OBSTETRICS FOR PAEDIATRICIANS

Premature labour

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The survival of premature infants has improved dramatically over the last 20 years, primarily as a result of the development of neonatal intensive care. As papers documenting improved survival appeared, obstetricians began taking more care over the delivery of preterm infants, leading to improved conditions at birth and thus to further improvements in survival.¹ Caesarean section rates of 40% for babies of less than 32 weeks' gestation are now common. The pace of advance has slowed over the last few years, however, and below 26 weeks' gestation or 750 g birth weight or both, major improvements in survival now seem unlikely unless there are fundamental advances in technology. This has lead obstetricians to re-evaluate their strategies with the twin aims of reducing the number of babies that are born who will survive grossly handicapped, and minimising maternal morbidity. In this paper I will survey current obstetric views on aetiology, prevention, and management of preterm labour, including the use of tocolytics and steroids, and speculate briefly on 'the way ahead'.

Aetiology

The aetiology of some preterm labours is not difficult to understand. Cervical incompetence can occur after operations (for example, conisation for cervical intraepithelial neoplasia) or as a result of congenital weakness (for example, after intrauterine exposure to diethylstilboestrol). The equivocal results of trials of cervical cerclage, however, indicate that genuine incompetence is rare, being implicated in less than 5% of cases. Uterine malformations may also give rise to preterm labour, but common ones such as a bicornuate shape are often compatible with term labour, while those such as a thin uterine septum that renders implantation insecure, are rare. The chorionic membranes become inflamed in 50–80% of premature labours, but the incrimination of specific organisms, which would then be susceptible to prophylaxis, has been unsuccessful. Beta haemolytic streptococci commonly cause serious infections in both mother and baby during preterm labour, especially if there is premature rupture of the membranes, but there is no convincing evidence that they cause the labour itself. Studies in the 1970s suggested that *Mycoplasma hominis* and *Ureaplasma urealyticum* might have a role in the aetiology, but this has been difficult to substantiate. Because preterm labour is more common among women of lower socioeconomic status, there is an association with *Chlamydia tracho-*

omatis and *Neisseria gonorrhoeae*, but there is no evidence that either is causative.

Failure to identify specific organisms that have a consistent association with preterm labour has suggested that the primary problem may lie within the immune system of the mother rather than in the nature of the infecting organism. Despite this, immunotherapy of various sorts has so far failed to prevent preterm labour. Disorders of placentation, which cause placental abruption and midtrimester bleeding, are a potent cause of preterm delivery but fortunately are uncommon, so in most cases preterm labour remains 'idiopathic', its specific aetiology unknown. It may be that in many cases it is a response to a hostile intrauterine environment and the trigger of labour lies within the fetus itself (as is probably true of term labour). This would explain why preterm labour is more common among women of lower socioeconomic status, those who smoke, those who are underweight, and those whose babies are born with retarded growth.

Interference with fetal growth associated with poor placental perfusion may occur secondary to maternal disorders such as collagen diseases, heart valve defects, diabetes, and pre-eclampsia. In such cases the risk of spontaneous premature labour is increased, and in addition it is often effected deliberately by the obstetrician to safeguard maternal or fetal health. By keeping it in its unsuitable environment, prolonging the pregnancy may place the baby at greater risk than if it is born. It seems likely that some babies respond to restricted intrauterine nutrition by reducing their growth rate, others by initiating labour, and still others by initiating labour when restricting growth is no longer a sufficient response to impaired placental function. These variations in response may reflect a genetic difference, and could be one reason why women who are born with retarded growth are more likely to have small babies themselves, whereas women who are born preterm have larger than average babies provided they carry to term. Most surveys show that clinicians choose not to give tocolytics in about half their cases of preterm labour because they are concerned about the safety of the intrauterine environment.

