Medical problems in obstetric practice

A joint conference entitled 'Medical Problems in Obstetric Practice' was held by the Royal Colleges of Medicine and Obstetrics and Gynaecology, at the Royal College of Physicians of London in February 1998.

Pre-eclampsia: mistakes physicians make

Professor Chris Redman (University of Oxford) described pre-eclampsia as an unpredictable and poorly understood disease of the placenta that causes placental ischaemia. This leads to the production of a putative factor X causing widespread endothelial dysfunction, a single pathological process that can account for the diverse clinical manifestations of pre-eclampsia: hypertension (increased vascular tone), oedema and proteinuria (increased vascular permeability) and disseminated intravascular coagulation (DIC) (increased pro-coagulant expression).

Using illustrative case histories, Professor Redman showed that the severity of pre-eclampsia is not related to the degree of hypertension, and that the progression of the disease is not affected by antihypertensive treatment (although, of course, antihypertensive treatment may be indicated in its own right to prevent stroke). An eclamptic crisis may strike without the classic prodrôme of pre-eclampsia1, and the HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count) described by Weinstein2, can present with epigastric pain and be misdiagnosed as gallbladder disease or heartburn. As a result, doctors can (and do) miss the opportunity for a useful therapeutic intervention.

The only certainty in pre-eclampsia is that it is caused by pregnancy and relieved by delivery.

A seizure in pregnancy

Professor Peter Rubin (University of Nottingham) reinforced the message that an eclamptic fit may not be heralded by either hypertension or proteinuria. A first fit occurring in pregnancy is most likely to be due to eclampsia, and if they are not already present, other features of endothelial dysfunction such as proteinuria and hypertension may rapidly ensue.

Professor Rubin recommends diazepam for the acute treatment of a pregnant woman who is actively fitting. The Collaborative Eclampsia Trial3 showed that magnesium sulphate is better than phenytoin for secondary fit prevention. A show of hands from the audience confirmed that this evidence has been generally incorporated into management policy.

If not due to eclampsia, first fits in pregnancy will usually be due to epilepsy. However, it should not be forgotten that cerebral arteriovenous malformations and berry aneurysms, subject to the softening and trophic effects of progesterone, can burst, and the hypercoagulable state of pregnancy can cause cerebral vein thrombosis.

Most of the problems of treating epilepsy in pregnancy stem from the failure of patients (and some of their doctors) to recognise that a fit in pregnancy is far more dangerous to both mother and fetus than is the teratogenic risk from adequately supervised anticonvulsant therapy. Increased seizure frequency in pregnancy, therefore, is nearly always due to reduced plasma levels of anticonvulsant, either because the woman has stopped taking it, or her doctor has failed to detect the need for a higher dose due to increased clearance in pregnancy.

Deranged liver function in pregnancy

Dr Catherine Nelson-Piercy (Guy's and St Thomas' Hospitals, London) pointed out that the 'normal ranges' for commonly assayed liver enzymes are different in pregnancy. Total protein and albumin concentrations are decreased by 20 to 40%, and there are increased levels of binding proteins. Placental production of alkaline phosphatase leads to a two- to four-fold rise in the serum level at term. The upper limit of normal of serum transaminases is lower in pregnancy, but bilirubin and amylase levels are unchanged4. Dr Nelson-Piercy alerted us to the risk of obstetric cholestasis (OC, intrahepatic cholestasis of pregnancy) to the fetus. OC is a disease of multifactorial aetiology and marked geographical variation, and appears to be increasingly common in this country – a view upheld by several delegates in the discussion. The two most serious causes of deranged liver function in pregnancy are the HELLP syndrome, and acute fatty liver of pregnancy (AFLP), which is less common but has a higher mortality than the HELLP syndrome.

Hyperemesis gravidarum (HG) can cause a mild elevation of serum transaminase levels. But all women with HG severe enough to require admission to hospital for intravenous fluid replacement are at risk of developing Wernicke's encephalopathy and should therefore be treated with thiamine, orally if possible (50–100 mg three times a day), but intravenously if necessary.

