catch-up growth is not possible or will be delayed or be partial, all of which are likely to compromise the realization of the long-term cognitive benefits that result from catch-up growth. Therefore it is advisable to strive for intakes of protein that enable full catch-up growth to occur in a timely fashion. Unfortunately, empirical studies specifically examining the nutrient needs for catch-up growth have not been performed to date.