Primary prevention

Strategies for the prevention of preterm labour (as opposed to its control, once started) have therefore had to be aimed at improving the intrauterine environment from the beginning of

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pregnancy without the advantage of knowing the precise aetiology in most cases, so they have of necessity been wide ranging. Most studies have been educational, in attempts to reduce high risk behaviour and improve diet, and have provided emotional support from social workers, midwives, and specially trained nurses. Unfortunately most of them have failed to show any significant reduction in the number of preterm births; many wide ranging strategies are costly, and most have now been abandoned. More recently there has been a resurgence of interest in the use of antibiotics. Several small trials have suggested that some benefit may be gained from using antibiotics such as erythromycin, which is active against chlamydia and mycoplasma, as prophylaxis in early pregnancy, and broad spectrum antibiotics such as amoxycillin for preterm rupture of the membranes. These findings need confirmation by larger studies before they can be recommended.

Assessment of risk

The search has therefore continued for treatments that can be applied in a more cost effective way to smaller groups of women who have been identified as being at increased risk of preterm labour. A wide range of techniques of identifying these risks have been published during the last 20 years; careful analysis of a woman's medical and social history at the initial antenatal consultation is of some predictive value, and numerous papers have shown that smoking and a low body mass index (weight (kg)/height (m)²) indicate the largest risk. Unfortunately it is difficult to persuade those women who are most at risk to give up smoking, and underweight women are twice as likely as women of normal weight to eat poorly in pregnancy and fail to gain weight. Social factors have some influence, but are difficult to categorise and rarely generalisable. It used to be thought that pregnant women should give up work outside the home at 28 weeks, and that failing to do so could increase the risk of preterm labour. Most studies suggest, however, that women who continue in employment fare better than women who stay at home, the only exception being those engaged in heavy manual work.

The single most important predictor in multiparous women is the birth weight and gestational age at delivery of the previous baby. Chng *et al*, however, has shown that these are usually ignored by midwives and doctors at 'booking' clinics.² This may be partly because previous birth weights are usually recorded from the mother's recall, in pounds and ounces, whereas most of us are now calibrated to normal values in kilogrammes. More complex screening systems, such as those of Hobel *et al* in the USA,³ have been widely used but recent evaluations have shown them to be of no practical value.⁴

Disillusionment with historical methods has led to experiments with strategies such as the recording of preterm uterine activity with external tocodynamometers, and regular assessment of cervical compliance and dilatation by

digital examination. The latter is currently routine in many European countries including France, Belgium, and Spain. While there is a reasonable correlation between increased frequency of Braxton-Hicks contractions or an inappropriately dilated cervix and preterm delivery, up to half the women who have abnormalities of these measures will carry to term, and the techniques carry a substantial penalty in terms of cost, time, and discomfort for pregnant women. Even more importantly, they are only of real value if they allow the application of an effective treatment; currently, such treatment does not exist.

Diagnosis of preterm labour

The diagnosis of preterm labour is difficult. Placebo controlled studies of tocolytics have shown that 70% of women in apparent preterm labour and allocated to receive placebo go on to deliver at term, and therefore were not truly in labour when the diagnosis was made. The only sure way to diagnose labour remains the demonstration of progressive cervical dilatation. Careful cervical assessment should be made on all women admitted to hospital with abdominal pain, vaginal discharge or bleeding, or any other symptom suggestive of preterm labour. The assessment should be repeated if there is any sign that labour might be progressing, and again before discharge from hospital. Such examinations are often omitted on the grounds that they might provoke labour or cause infection. There is no evidence that any number of examinations when the membranes are intact, and up to three when they are ruptured, have any such effect provided that appropriate aseptic technique is used. On the other hand, there is good evidence that knowledge that delivery is imminent, thus allowing choice of an appropriate place for delivery and the attendance of paediatricians at the time of delivery, improves the chances of survival. It has been suggested that fetal breathing movements, which usually disappear in labour, might be a useful diagnostic variable. Lack of appropriate ultrasound equipment and trained personnel on labour wards out of hours have, however, prevented this from being tested in realistic clinical trials.

