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Editors' highlights

Germany is presently fighting for a change in the law on stem cell research. On Thursday February 14, the discussion in the Bundestag, the German parliament, addressed one of science's most sensitive issues. Pressure is growing for an easing of restrictions that local scientists complain prevent them from keeping up with global advances. The Bundestag sees the stem cell question as one which carries historic overtones of the Nazis' genetic experiments linked to the creation of a ''master race''. Six years ago a law was passed banning the production of embryonic cells from pre-existing stem cell lines. The recent debate was without a satisfactory conclusion and a vote on whether the law should be changed has been scheduled for mid-March.

Other European countries, such as Britain and Sweden, have less strict laws. Researchers in Germany complain that their country's tight laws prevent them from taking part in international projects using stem cell lines created elsewhere after the current law was introduced in 2002. The proposal which has won most support from lawmakers so far is one which introduces a more recent cut-off date, probably May 2007, for the import of stem cell lines. But under these conditions the law remains, like Janus, a body with two heads looking in different directions.

What is new? Phenylketonuria (PKU) is the most hereditary form of metabolic disorder with an incidence of 1 in 6000–7000 newborns. Affected people are unable to metabolize the amino acid phenylalanine. The classical form exists in 98% of cases. Deficiency or reduced activity of the enzyme phenylalanine-hydroxylase leads to accumulation of phenylalanine in the body and, if untreated, to mental retardation and epilepsy. The atypical form of PKU occurs in 2% of cases and is caused by a disorder of the coenzyme tetra-hydrobiopterin. Classical PKU is caused by mutation of the gene on the long arm of the chromosome 12. On page 131 the review by Hanley from Toronto, Canada, highlights two groups of women with PKU who are at risk in producing offspring with embryopathy: (a) those not yet diagnosed and (b) those lost to follow up. He reviews the literature including the International Maternal PKU Collaborative Study. Blood phenylalanine concentrations of 200–600 μmol/l seem not to affect the offspring, but virtually all the 119 offspring from 60 women with previously undiagnosed PKU (most of whom had relatively normal intellectual function) were profoundly damaged. The author recommends selective prenatal screening or case finding for fertile women with PKU and presents a template.

Obstetrics and Maternal-Fetal Medicine: Fetal loss has many causes, such as chromosomal aberrations in about 50% of cases in early pregnancy and infections at later gestational ages. Immunological disturbances are difficult to define but are surely one cause of early fetal loss. Vora and colleagues from Mumbai, India (page 136) conducted a comprehensive screening analysis of antiphospholipid antibodies (APA) to investigate their relation to fetal loss in 430 women. Conventional lupus anticoagulant (LA) and anti-cardiolipin antibody (ACA) tests were positive in 23.2% of cases compared to 1% of controls. It is important to find a diagnosis for miscarriages if all conventional causes have been ruled out, even if no treatment is presently available.

Perinatal audit is an important part of quality assurance in the obstetrical service. Alderlisten and colleagues from Amsterdam describe on page 141 a regional audit of perinatal death in a blinded study to investigate whether substandard care was the cause of the perinatal death. They reviewed 137 perinatal deaths after 23 weeks of gestation and found factors of substandard care in 25% of cases. Analyses of substandard care, however, can be effective only if the observations of causes are translated into better management.

The pathophysiology of preeclampsia (PE) is a vasoconstriction of the maternal circulation including the uterine vascular system. There is still speculation about the causes of the disease and although many facts are put together, a clear concept is still missing. PE occurred in 2.4% of pregnancies in a study by Deis and colleagues from Paris on page 146. Vasoconstriction of the uterine vessels reduces blood flow and affects the fetus by reducing the oxygen supply. The effects on the fetus were measured by Deis, and used for a nomogram to predict preeclampsia. In general, however, preeclampsia is detected by an increase of systolic and diastolic blood pressure which was also used for the nomogram. Deis recommends planning a preventive trial and we await this with interest although we are not sure how prevention can be achieved. On page 157 Chavarria and colleagues from Mexico City report another indicator for the development of preeclampsia. They investigated adhesion molecules at 20 weeks' gestation and again in the third trimester in 200 nulliparous women, of whom 75 developed preeclampsia and 125 served as controls. In women with subsequent preeclampsia, sL-selectin and sVCAM-1

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concentration were significantly lower, whereas sE-selectin, sP-selectin and sICAM-1 levels were significantly higher in midpregnancy compared to controls. The authors concluded that low sL-selectin levels at 20 weeks of gestation may be an indicator for the development of preeclampsia. It may be that biochemical markers are better predictors than biophysical measurements.

