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Premature babies and their problems

The World Health Organization (WHO) defines prematurity as babies born before 37 weeks from the first day of the last menstrual period. Worldwide, it is estimated more than 1 in 10 infants were born preterm in 2013, accounting for approximately 15 million premature babies [1].

In England and Wales in 2019, there were almost 50,000 infants born at less than 37 weeks of gestation, which was about 8% of all live births. 10,500 were born at less than 33 weeks and 3,000 were born at less than 28 weeks [2].

There is a marked gradation in terms of severity of the problem with increasing prematurity:

- A baby born at 36 weeks will probably be a little slow to feed.
- A baby born before 33 weeks will have more serious problems including, possibly, immature lungs.
- Birth before 28 weeks causes very significant problems but the survival rate is quite remarkable.

It is not uncommon for babies to be both early and to have intrauterine growth restriction (IUGR), which adversely affects their prognosis. IUGR is a condition where the baby's growth slows down or becomes static while still in the uterus. It is part of a wider group referred to as small for gestational age (SGA) fetuses where the fetus is smaller than expected for the gestational age. The SGA includes fetuses which are constitutionally small and those whose growth has been restricted.

Preterm survival at the earliest gestational ages has improved dramatically in developed countries, where the limit of viability has extended to 22-23 weeks of gestation. However survival at these gestational ages in developing countries is rare. Quoting survival figures may be misleading as they will vary considerably amongst units and with gestational age, ethnicity, sociodemographic and genetic factors [1] .

Improving survival at lower gestations and weight makes it challenging for health professionals and parents to choose the right course of action for babies born at limits of viability. The Royal College of Obstetricians and Gynaecologists (RCOG) has published new guidance to help with this difficult issue [3]. The RCOG guidance recommends that if the birth weight is less than 500 g, resuscitation should only be performed after most careful consideration.

Presentation

The baby who is also small for gestational age (SGA) may have little subcutaneous fat and the skin may appear wrinkled.

Because mortality rates have fallen, the focus for perinatal interventions is to reduce long-term morbidity, especially the prevention of brain injury and abnormal brain development. The premature baby faces a number of problems (these may be accentuated if there is also IUGR):

- Hypothermia is a great risk, especially if there is little subcutaneous fat. A premature baby is less able to shiver and to maintain homeostasis.
- Hypoglycaemia is also a risk, especially if SGA. There may also be hypocalcaemia. Both can cause convulsions that may produce longterm brain damage.
- The more premature the baby, the greater the risk of respiratory distress syndrome. Steroids before delivery may reduce the risk but it is still very real. If the baby requires oxygen it must be monitored very carefully as, if the levels are too high, the premature baby is susceptible to retrolental fibroplasia and blindness.
- The premature baby is more susceptible to neonatal jaundice and to kernicterus at a lower level of bilirubin than a more mature baby ^[4].

- They are susceptible to infection and to necrotising enteritis.
- They are susceptible to intraventricular brain haemorrhage with serious long-term effects.

All these are problems faced by the neonatologist in the Special Care Baby Unit (SCBU) but, when the baby is eventually discharged from hospital and goes home with the family, that is not the end of problems. The baby who is just slightly premature will probably have few or no long-term problems but those who are very premature and who have a stormy start to life often suffer many and serious problems.

Long-term problems of premature babies

Morbidity is inversely related to gestational age; however, there is no gestational age (including term) that is wholly exempt $^{\left[5\right]}$. Data from EPICure studies confirm that prevalence of neurodevelopmental impairment was significantly associated with the length of gestation, with greater impairment as length of gestation decreased (45% at 22–23 weeks, 30% at 24 weeks, 25% at 25 weeks and 20% at 26 weeks $^{\left[6\right]}$. Cerebral palsy was present in 14% of the survivors from this group. There is some evidence that the incidence of cerebral palsy is falling in premature babies born between 28–31 weeks $^{\left[7\right]}$. Figures about outcomes for premature babies have to be interpreted with a degree of circumspection to be sure that like is being compared with like:

- Percentages should be taken with caution.
- Different studies use different criteria for the degree of prematurity for inclusion.
- There is a gradation of risk.
- Being both premature and small for dates would seem to add further to the risk.

A large French study followed up 5,567 neonates born alive in 2011 at 22–34 completed weeks of gestation, with 4,199 survivors at 2 years (corrected age) included in follow-up. The rates of survival and survival without severe or moderate neuromotor or sensory disabilities increased during a period of two decades, but these children remained at high risk of developmental delay. There was a statistically important decrease in the rate of cerebral palsy but the risk of developmental delay was high, even in children born moderately preterm [8] .

Cerebral palsy [9]

Children born preterm are at increased risk of cerebral palsy. The prevalence increases with decreasing gestational age. Independent risk factors include:

- Grade 3 or 4 intraventricular haemorrhage.
- Cystic periventricular leukomalacia.
- Neonatal sepsis.
- Bronchopulmonary dysplasia for which mechanical ventilation was still needed at 36 weeks' postmenstrual age.
- Antenatal steroids not given.
- Postnatal steroids given to babies born before 32+0 weeks of gestation.

Sight and hearing

About 1 in 4 babies with birth weight below 1.5 kg have peripheral or central hearing impairment, or both [10].

Infants who undergo early screening and treatment for retinopathy of prematurity (ROP) have improved long-term functional and structural outcomes compared with those who receive conventional screening and treatment $^{[11]}$. However, the increased survival of lower birth-weight infants has increased the prevalence of aggressive, posterior ROP that may be unresponsive to conventional treatment. In a multicentre study, 66% of babies under 1.25 kg developed ROP, but only 6% required treatment $^{[12]}$.