Tocolysis and corticosteroids

Tocolytic therapy for the prophylaxis and suppression of preterm labour became popular in the 1970s when some tocolytics such as ritodrine were massively promoted and achieved substantial 'market penetration'. Papers have now been published about at least 18 different tocolytics ranging from β sympathomimetics such as ritodrine, to prostaglandin synthetase inhibitors such as indomethacin, calcium channel blockers such as nifedipine, and direct muscle relaxants such as magnesium sulphate. While most of them can achieve suppression of uterine contractions for a limited period (usually 48 to 72 hours), which is long enough to allow corticosteroids to promote release of fetal lung surfactant, and the preparation of appropriate circumstances for delivery, none of the currently

available evidence suggests there is any improvement in neonatal survival from long term treatment. The risk to the mother of serious complications such as pulmonary oedema and hyperglycaemia is such that Kierse *et al*, after an extensive review of evidence from randomised controlled trials, recently recommended that long term treatment with any contraction suppressing agent should not be used outside clinical trials.⁵ Such a conclusion is in sharp contrast to that for corticosteroids, which are of proved benefit in all racial groups and in fetuses of both sexes, from at least 26 weeks (and possibly before) to 32 weeks' gestation.

Cervical cerclage

Cervical cerclage (putting a 'stitch', usually branded polyester (Mersilene) tape, around the cervix) has also waxed and waned in popularity during the last 20 years. Most obstetricians use the simple MacDonald procedure, in which the knot remains exposed and the suture can be removed in late pregnancy, rather than the 'Shirodkar' suture, in which there is extensive dissection of the bladder from the cervix, a buried knot, and usually caesarean delivery. It now seems that it may be of benefit where there is evidence of true cervical incompetence (for example, after previous traumatic termination of pregnancy, or cervical surgery for neoplasia), although the outcome is changed in only about 5% of those who undergo the procedure. The realisation that in cases of previously otherwise unexplained preterm labour there is no demonstrable benefit has led to a pronounced decline in the use of cerclage in such cases.

Preterm premature rupture of the membranes

The increasing success of neonatal intensive care in the 1970s led to an interventionist approach in the management of preterm rupture of the membranes, treatment with corticosteroids being followed by elective delivery after 48–72 hours. Despite the confirmed value of corticosteroids, however, hyaline membrane disease remains a major problem with early delivery, and the balance has once again swung back to conservative management. In the USA, amniocentesis is often used to detect amnionitis, but evidence of its value is lacking and it has not yet been generally accepted in the UK. This is particularly true outside teaching hospitals where there are no facilities for scanning out of hours, amniocentesis, or Gram staining and immediate culture of samples. A current worry is that the lungs of fetuses in which the liquor has been profoundly reduced for more than three weeks may fail to develop properly; this is a particular problem when the membranes rupture before 24 weeks when early delivery is not a reasonable option. In such cases termination of pregnancy may be a preferable course of action.

Management of very preterm labour

The management of established preterm labour (strictly, a 'threatened miscarriage') between 22 and 28 weeks' gestation is a particular problem.

Important decisions have to be made that centre on the viability of the infant. A recent national survey has shown that over 80% of obstetricians in this country do not favour surgical intervention (caesarean section) on fetal grounds alone at less than 26 weeks' gestation. This decision depends on accurate dating of the pregnancy, however, and preterm labour is over-represented in women who have failed to attend for antenatal care. In addition, most obstetricians would not be keen to intervene if the fetus weighed less than 650 g, principally because it is usually necessary to resort to a classical caesarean section for these very small babies, as the lower segment of the uterus is not sufficiently formed to allow the usual lower segment approach. Classical caesarean section is associated with substantial maternal morbidity, particularly in relation to subsequent pregnancies in which uterine rupture can be a catastrophic complication and repeat caesarean section is mandatory. A third of babies below 28 weeks' gestation present by the breech, so determining presentation is also vital. Estimation of fetal size and presentation, therefore, remain the cornerstone of appropriate management. Unfortunately these require good ultrasound equipment and obstetricians who are skilled ultrasonographers; currently these are available for 168 hours a week in only a minority of British maternity units.

Fetal monitoring and resuscitation

It is now well established that if fetuses of 26 to 36 weeks' gestation are monitored with continuous cardiotocography and fetal blood sampling, the criteria for normality are similar to those for term fetuses. The differences are that very preterm fetuses have less baseline variability in fetal heart rate, the normal quiet/active sleep cycling is often absent, and there are often small (<40 beats/minute), short (<20 seconds), decelerations that do not seem to have sinister implications. Normal ranges of fetal blood gas and pH values are similar to those at term. Whether babies of less than 26 weeks' gestation or with an estimated weight of less than 650 g should have continuous fetal monitoring is controversial. One view is that if intervention on fetal grounds is not contemplated, then the fetus should not be monitored as it may upset the mother and staff if it becomes abnormal and there is no intervention. Those who believe this also advocate the view that if the fetus has been 'written off' in this way by the obstetrician, the paediatrician should not be asked to attend the delivery. They suggest that if the paediatrician attends, and sees signs of life even in a very tiny baby, resuscitation is obligatory.

