The physician in the antenatal clinic

The conference was held at the Royal College of Physicians on 1 November 1991. It brought together physicians and obstetricians to discuss their interaction in the antenatal clinic. A show of hands suggested that 60% of the audience were obstetricians and 30% physicians; the remainder may have been both or neither. Many of the talks illustrated that changes in the intrauterine environment may have long-term consequences on fetal well-being and emphasised the importance of defining ‘normal ranges’ during pregnancy.

Risk assessment

An overview of risk assessment was provided by Professor G. M. Stirratt (Bristol Maternity Hospital). Risk is the probability that a particular event will occur; therefore an ‘at risk’ pregnancy is one in which the probability of an adverse outcome in the mother and/or her baby is greater than for pregnant women in general. Risk assessment may put too great an emphasis on the death of a baby, yet the low risk of a serious condition with a bad outcome should be given more weight than the high risk of a condition with low morbidity. Risk markers are factors associated with a particular risk event and can be assessed in three ways: first, and most important, by history and examination; second by screening tests; and third by diagnostic tests. Diagnostic and therapeutic interventions have their own intrinsic risks and must be justified by risk benefit analysis in their own right. It is also imperative to consider the ethical dimension, especially in view of technical advances in medicine: although we can do this, ought we to do it? Two interesting points were raised during the discussion of this paper: first, that litigation is also a factor in risk benefit analysis; and second, that those who most need risk assessment by pre-conceptual counselling often do not receive it.

Cardiovascular disease and pregnancy

A recurring theme through the conference was that intrauterine events may be associated with morbidity in the offspring many years later. Mr S. R. Robson (University College Hospital, London) discussed the haemodynamics of normal pregnancy. Doppler analysis of blood flow provided a reliable, cheap, reproducible and non-invasive measurement of cardiac output in pregnancy. There is a slight fall in the first trimester, followed by an increase in maternal blood pressure associated with an impressive fall in vascular resistance; this is associated with a 50% increase in cardiac output. In pre-eclampsia, cardiac output is reduced, peripheral resistance is high and stroke volume may be reduced. Histologically, pre-eclampsia is associated with failure of infiltration of the trophoblast by the spiral arteries, which develop into ‘stem pipe’ vessels which do not dilate, thus causing relative ischaemia of the placenta.

Does this information about blood flow influence therapy? Patients with evidence of increased vascular resistance and an abnormally notched wave form of placental blood flow have a 25% chance to go on to develop hypertension. Vasodilation should not be attempted when a low central venous pressure gives evidence of a reduced plasma volume, as this may lead to oliguria and fetal distress. Patients with severe peripheral resistance and normal cardiac output may benefit from hydralazine, whereas those with an increased cardiac output should benefit from atenolol. These predictive measurements are not easy to carry out. However, with a low central venous pressure and oliguria, plasma volume expansion would seem sensible, but with a normal or high central venous pressure in the presence of oliguria it may be necessary, before deciding on the appropriate action, to use Swann–Ganz catheterisation for further information on the cardiovascular status.

Pregnancy-induced hypertension does not increase fetal risk but pre-eclamptic toxaemia (PET) does increase the risk. It would therefore be useful to be able to identify both of these situations. Dr M. de Swiet (Institute of Obstetrics and Gynaecology, London) showed that they inevitably overlap. Maternal hypertension is the commonest cause of maternal mortality. It is responsible for 9.4 deaths per million pregnancies, from seizures, renal failure, and especially from cerebral haemorrhage. Despite the great proliferation of hypotensive therapeutic options over the past 15 years, hydralazine remains the most commonly prescribed drug, followed by nifedipine. Diazepam is the most used anticonvulsant despite its sedative effect on mother and fetus, followed by chlorpromazine. Magnesium sulphate and phenytoin are commonly used after a seizure. Control of hypertension is therefore of paramount importance for the mother, and gentle rehydration to increase the plasma volume could be used before introducing a vasodilator drug. Although diuretics may reduce the risk of maternal oedema they exacerbate hypovolaemia which may be detrimental to the fetus.