Pregnancies in young women are always thought to be of high risk. This seems not to be true as shown by Gupta and colleagues from Cardiff, UK on page 165. They investigated primigravid women less than 20 years of age. Compared to a control group of women aged 20–34, there was a lower incidence of multiple pregnancy, spontaneous rupture of membranes and pregnancy induced hypertension, but a higher incidence of anaemia and pyelonephritis. Teenage women were more likely to have a spontaneous delivery and had a lower incidence of caesarean section without compromising maternal or neonatal outcome.

Postpartum haemorrhage (PPH) is usually an unexpected event and fast action is necessary to explore the causes and prevent major blood loss. Bouma and colleagues from Amsterdam (page 172) investigated PPH and found uterine atony to be the main cause in 82% of cases. To treat the blood loss and prevent hysterectomy they used recombinant activated factor VII (rFVIIa, NovoSeven) from Novo Nordisk, Denmark. Its haemostatic effect is thought to be mediated by enhancing the rate of thrombin generation leading to a full thrombin burst providing a fully stabilised fibrin plug with a tight fibrin structure resistant to premature lysis. The dose of rFVIIa used ranged from 16 to 128 μg/kg. The authors see a role for this substance in PPH unresponsive to conventional therapy.

Reproductive Medicine and Endocrinology: In modern antenatal care the diagnosis of twin gestation is usually made by vaginal ultrasound investigation at a very early gestational age, i.e. 8–10 weeks, when fetal viability can easily be confirmed. On page 185 Goktolga and colleagues from Ankara describe the prediction of twin pregnancy outcome by investigating the progesterone level. They speculate that the number of ultrasound examinations may be reduced by this method. Why leave a reliable and fast method of fetal surveillance in twin pregnancy and change to an insecure procedure of hormone investigation with a wide variance? The opinion of readers would be appreciated.

An interesting paper is presented by Liedman and colleagues from Lund, Sweden on page 189. They investigated gene expression for vasopressin and oxytocin in endometrial tissue in patients with dysmenorrhoea. Gene expression for oxytocin receptor was significantly lower in women with dysmenorrhoea compared to controls and it might be involved in the aetiology of primary dysmenorrhoea.

Gynaecology and Gynaecological Oncology: Estimation of uterine weight can be useful if the surgical approach has to be decided. Bimanual examination is usually more an approximation than an exact measure. Rovio and colleagues from Tampere, Finland (page 193) measured the size of the uterus by transvaginal ultrasound, applying two formulas for calculation. There was rather good agreement of measured and estimated weight up to 400 g. But above this limit the variation of the estimated weight increased so that estimation became unreliable.

Endometriosis is still a disease without effective drugs to cure it. There are several papers on the topic in this issue. Promising experiments on an endometrial stromal cell line have been conducted by Wu and Guo from Milwaukee, USA (page 198). The histone deacetylase inhibitors (HDACIs) trichostatin A (TSA) and valproic acid (VPA) suppressed proliferation of these cells and the authors speculate that HDACIs may be promising for treating endometriosis. Othman and colleagues from Galveston, USA, Lübeck, Germany and Assiut, Egypt investigated serum cytokines as biomarkers for endometriosis. The serum of patients with endometriosis contains significantly higher levels of interleukin-6, monocyte chemotactic protein-1 and interferon-gamma than that of control women. Discrimination between early and severe forms is not possible, however, because of the wide variation of the investigated cytokines. Adenomyosis is a special type of endometriosis with migration into the uterine musculature. Kissler and colleagues from Frankfurt am Main, Germany, (page 204) visualised adenomyosis with magnetic resonance imaging in cases of dysmenorrhoea in a prospective study. They studied the enlargement of the junctional zone (JZ) in relation to duration of dysmenorrhoea in 70 women. The thickness of the JZ in cases of long duration was 11 mm and in cases of short duration 6.4 mm. The prevalence rate of adenomyosis in endometriosis after more than 11 years of dysmenorrhoea was 87%.

Vulvar cancer is in general a disease of elderly women, often treated with the wrong methods and sometimes discovered very late. Involvement of the lymph nodes is related to the size of the tumour and can be ascertained only by removal and histological examination of the nodes. Six and colleagues from Vienna (page 217) investigated whether lymph node status is associated with the serum level of C-reactive protein (CRP). The investigation provides a clear answer: CRP is closely associated with lymph node status but cannot be used as a prognostic marker.

Enjoy reading the papers.

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