A second view is that a senior paediatrician should attend all such deliveries, and then make an objective decision as to whether the baby should be actively supported or not. He may be helped in such a decision by knowledge of the fetal heart rate pattern, and even occasionally by measurement of blood gases and pH from the umbilical cord. An extension of this approach is that the baby should be resuscitated and stabilised, after which a decision to continue or

remove support can be made. This course of action, however, runs the risk that the 'window of opportunity' during which nature can be allowed to take its course may pass. In the light of finite resources and the need to use those available most effectively, obstetricians and paediatricians must coordinate their efforts closely if this issue is to be resolved.

Mode of delivery of a preterm infant

The mode of delivery of a preterm infant has been a contentious issue during the 1980s. A recent survey showed that it is now widely accepted that—for the baby being born head first—there is no need to do a routine forceps or caesarean section, whatever the gestation, unless there is a specific fetal indication such as a severely abnormal heart rate pattern or acidosis. At one time it was widely believed that because preterm infants have a much higher incidence of low Apgar scores at birth, this reflected 'birth asphyxia' and thus labour was intrinsically more stressful for the preterm than the term infant. Two factors have changed this view. Firstly, it is now appreciated that low Apgar scores do not necessarily indicate 'birth asphyxia' if biochemical disturbance including hypoxia and acidosis is meant. Half of all mature babies born with low Apgar scores do not have acidosis, and this proportion is even greater among preterm infants who usually have cord blood oxygen tension and pH similar to those of term babies at birth.⁶ Secondly, we now know that the reason for the increased incidence of low Apgar scores in preterm babies is usually immaturity such that respiratory effort, tone, and reflex irritability are less well developed than in the term baby. This is an effect of gestational age and is not produced by impaired placental gas exchange.

The picture in relation to the preterm fetus in the breech position is not so clear cut. A substantial number of retrospective studies have reported lower mortality and morbidity when preterm fetuses in the breech position were delivered by caesarean section. Unfortunately the studies were all retrospective and uncontrolled, and it is inappropriate to compare a planned caesarean section with senior obstetric and paediatric staff present with an unexpected vaginal delivery supervised by less experienced staff in a cold accident and emergency department. For the last 20 months a multicentre randomised controlled trial of the mode of delivery of the preterm (26–32 weeks' gestation) breech has been underway in 22 centres in the UK. Recruitment has, however, been slow, with only 10% of eligible cases being randomised, which seems to reflect obstetricians' reluctance

to abandon individualised management even in the presence of uncertainty. The need for the trial has been emphasised by the finding that so far two babies allocated to vaginal delivery remained undelivered until after 32 weeks, and a further two were in cephalic presentation at delivery.

In utero transfer

The benefit of in utero transfer for the baby is well attested. The risks to the mother of delaying delivery to allow transfer are sometimes less well appreciated. This is particularly true of those with fulminating pre-eclampsia or eclampsia; during the last 15 years hypertensive disorders of pregnancy have been the leading cause of maternal mortality. The onset of eclampsia indicates that immediate delivery is necessary to safeguard maternal health; transfer by ambulance of women at risk of fitting is too dangerous to be justified. In a recent national survey of triplet pregnancies, the case was reported of a woman whose delivery was delayed for some days until a neonatal unit able to take her babies was found; after delivery she died from the complications of her pre-eclampsia.

The way ahead

It seems unlikely, given the complexity of the problem, that there will be any sudden 'break-throughs' in the prevention of preterm labour. Work must continue to elucidate the various causes in the hope of finding specific treatments for specific causes. In the meantime we must attempt to improve our management by properly designed controlled trials such as those that have confirmed the efficacy of treatment with corticosteroids. The greatest practical benefits in the short term are likely to flow from the increasing involvement of senior obstetricians, and the provision of adequate ultrasound and fetal monitoring facilities on all labour wards.

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