Methyldopa reduces fetal mortality, although treating the mother’s hypertension is not the whole answer for the fetus. Methyldopa remains the most commonly prescribed hypotensive agent. Atenolol has been associated with intrauterine growth retardation, hypogly-
caemia and fetal distress. A comparison of oxrenolol with methyldopa gave a similar fetal outcome, but an increased fetal weight in the oxrenolol treated group, although other trials failed to show which of them was the more suitable treatment. Dr Swiet’s preference remains for methyldopa treatment with angiotensin converting enzyme inhibitors was associated with intrauterine death, oligohydranmios and renal failure. Early delivery is a realistic therapeutic option since fetal survival even of a very preterm infant has greatly improved.

Aspirin has been tried in the prevention of pre-eclampsia toxemia on the grounds that it increases prostacyclin levels which may produce vasodilatation. Meta-analysis of several studies has demonstrated that aspirin will improve birth weight and reduce the risk of proteinuric hypertension, but there is no proof of benefit on perinatal mortality. A collaborative low dose aspirin study (CLASP) is still in progress.

Thromboembolic disease is the second most common cause of maternal mortality. Professor I. A. Greer (Glasgow Royal Infirmary) explained that because total mortality had diminished there was now a relatively greater risk of maternal mortality from thromboembolic disease which is the result of an increase in caesarean sections. Nevertheless, the actual incidence of thromboembolic disease is rare. The incidence of deep vein thrombosis (DVT) varies from 0.07% to 2.6% depending on the method of diagnosis and mode of delivery; over the next 10 years the risk of a further DVT is 26.6%. Deep venous insufficiency may occur in 65% of legs after a treated DVT compared with 22% of non-affected legs. Virchow’s triad of stasis, vascular damage and hypercoagulability are the basis of risk factors such as operative delivery, prolonged labour, dehydration, PET, obesity, increased age and parity, and a previous history of DVT. The correct diagnosis of DVT is crucial but, because clinical diagnosis is unsatisfactory, venography and real time Doppler ultrasound assessment are the most suitable investigations. Similarly, a clinical diagnosis of pulmonary thromboembolism is unreliable and ventilation perfusion scanning is required to confirm it.

Treatment with anticoagulants is necessary in established thromboembolism or for prophylaxis. Warfarin crosses the placenta and is a teratogen, causing embryopathy in 4-5% of cases if used between 6 and 9 weeks of gestation; used late in pregnancy it may be associated with abruption of the placenta and increased risk of fetal intracerebral bleeding. Unfortunately, heparin also causes problems, although it does not cross the placenta; it may cause maternal osteoporosis, thrombocytopenia or allergic reactions. The low molecular heparins may reduce the haemorrhagic risk, but twice daily dosage is probably needed and there is little information on their use during pregnancy. Patients with recurrent problems should be warned before pregnancy. Delivery itself presents particular problems; after delivery, warfarin can be used as it does not pass into breast milk, and treatment should be continued for 6 weeks after delivery.

Management of medical disorders in pregnancy

Epilepsy and the pharmacokinetics of anti-epileptic drugs in pregnancy were reviewed by Professor P. C. Rubin (University Hospital, Nottingham). Phenytoin is associated with craniofacial and limb defects, carbamazepine is associated with craniofacial and fingernail defects, and sodium valproate is associated with neural tube defects. Drugs are only teratogenic if given during the period of embryogenesis. Early ultrasound diagnosis is now feasible for nearly all these defects, so that with suitable pre-pregnancy counselling the patient with epilepsy can come to an informed decision about her treatment. At pre-pregnancy counselling the treatment needs for epilepsy should be assessed and, if deemed suitable, treatment should be slowly withdrawn; if not, suitable treatment should be optimised, preferably with a single antiepileptic drug. It should be remembered, of course, that the seizures of untreated epilepsy are associated with maternal death and fetal hypoxia. Potential mothers with epilepsy must also be warned that they risk losing their driving licence should they have a seizure. Anticonvulsants are associated with neonatal haemorrhage, which tends to be early and severe. Vitamin K, 20 mg a day, should therefore be administered for 2 weeks before delivery. Behavioural teratogenesis was once thought to be a problem associated with these medications; however, the children of untreated and treated mothers showed no difference in intelligence. Phenytoin and carbamazepine clearance may as much as double during pregnancy; it is therefore necessary to measure plasma levels of these medications to ensure correct dosage. Phenytoin, valproate and carbamezepine are all compatible with breast feeding.

