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Editors' highlights

What's new?

In previous issues we have had the pleasure of offering reviews about a wide variety of subjects and this month we are happy to continue with five reviews ranging from the methodology of systematic reviews to COX-2 expression in ovarian malignancies. On page 121, [Knox and colleagues](#) from Birmingham, UK, memorably describe systematic reviews of fetal medicine as “a tool for translation of research findings from a few expert centres to a wider health care specialty”. They identified 84 reviews which met their inclusion criteria – over half being in the field of fetal pathology. The authors say there is a paucity of good quality reviews in fetal medicine research, that reporting of methodological features is poor and that not enough attention is paid to assessment of the validity of included studies or to the appropriate use of meta-analysis.

Isolated tubal torsion is a rare cause of acute abdomen in pregnancy, with an incidence of about 1/1,500,000 women. Many obstetricians will never see a case during their lifetime. [Origoni and colleagues](#) from Milan, Italy (page 116) report 19 cases from 1936 until today, including one which they observed. In 90% of cases the right tube was involved and in recent years pain was accompanied by an adnexal cyst detectable on ultrasound. Isolated tubal–paratubal cyst torsion should be considered when Doppler flow ultrasound shows normal ovaries and a pelvic cyst, and this may allow the obstetrician to plan ovary-sparing surgery.

Because splenic artery aneurysm (SAA) is asymptomatic, its prevalence is unknown. Estimates vary from 0.01% to 10.4%. It may be found at angiography, at laparotomy or post-mortem, but up to 95% present during pregnancy. [Fong Ha and colleagues](#) from Subiaco, Australia (page 133) review 32 pregnancy-associated cases, of which only one was found incidentally. The rest were found following rupture, which was usually spontaneous. The maternal mortality rate was 21.9% and the fetal death rate 15.6%. Ruptured SAA should be always considered in a pregnant patient with severe and unexplained abdominal pain, and surgery should be performed without delay. Salvage of the spleen is now advocated.

There are so many aspects to preterm birth that research on this subject is a never ending story. [McDonald and colleagues](#) from Canada and China (page 138) present a systematic review of preterm birth and low birth weight after in vitro fertilization. They included 17 studies with 31,032 IVF singletons and 81,119 spontaneously conceived singletons. After controlling for maternal

age and often other factors, they showed that IVF singletons had increased risks of preterm birth (RR 1.84, 95% CI 1.54, 2.21), low birth weight (<2500 g, RR 1.60, 95% CI 1.29, 1.98) and intrauterine growth restriction (RR 1.45, 95% CI 1.04, 2.00). At present there seems to be no way to influence this outcome, but further research should be conducted to clarify the causes and offer treatment to IVF patients, and the authors also recommend more research on preventable causes of infertility. We doubt if many couples will be satisfied, or deterred, by their final statement that: “All couples considering IVF should be counselled about the increased perinatal risks so that they are truly informed when they consent for the procedures”.

On page 129, [Joseph Menczer](#) from Holon, Israel, reviews the clinical aspects of COX-2 expression. COX-2 is an inducible enzyme expressed only in response to stimuli such as mitogens, cytokines, growth factors or hormones, and it is expressed in ovarian and peritoneal carcinoma and in ovarian tumours of low malignant potential. Its overexpression stimulates angiogenesis by promoting the production of, among others, vascular endothelial growth factor. The association between COX-2 expression and response to treatment, however, is inconsistent and studies on the use of COX-2 inhibitors in epithelial ovarian cancer are needed.

European view

From time to time, under the heading “European view”, we publish activities and investigations conducted by researchers from different countries in Europe. In this way we are supporting a European perspective on various aspects of our specialty, as we feel it is important for us to identify ourselves as part of the European community. Comparison of medical practice among European countries is surprisingly difficult, but it facilitates communication and understanding and is a stimulus to better quality of medical services.