In summary, it is always advisable to measure liver function in a pregnant woman with epigastric pain, nausea or vomiting; and in those with an itch but no rash. The deranged liver function of HG resolves as the HG ceases, but the deranged liver function of AFLP or HELLP is an indication for delivery. The correction of deranged liver function in OC does not eliminate fetal risk.

New drugs

Dr Nick Bateman (University of Newcastle upon Tyne) recalled the specific problems caused by thalidomide,
debendox and the retinoids. The teratogenic effect of a given drug is dose dependent, and the timing of fetal exposure is critical in determining the extent of harm done. The criteria for defining a teratogen require a distinctive pattern of defects to be consistently associated with exposure to the substance, with clear animal correlates, and a known mechanism of teratogenicity. As a result, it is easier to identify a drug that causes a rare birth defect than one which increases the incidence of a more common congenital malformation.

Advice can be obtained from the European Network of Teratology Information Services (ENTIS). To complement this service, it would be helpful if a system were initiated that reports and records the use of drugs in pregnant women with good outcome.

The use of anticonvulsants in pregnancy aroused great interest among the audience. Nakane et al. had shown that the teratogenic risk of anticonvulsant therapy increases dramatically when multiple drugs are used (presumably because each new drug carries its own risk); hence the least number of drugs possible to achieve seizure control should be used for epilepsy in pregnancy. Data on the newer drugs, such as lamotrigine and gabapentin, are still scanty, and likely to be biased against the drugs due to the reporting of adverse events rather than good outcomes, and also because these drugs tend to be used in cases where seizure control has been difficult and multiple drug regimens are more common. It is important to continue folic acid supplements throughout pregnancy when anticonvulsants are prescribed.

Travel medicine

Miss Pauline Hurley (John Radcliffe Hospital, Oxford) gave a comprehensive review of commonly and uncommonly requested travel vaccines, with regard to their safety in pregnancy. The take-home message appears to be ‘weigh up the risks in the individual case, but there are a few vaccines (usually the live forms) which are contraindicated’.

For malaria, Miss Hurley stressed the importance of non-pharmacological methods for avoiding mosquito bites: mosquito nets, avoiding high risk geographical areas, and the use of insect repellent. Malaria is often a more serious disease in pregnancy, and there is an increased risk of second trimester abortion and premature labour. Chloroquine is safe in pregnancy, but this drug is useless in areas where the parasite has become resistant.

In severe travel sickness, promethazine theoclate is safe and effective.

If delivery occurs abroad, the woman should be advised to contact the British Embassy of the country in question. Leading on from this, a member of the audience pointed out that travel insurance may exclude medical disorders and treatment related to pregnancy and delivery, and will almost certainly not cover the neonate.

Debate: All pregnant women should be screened for gestational diabetes

For the motion

Dr Michael Maresh (St Mary’s Hospital for Women and Children, Manchester)

In Dr Maresh’s view, screening should be routinely performed as part of antenatal care to avoid the adverse effects of gestational diabetes mellitus (GDM) on maternal and fetal outcome. He cited an increased caesarean section rate for women with diabetes, and highlighted the long-term increased incidence of Type II (non-insulin-dependent) diabetes in women who have had GDM. For the fetus there is a higher perinatal mortality rate, morbidity associated with macrosomia and its complications, and, in the long term, possible obesity and diabetes. He used the data of O’Sullivan’s to support his argument that if detected and treated aggressively with diet and insulin, the risks are reduced. Dr Maresh concluded by pointing out that one form of screening, namely detection of glucose in random urine specimens, is already routine; and that screening is essential to reduce maternal and fetal risk.