Gestational diabetes: fact or fiction?

Gestational diabetes is regarded as fiction by Professor D. R. Hadden (Royal Victoria Hospital, Belfast) and as fact by Dr M. J. A. Maresh (St Mary’s Hospital, Manchester). Professor Hadden considers that gestational diabetes is a confusing term and should not be used. There are large differences in the prevalence of diabetes first diagnosed in pregnancy, from 0.15% in Newcastle to 0.22–3.5% in Belfast, and up to 12.3% in Los Angeles; this variance may be due to the diagnostic method used as well as to real population differences. Some workers demonstrated that as many as 70% of former gestational diabetics will develop diabetes within 25 years. Yet when oral GTTs were performed on a random selection of US women, 2.5% of 20–44 year olds had diabetes, which suggests that some women already have diabetes before pregnancy and calls into question the ‘gestational’ label. Perhaps preg-
nancy *per se* has no role and advancing age identifies the diabetics. Diabetes in pregnancy is a window for the early diagnosis of non-insulin dependent diabetes (NIDDM). Interestingly, the offspring of these women are more likely to become obese in later life. Major controversy continues to surround screening and diagnostic criteria for diabetes in pregnancy. There are certainly large geographical differences in the type and incidence of diabetes in pregnancy. In the USA all pregnant women tend to be screened and, if found positive, to have a 100gm OGGT; however, in the UK clinical screening criteria are most commonly used, even though this method will inevitably be less sensitive. A random blood glucose or a test meal may have a role. We were left with the thought that to screen means to shelter, to protect from blame.

Dr Maresh pointed out than an abnormal oral GTT may identify true gestational diabetes, or undiagnosed impaired glucose tolerance already present before pregnancy, or undiagnosed type II diabetes, or the prodromal phase of type I diabetes. Fetal morbidity is influenced by an interaction of maternal age, maternal race, weight and gestational diabetes. There are obvious risks to the mother from undiagnosed type I or type II diabetes, possibly leading to ketoads. The higher caesarean section rate in diabetic pregnancy is associated with increased morbidity and mortality. Maternal obesity is more closely associated with fetal weight than with gestational diabetes, but neonatal morbidity is influenced by gestational diabetes itself. Fetal macrosomia can lead to traumatic delivery and may be avoided by early diagnosis and treatment of maternal diabetes. The 2-hour glucose concentration in pregnancy, during GTT, is proportional to the glucose levels of the child. Dr Maresh concluded that the prevention of neonatal morbidity and the unique opportunity for the early diagnosis of NIDDM in the mother lends support to the importance of diagnosing diabetes in pregnancy, whether or not it is called gestational diabetes.

**Liver disease**

Problems in the diagnosis of liver disease in pregnancy arise because physical signs and various special investigations have altered normal ranges in pregnancy. **Professor Carol Seymour** (St George’s Hospital, London) finds that helpful laboratory tests include the plasma enzymes AST and gamma GT, prothrombin time and platelet count. Jaundice in pregnancy can be classified into pre-existing liver disease, jaundice peculiar to pregnancy, and jaundice intercurrent in pregnancy. Hyperemesis gravidarum normally occurs in the first trimester and may be confused with early viral hepatitis. The raised level of alkaline phosphatase is of placental origin, although the transaminases may also be slightly elevated.