On page 149 the EURO-PERISTAT Report Writing Committee ([Meagan Zimbeck](#), [Ashna Mohangoo](#) and [Jennifer Zeitlin](#)) present the key findings of the first-ever European Perinatal Health Report, with data allowing comparison of perinatal health among European countries. So, for example, the proportion of preterm births varied from around 5.5% in Ireland, Finland, Lithuania and Latvia, to 8.9% in Germany and 11.4% in Austria. Rates of low birth weight (below 2500 g) among live births ranged from 4.2% to 8.5% and showed an increasing trend from north to south, raising questions about the appropriateness of applying a single birth weight standard in different populations. EURO-PERISTAT plans to

carry out further analyses of these variations and to evaluate the report's usefulness to the people who have power to make changes.

Obstetrics and maternal–fetal medicine

“A higher rate of neural tube defects was found in the offspring of mothers with severe diseases of the biliary system during pregnancy” is the result of an investigation by [Acs and colleagues](#) from Budapest (page 152). Notification of congenital abnormalities is compulsory in Hungary and cases were collected from the Hungarian Congenital Abnormality Registry, 1980–1996, with controls ascertained from the National Birth Registry. The aim was to evaluate the possible association between maternal cholecystitis and cholelithiasis with related drug treatments and congenital anomalies in their offspring. The authors suggest that fever may be the explanation for the higher rate of abnormalities but they point out that details of the biliary disease, such as its aetiology or the presence of fever, were often lacking. They conclude that their finding needs to be confirmed by further studies to determine whether it is a causal or a chance event.

Interesting results regarding the treatment of myelo-meningocele in an experimental model are reported on page 174 by researchers from Barcelona, Spain. [Fontecha and colleagues](#) used a surgical approach to treat lumbar myelo-meningocele with an inert bio-adhesive patch in 15 fetal sheep. Untreated animals were unable to walk, had sphincter incontinence and showed histological spinal cord damage and a large Chiari malformation, but all the covered animals were able to walk, had sphincter continence and showed almost complete closure of the defect. This approach is promising but the authors comment that further work is needed on absorbable material and a less invasive approach using fetoscopy.

Premature delivery is a major concern for obstetricians and neonatologists. Giving the right treatment at the right time when premature labour threatens has been the goal for many years, and an early diagnostic tool would be helpful. Estimation of fetal fibronectin has been recommended and on page 180 [Bolt and colleagues](#) from London report that in practice use of this test has a significant effect on clinical management. A longer-term approach is reported on page 169 by [Toricelli and colleagues](#) from Siena, Italy, who measured stress-related hormones in amniotic fluid obtained by amniocentesis in the mid-trimester. Urocortin concentrations were significantly lower among women who subsequently went into premature labour compared with those who delivered at term. The difference is convincing but further studies will be necessary to find easier methods of access to fetal urocortin. If it can be measured in maternal serum, this would open up the possibility of a longitudinal study to predict premature labour.

A stone plaque at the Chicago Lying-In Hospital is still waiting for the name of the individual who will discover the cause of pregnancy-induced hypertension. It seems unlikely that a single cause will ever be “discovered”, as teams of researchers investigate the mosaic of many coloured stones, each of them contributing to the syndrome. Levels of fetal DNA in maternal serum have been found to be elevated in pre-eclampsia due to leakage through the placenta but so far, studies have been limited to women carrying male fetuses, whose DNA is easier to identify. Now [Karina and colleagues](#) from Poland (page 165) have investigated female fetal DNA concentration in the plasma of pregnant women with and without pre-eclampsia. They were able to quantify fetal DNA in both groups and to confirm for the first time that in women carrying female fetuses, development of severe pre-eclampsia is associated with an increase in fetal DNA in maternal serum.

Reproductive medicine and endocrinology

Ultrasound and laparoscopy now enable early diagnosis of ectopic pregnancy, giving more opportunity for conservative treatment options. Among these, the antimitotic drug methotrexate (MTX) is widely used but its side effects on ovary and tubes have not been carefully investigated. [Yang and colleagues](#) from Wenzhou, China (page 193) investigated its effect on 108 female rats at different doses (1, 2 and 5 mg/kg bodyweight of MTX i.p.) and found a dose-dependent influence on oestrogen receptor expression in the endosalpinx. They conclude that more than 5 mg/kg of MTX can induce long-term irreversible changes to steroid hormone receptors and suggest that it should be used clinically in a reasonably small dose.

