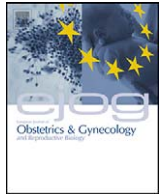


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Editor's highlights

Next month there will be two important European meetings within 100 km of each other. On 5–8 May the EBCOG Congress will be held in Antwerp, Belgium, and we hope that many readers, encouraged by our comments in last month's issue, are planning to attend. Shortly after that, on 19–22 May, the European Society of Contraception and Reproductive Health will hold its eleventh Congress in The Hague, The Netherlands. The Congress's theme, *Culture, Communication, Contraception*, reflects its focus on diversity, and its co-presidents point out that preventive strategies must increasingly "take into account the specific cultural, sub-cultural, economic, ethnic and religious characteristics of sub-populations within the European community." This is an important message. Our colleagues in sexual and reproductive health are the first to be aware of the cultural undercurrents that lie beneath the surface of life in Europe but these issues are of course highly relevant to obstetricians and gynaecologists. The ESC Congress programme is available at www.contraception-esc.com. Contraceptive provision is a particular challenge in Eastern Europe and we were pleased to see Cyrillic script on the programme cover, announcing that simultaneous translation into Russian will be available.

What's new?

Obstetricians are familiar with the "fetal programming" hypothesis of Professor David Barker of Southampton University, UK. Twenty years ago he published his first studies showing that people who had a low birth weight have high risks of cardiovascular disease later in life. Evidence to support his hypothesis has steadily grown and it is now widely accepted that coronary heart disease originates through undernutrition in the uterus. Ironically, as the importance of the antenatal period has become clearer, there has been a trend to reduce medical supervision of pregnancy, and very little effort is now being put into the detection of intrauterine growth restriction in so-called "low risk" pregnancies, where most cases occur.

Although the epidemiological evidence has become stronger, the exact mechanism of fetal programming is still a mystery. Growth-restricted fetuses are subjected in utero to oxidative stress which may cause arterial endothelial dysfunction, and this in turn leads to subsequent atherosclerosis. In this month's first review (page 127) [Leduc and colleagues](#) from Montreal, Canada, present evidence that mitochondrial damage is central to this process. Not only do mitochondria have a critical role in the endothelial dysfunction that causes atherogenesis, but the authors also propose that placental mitochondrial dysfunction is part of

placental insufficiency. Oxidative stress, they suggest, causes damage to mitochondrial DNA and this may be the link between malnutrition in early life and disease in adulthood.

Oxidative stress may also be involved in the formation of intraperitoneal adhesions, which are the subject of our second review. All gynaecologists know that re-operating after a previous laparotomy is likely to involve dealing with at best a few, or at worst extensive, adhesions but many share a feeling that using agents to try to prevent adhesion formation is probably a futile gesture. Many strategies are available, however, and on page 131 [Imai and colleagues](#) from Gifu, Japan, focus on topical non-barrier agents. They point out that although synthetic barriers have been widely studied, their disadvantage is that patients still develop adhesions in uncovered areas in the abdomen. Liquid anti-adhesive agents, on the other hand, can cover all potential peritoneal lesions and have been effective in animal models, but as yet they are not widely used in clinical practice. The authors suggest that a combination of barrier and non-barrier agents may prove effective, and call for further studies in human subjects. Later in this issue (page 195) [Aysan and colleagues](#) from Istanbul report that aloe vera gel is effective in reducing adhesions, though this too is an animal study.

Obstetrics and maternal–fetal medicine

Indications for caesarean section (CS) include prematurity and acute fetal distress, and both of these are the subjects of reports from large multicentre studies in this issue. On page 147 [Zeitlin and colleagues](#) report data from a study of very preterm babies in ten European regions. The MOSAIC study (which stands for "Models of Organising Access to Intensive Care") looked at a cohort of very preterm babies born in 2003 and the focus of the present paper is on births at 28–31 weeks. The use of CS at this gestation is variable, with rates reflecting the regional CS rates for births at all gestations: these ranged from 14% to 38%. The study found no regional correlation between CS rates and neonatal mortality and morbidity. The authors point out that very preterm CS may carry higher risks to the mother, and in view of the evident lack of consensus more research is necessary on the optimum use of CS at this gestation.

Acute fetal distress, by contrast, does not stimulate debate about whether or not CS is the right thing to do but about how quickly it can be carried out. The recommended decision-to-delivery interval (DDI) in the UK is 30 min and in Germany is 20 min, while in France there is no specific guideline because of the great diversity of practice settings. This is the background to a

report by [Huissoud and colleagues](#) from Lyon, France, of a prospective multicentre study in the 31 hospitals of the Aurore perinatal network in the Rhone-Alpes region of France (page 159). The network includes two level III maternity units with neonatal intensive care, twelve level II units (which include facilities for infants born at 32 weeks or later), and 17 level I units with no paediatric facilities. This study of 666 unplanned CS deliveries found that the median DDIs for emergency CS in level I, II and III units were 48, 40 and 22 min, respectively. For very urgent CS in a level III unit the median DDI was 13 min. This appears to argue in favour of large units but the authors found that the neonate's condition did not differ significantly according to the DDI.