Although benign intrahepatic cholestatis (BIC) may occur from the 6th week onwards, it normally occurs in the third trimester. It must be differentiated from gallstones or viral hepatitis. Pruritus is an early feature, followed by jaundice and irritability. Although BIC has a benign course it may recur in successive pregnancies. Biochemically, the alkaline phosphatase may be 20 times normal maximum, with the transaminases only mildly elevated. After delivery the bilirubin level decreases, but the alkaline phosphatase may remain elevated. Liver biopsy is not indicated. Acute fatty liver of pregnancy occurs in the last trimester, more commonly in primiparous women. Although rare, mortality is high; the differential diagnosis is with viral hepatitis. Early features include vomiting, haematemesis, headache, abdominal pain, followed by preterm labour and vaginal bleeding. Jaundice occurs in 95%, but pruritus is rare. Bilirubin levels are raised, the prothrombin time is reduced, alkaline phosphatase levels are commonly very high, transaminases are slightly increased, and there is hypoglycaemia. On histology, the liver architecture is normal but with diffuse fatty change in the hepatocytes. Attention should be paid to the mother’s state of hydration, her caloric intake, and clotting status, diffuse intravascular coagulation must be corrected and, if caesarean section is indicated, a local rather than general anaesthetic should be used.

Viral hepatitis is a common cause of jaundice, especially type A, and it may occur in any trimester. The transaminase levels are often very high and some of the features may be similar to intrahepatic cholestasis. The virus can be transmitted through the blood or with breast feeding, and neonates can become chronic carriers. Children should be given hyperimmune gamma globulin.

**Pregnancy and the immunocompromised patient**

HIV in pregnancy was discussed by **Professor F. D. Johnstone** (Centre for Reproductive Biology, Edinburgh). Although transmission of HIV through the placenta is well documented, the relevance of transmissions to the child through the birth canal or through breast milk is unproven. Any discussion with a pregnant woman considering have an HIV test has to take into account her lifestyle, change to safe sexual practices, whether she would consider termination of the pregnancy, and her views on breast feeding. HIV in pregnancy may affect placental function or induce preterm labour. It is uncertain whether a dysmorphic syndrome is associated with HIV or whether this is due to the lifestyle of the women likely to have HIV. HIV infection makes one consider the method of delivery and protection of staff, without depersonalising care during pregnancy and delivery.

HIV testing may be done for epidemiological reasons, for public health purposes, for personal benefit, to prevent transmission to the infant, or to control infection. Tests should only be performed where specific consent is given. Their sensitivity is 95% and
specificity is 98%, creating problems when false-positive and false-negatives emerge.

There is only one recorded case of infection from staff to patient. Patient to patient infection is probably equally rare and segregation is not necessary except for toilet facilities because blood and lochia may be infectious. There are 30 documented cases of patient to staff infection; the risk in a lifetime may be as great as 1 in 3,700. Great care should be taken with needles as infection can only occur through non-intact skin or mucous membranes. Overall, HIV positive mothers should be able to enjoy normal midwifery care but special care should be taken of blood and amniotic fluid and lochia.

Viral diseases in pregnancy were discussed by Professor J. E. Banatvala (St Thomas's Hospital, London). Although around 500 pregnant women have been inadvertently infected with live rubella vaccine there is no evidence that the offspring sustained any congenital malformations. However, if possible, it is probably best to avoid live vaccines in pregnancy. Rubella is a disappearing disease, with only 1-2% of women now seronegative. The parvoviruses may cause a rubella-like syndrome with erythema infectiosum, arthritis and hydrops fetalis due to aplastic anaemia. If it is not fatal for the fetus, the fetus remains unharmed, and there is no resultant morbidity.

Influenza appears to be associated with excessive mortality in pregnant women, especially if they have pre-existing cardiac disease. Varicella can now be quickly diagnosed by examining vesicle fluid with an electron microscope. Three to four percent of infections will be teratogenic if they occur early in pregnancy when it is difficult to make a diagnosis. If, from the history alone, varicella is a possibility, immune globulin should be given by intramuscular injection.