Against the motion

Professor Robert Tattersall (University of Nottingham)

Professor Tattersall began by saying that the views he expressed in the spirit of the debate are based on fact but are not necessarily his own. With the possible advantage of speaking second, he began by challenging the obstetrician’s view that ‘because we are doing it, it must be right’. Screening for GDM does not fulfil any of the criteria for a beneficial screening programme: specifically, GDM is not a significant public health problem; there is no sensitive and specific test suitable for mass screening; the natural history of GDM is poorly understood; there is no effective treatment for it, and therefore screening could never be cost effective. He disagreed with some of O’Sullivan’s conclusions with regard to the effectiveness of aggressive treatment of GDM at reducing fetal complications. He suggested that women labelled as ‘diabetic’ in pregnancy are more likely to be delivered by caesarean section simply by virtue of the label itself. He concluded his argument with the recommendation that slim Caucasian women under the age of 25 should not be screened for GDM.

A lively and entertaining debate continued from the floor. Professor Tattersall maintained that screening for glycosuria is not sensitive or specific enough for GDM, and is only of value in detecting previously undiagnosed Type I (insulin-dependent) diabetes in the first trimester. Dr Maresh stressed that selective screening will miss cases of GDM, and a speaker from the floor felt that the prevention of even one episode of traumatic delivery would justify any cost implications. The camp in favour of screening had no consensus view on which test to use, and Dr Nelson-Piercy stated that this was a reflection of the situation nationally.
The lobby against screening held the view that the oral glucose tolerance test (OGT) would be both impractical and non-viable on cost grounds. From the floor, it was suggested that pre- and post-prandial blood glucose measurement could be a cheaper alternative. Professor Tattersall replied that the resource implications of this suggestion would probably be even greater than those of the OGT. Professor Redman stated that the pregnant woman has a right to be healthy and protected from harm, but also from unnecessary intervention; and we were again reminded of the uncertainty that intervention in GDM is effective, or that women with GDM and their babies are at increased risk in the short term.

On a show of hands, the audience was approximately equally for and against the original motion, but unanimously rejected a motion that all women should be screened with an OGT.

**HIV**

**Dr Frank Johnstone** (University of Edinburgh) began by emphasising that HIV infection and AIDS are now treatable diseases, and that materno-fetal spread is largely preventable. He recommended the use of the AIDS information site on the world wide web, which is frequently updated and of high quality.

Vaginal delivery is the main risk for fetal infection, due to exposure to virus in the birth canal. However, elective caesarean section to avoid this risk is probably only indicated in cases where the maternal viral load is known to be high. Zidovudine is safe in pregnancy and decreases the risk of materno-fetal transmission, possibly by post-exposure prophylaxis. For this reason it should be given in labour and to the neonate.

Combination therapy for AIDS has dramatically altered the prognosis of the disease in adults. The clinical ethos is that maternal need predominates, so therapy should not be stopped in pregnancy. Some suggest withholding therapy until 10 weeks gestation if pregnancy is confirmed, to avoid exposure of the fetus to drugs during organogenesis. Monotherapy with zidovudine in the third trimester is reasonable to prevent vertical transmission, even in women whose CD4 count would not normally merit treatment.

Finally, Dr Johnstone addressed the issue of antenatal screening for maternal HIV infection. Countries with the highest uptakes are those which operate an opt-out system rather than opt-in, but so far in the UK the main barrier is cost.

**Thromboembolism**

**Dr Michael de Swiet** (Queen Charlotte's and Chelsea Hospital, London) pointed to thromboembolism as the leading single cause of death in the Confidential Maternal Mortality Report of 1991–1993.

Pregnancy and operative delivery are risk factors, together with thrombophilias, disorders of homocysteine metabolism, age, parity and a positive personal or family history.

Newer developments in the area of diagnosis include the use of Doppler ultrasound for deep vein thrombosis and magnetic resonance imaging for pulmonary embolism. In the area of treatment and prophylaxis, the new fractionated low molecular weight heparins are being used to reduce monitoring requirements, and for ease of administration. However, the effect of these drugs on bone demineralisation is as yet unclear, so they are not recommended as an alternative to unfractionated heparin simply to protect bone.

**References**

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