The psychological aspects of pregnancy are important but research on them is difficult. On page 136 [Pozzo and colleagues](#) from Milan, Italy, explore the experiences of women hospitalised with "high risk" pregnancy, and of the staff looking after them. Women experienced loneliness and staff realised that they were not communicating with women as well as they should. The authors point out that the doctor–patient relationship in these circumstances is not one-to-one but involves the whole team. Some doctors described feelings of powerlessness and even guilt at being unable to meet patient's needs, but more than half the doctors questioned did not seem to recognise the emotional component of their work.

Reproductive medicine and endocrinology

Assisted reproduction only rarely involves life-and-death issues but two papers this month address different aspects of mortality. On page 175 [Michaan and colleagues](#) from Tel Aviv review 22 patients who underwent ovarian stimulation and emergency IVF before chemotherapy, for cancer in all cases but one. The mean age was 33. Twelve of the women had breast cancer and six of the twelve were taking tamoxifen. The study compared the outcomes in these cases with 22 patients undergoing IVF for tubal factor infertility. No significant differences were found regarding the main outcome measures including number of oocytes retrieved. Four of the cancer patients have had thawed embryos transferred and two of them have had healthy babies. The authors comment that current treatment protocols offer a minimal time delay before chemotherapy is commenced, but they stress that stringent patient selection is necessary to ensure that no unnecessary procedures are undertaken.

Ovarian stimulation for IVF carries a risk of ovarian hyperstimulation syndrome (OHSS) and the chance of severe OHSS is estimated at 1.5–3.5%. This complication can be fatal and various strategies are used for OHSS prevention, including coasting and cycle cancellation. A new concept is suggested on page 190 by [Griesinger and colleagues](#) from Luebeck, Germany, who report 40 patients considered at risk of severe OHSS, with their chance of recurrence being at least 10%. This high-risk group underwent ovarian stimulation in a GnRH-antagonist protocol and final oocyte maturation was triggered by a GnRH agonist rather than by HCG. Because GnRH-agonist triggering has been linked to a defective luteal phase and reduced pregnancy rates, it was followed in this study by oocyte cryopreservation and later frozen-thawed embryo transfer. This protocol has been used for 4.5 years and the authors report a cumulative live birth rate per patient of 35% with a 0% incidence of OHSS.

Gynaecology and gynaecological oncology

Endometriosis continues to baffle and fascinate researchers and is the subject of two papers in this month's issue. The causes of

endometriosis are recognized to involve genetic factors, ovarian steroid hormones and inflammatory mediators, and all of these endogenous factors have been extensively researched. Less attention has been paid to exogenous factors such as bacterial or viral infection, and on page 204 [Khan and colleagues](#) from Nagasaki, Japan, report a study on the effect of semen. They collected seminal fluid from 18 healthy men, and biopsy specimens of endometriosis at laparoscopy from 45 women. They also collected eutopic endometrium, peritoneal fluid and serum from these women and from 20 women without endometriosis, and studied the effects of seminal plasma (SP) on cultures of stromal and epithelial cells from the endometria. SP stimulated growth of both eutopic and ectopic endometrial cells but its effect on eutopic cells was much greater in women with endometriosis than in women without endometriosis. Growth factors in SP may be responsible and antibodies to these growth factors suppressed the effect of SP. The clinical relevance of this painstaking work is that unprotected sexual intercourse may have detrimental effects on endometriosis.

Endometriosis affecting the bowel is one of the most severe forms of the disease and is estimated to affect 5.3–12% of women with endometriosis. Bowel resection may be required and nowadays this can be carried out laparoscopically. There is a lack of information on pregnancy rates after this procedure. On page 210 [Darai and colleagues](#) from Paris report on 83 women who underwent colorectal resection for endometriosis, exclusively by laparoscopy in 77 cases and with laparoconversion in six. Twenty-nine pregnancies occurred in 24 patients, of which 20 were spontaneous and nine were by IVF. The pregnancy rate was higher in younger women and was reduced by the presence of adenomyosis, by laparoconversion and by more severe disease (as shown by a higher ASRM score). These results, say the authors, support the use of radical laparoscopic excision of endometriosis plus colorectal segmental resection in symptomatic women wishing to conceive.

Gynaecological urology

Much research is continuing not only on the treatment of pelvic organ prolapse (POP) but also on its causes. Some people are more susceptible to POP than others, and it seems that both genetic and environmental factors are involved. Connective tissue metabolism, and in particular the remodeling of vaginal connective tissue, are important in the development and progression of the condition. Matrix metalloproteinases (MMPs) are enzymes directed against connective tissue components such as collagen and elastin and one of these, MMP-9, is thought to be specially important in the remodeling process. On page 222 [Chen and colleagues](#) from Taichung, Taiwan, report an investigation of MMP-9 gene polymorphism in 92 women with POP and 152 women without POP. The authors found a significant difference between the two groups in the MMP-9 genotypes evaluated. They suggest that the ability to identify women at increased risk of POP could help clinicians in counselling women who request elective caesarean section to preserve the pelvic floor.

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