“Anti-aging” creams are widely used by postmenopausal women. The oestrogen beta receptor exists in large quantities in the skin, and in smaller quantities in the breasts and uterus, and phyto-estrogens such as soy isoflavones may induce proliferation of the epidermis and increase dermal collagen. [Moraes and colleagues](#) (page 188) from Sao Paulo, Brazil, investigated the effect of topical isoflavones ($n = 18$) in comparison with estrogen ($n = 18$; beta-estradiol 0.01%) by performing preauricular skin biopsies. There was an increase in histo-morphometrical parameters in both groups but estrogen had the stronger effect. The authors conclude that both therapies produced positive effects on the facial skin with no significant systemic repercussions.

Gynaecology and gynaecological oncology

X-linked inhibitor of apoptosis protein (XIAP) is one of the most potent inhibitors of caspases and apoptosis identified to date and is known to be upregulated in various malignancies including ovarian cancer. It promotes invasion, metastasis, growth and survival of malignant cells. On page 222 [Ma and colleagues](#) from Xian, China, present a study of the impact of XIAP gene RNA interference on ovarian carcinoma cells. Blocking XIAP gene expression inhibited proliferation of these cells and caused them to be more sensitive to cisplatin through reduction of its mRNA and protein. These results suggest that XIAP is an ovarian cancer-related gene and that XIAP is a potential target for anti-cancer drugs.

It is well known that the recurrence rate of cervical cancer is related to the stage of the disease, and one of the most important prognostic factors is the presence of lymph node metastases. Many recurrences, however, occur in women without such metastases and [Fregnani and colleagues](#) from Brazil (page 204) ask whether possible predictive factors can be defined in these women. They recorded 27 recurrences among 233 women with carcinoma of the cervix. The five-year disease-free survival rate among the study population was 88.4%. On multivariate analysis, independent risk factors for recurrence were postmenopausal status, absent or slight inflammatory reaction and invasion of the deepest third of the cervix. Postoperative radiotherapy was identified as a protective factor against recurrence. The authors comment that the effect of postmenopausal status needs confirmation with other studies.

Altered fibrinolytic activity has been suggested as a key factor in the development of endometriosis and there is controversy over the role of plasminogen activator inhibitor-1 (PAI-1) gene polymorphism 4G/5G. [Gentilini and colleagues](#) from Milan, Italy, (page 219) investigated 368 patients who underwent laparoscopy and 329 controls. They report that there is no greater susceptibility to endometriosis in patients harbouring the PAI-1 4G/5G and 4G/4G genotypes, and no significant role of polymorphism in endometriosis development. Their investigations present a clear view on this subject.

An interesting contribution to vaginal surgery is given by [Siva-Filhon and colleagues](#) from Belo Horizonte, Brazil, on page 200. Ninety patients undergoing vaginal hysterectomy for a non-prolapsed uterus were randomised to conventional suture ligation or a bipolar vessel sealing system (BVSS). Patients operated on with the BVSS had reduced operating time, less blood loss, better pain status and reduced hospital stay compared with the control group. This is a challenge to copy this approach.

Gynaecological urology

Vaginal vault prolapse may develop as a long-term complication after hysterectomy for various reasons and many methods

have been tried to cure this problem. On page 227 [Granese and colleagues](#) from Italy report their experience of 165 cases of laparoscopic sacro-colpopexy using polypropylene mesh. They report a number of side effects – 4.8% intraoperative and 21.1% postoperative complications – but finally conclude: “Our study shows that laparoscopic sacro-colpopexy, in the hands of an expert surgeon, can be considered a safe, effective procedure for the treatment of vaginal vault prolapse, allowing long-term anatomical restoration with a 94.9% success rate”. Each reader’s experience will decide which treatment to choose in future.

Enjoy reading all the articles.

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