Each year 1.6 million people travel to areas where hepatitis A is endemic. Non-A and Non-B hepatitis can also create problems, especially in Mexico, Africa and India. Hepatitis E is a more severe illness in pregnant women, and in the third trimester the mortality may be as high as 20%. Locally prepared immunoglobulins may be useful. Coxsackie B may cause a severe illness in the third trimester and is associated with myocarditis in some parts of the world. Japanese B encephalitis, found near rice fields, rain and pigs, may have a mortality as high as 20% or more in pregnant women. It is especially severe in the third trimester and may be associated with stillbirth. Haemorrhagic fevers may be especially severe in pregnant women with 30-80% mortality.

Renal disease and kidney transplantation

The contribution by Professor J. M. Davison (Princess Mary Maternity Hospital, Newcastle) dealt with an increasingly prevalent problem of pregnancy: renal disease and the kidney transplanted patient. A recurring theme of the day's talks had been the difficulty of interpreting laboratory data due to the physiological changes of normal pregnancy; this applies equally to the analysis of indicators of renal function. As with all other medical disorders in pregnancy, one has to consider the effect of chronic renal disease on the pregnancy and the effect of the pregnancy on chronic renal disease, take into account fetal and maternal prognosis, and consider pre-pregnancy counselling. It is useful, in terms of problems in pregnancy, obstetric outcome and long-term deterioration of the renal disease, to stratify the severity of renal disease before pregnancy in terms of the plasma creatinine—mild being a creatinine level less than 125, moderate 125-250 and severe greater than 250 μmol/l. In the moderate group as many as 25% have long-term renal problems related to that pregnancy, and in a severe group a successful outcome to the pregnancy could be expected only in 50%.

The problems of renal transplantation in pregnancy are best dealt with in a pre-pregnancy clinic, although it is pleasing to note that the incidence of congenital malformation is the same as in the population at large. Half will expect problems in pregnancy, but as many as 92% can expect a successful obstetric outcome. However, 12% will have long-term renal problems related to that pregnancy. The pre-pregnancy clinic assesses the general health, hypertension control and proteinuria; a creatinine level greater than 180 μmol/l, evidence of rejection and calyceal dilation would be causes for concern. The pre-pregnancy clinic should stress that parenthood extends beyond the pregnancy, and the mother should consider her own long-term health and her ability to take care of her future offspring. We were again reminded that the intrauterine environment can affect the long-term health of the fetus, and the offspring themselves may be reproducibly less successful. Cyclosporin, which is often used in the second or third transplant, is associated with 63% of pregnancy problems, 90% of successful pregnancies and 15% of problems in the long term.

Who should manage medical disorders?

A high point of the conference was the debate on the motion that medical disorders in pregnancy should be managed by physicians. Dr M. de Swiet (Institute of Obstetrics and Gynaecology, London) spoke for the motion and Professor T. Lind (Royal Victoria Infirmary, Newcastle) spoke against it. Before the debate, 25% of the audience were for the motion and 5% against it; the rest abstained. These proportions remained unchanged after the debate, perhaps because the protagonists had moved the goalposts. Both felt that medical disorders in pregnancy should be treated by physicians unless there was an obstetrician with a special interest in medical problems of pregnancy. The real argument, therefore, was whether medical diseases should be managed by a physician with a particular interest in obstetrics, or whether the
patient with a particular medical problem in pregnancy should be referred to a physician concentrating on that specialty. There could be very real problems in deciding which physician to ask for advice in the case of a pregnant woman with non-specific symptoms; furthermore, there are some particular medical problems of pregnancy. Dr de Swiet stressed that experience of working as a team with the obstetrician is essential. Professor Lind pointed out that there is not yet a training programme for the obstetric physician. He also referred to the failure of physicians to understand the physiology of normal pregnancy, misinterpreting the physiologic anaemia of pregnancy or not realising that glycosuria can be episodic and unpredictable. While there is a place for diabetologists, can a metabolic physician look after a cardiac condition? He then described the system in Newcastle, where a pregnant woman can be seen by almost any medical specialist, but it is not clear how well that would work in other district general hospitals.

It would be interesting to know how many of the audience considered themselves closer to being both obstetricians and physicians after the day’s talks.

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