Childhood hospital admissions

Extremely low birth-weight children (birth weight 500-999 g) have more hospital re-admissions and other health problems in the early years after discharge than do normal birth-weight children (birth weight >2499 g). Respiratory illnesses, including lower respiratory infections, are the dominant cause for hospital re-admission [13].

Initial severity of bronchopulmonary dysplasia (BPD) is an important predictor of pulmonary function abnormality and healthcare use during childhood [14].

Follow-up to school

Cognitive and neuromotor impairments at 5 years of age increase with decreasing gestational age. Many of these children need a high level of specialised care ^[15]:

- About half of infants born at 24-28 weeks of gestation have a disability at 5 years, similar to the proportion observed in the UKbased EPICure study [16].
- In the infants born later (29-32 weeks of gestation), about a third have a disability at 5 years.

Behavioural and psychomotor problems

A study from Liverpool has looked at children aged 7 and 8 who were born before 32 weeks and who were well enough to attend mainstream school [17]. They were compared with full-term children of similar age in their class at school:

- Disabilities can be subtle and numerous and so a range of tests was used.
- The preterm children had a higher incidence of motor impairment and this affected how well they did at school even when their intelligence was normal.
- Over 30% had developmental co-ordination disorder (DCD) compared with 6% of classmates.
- The preterm children were significantly more likely to be overactive, easily distractible, impulsive, disorganised and lacking in persistence. They also tended to overestimate their ability.

- Attention deficit hyperactivity disorder (ADHD) was found in 8.9% of the preterm children and 2% of controls.
- The children who had been the most premature were not necessarily those with the lowest scores.

Although major disabilities have been reduced, the levels of disability tested in this study did not seem lower than those found in children born 10 or 20 years earlier, despite improvements in care of the newborn.

Emotional development - teens and beyond

A study of teenagers in mainstream schools who were born before 29 weeks of gestation showed that, compared with mainstream classmates, they have higher levels of parent- and teacher-reported emotional, attentional, and peer problems well into their teens. Despite these problems, they do not show signs of more serious conduct disorders, delinquency, drug use, or depression [18].

A study of those aged 18 and 19 years who were born before 33 weeks of gestation showed that they had different personalities from controls with increased neuroticism and decreased extraversion scores. This was more marked in females than in males [12].

A study of preterm children who had reached 19-22 years of age showed that they were, on average, shorter than their contemporaries, more likely to use prescription medicines and less likely to have attended higher education [19]

Developmental follow-up^[9]

The National Institute for Health and Care Excellence (NICE) has published recommendations for the follow-up of babies born prematurely. In addition to identifying the types of problems and the likelihood of them being present, the guideline also suggests rationales for follow-up.

Enhanced surveillance by a developmental team up to 2 years (corrected age) is suggested for children born preterm who are at increased risk of problems:

• Have a developmental problem or disorder.

- Increased risk of developmental problems or disorders, based on the following criteria:
 - Born before 30+0 weeks of gestation.
 - Born between 30+0 and 36+6 weeks of gestation and one or more of the following risk factors:
 - Brain lesion on neuroimaging, likely to be associated with developmental problems or disorders (for example, grade 3 or 4 intraventricular haemorrhage or cystic periventricular leukomalacia).
 - Grade 2 or 3 hypoxic ischaemic encephalopathy in the neonatal period.
 - Neonatal bacterial meningitis.
 - Herpes simplex encephalitis in the neonatal period.

NICE recommends considering enhanced developmental support and surveillance by a multidisciplinary team up to 2 years (corrected age) for children born preterm who do not meet the above criteria but are suspected of being at increased risk of developmental problems or disorders.

NICE also recommends a face-to-face developmental assessment at 4 years (uncorrected age) for all children born before 28+0 weeks of gestation.

Prevention

Interventions to reduce the morbidity and mortality of preterm birth can be primary (directed to all women), secondary (aimed at eliminating or reducing existing risk), or tertiary (intended to improve outcomes for preterm infants)^[20]. Most efforts so far have been tertiary interventions.

- Primary problems of social deprivation, poor maternal nutrition and substance abuse must all be addressed. Smoking should cease and, as explained in the article on fetal alcohol syndrome, alcohol consumption should be avoided, as there may be no safe lower limit.
- Secondary antenatal care is important and should be easily accessible to all women.

Tertiary - interventions when complications arise - eg, regionalised care, treatment with antenatal corticosteroids, tocolytic agents and antibiotics. More recently the role of progesterone treatment for women at risk of preterm labour, to prevent preterm birth, has been recognised [21].

Parental support

When a baby is in the SCBU it is a very emotional and traumatic time for any parent. They should be encouraged to visit and stay with the baby as much as possible. Breastfeeding may be rather difficult but it should be encouraged. Breast milk is the best food for any baby but especially premature babies. Mothers who are producing more than their own baby's needs should be encouraged to donate to the local SCBU as it is always welcome.

The baby is attached to monitors and has tubes in and out of the body. It may not be possible to hold the baby or it may not be possible to do so for long. This should be encouraged as much as is compatible with the safety of the baby but bonding is much more difficult than with a normal, healthy, full-term baby.

Whilst trying to keep a positive attitude, a parent must also come to terms with the fact that the baby could die. There may also be difficult decisions about switching off ventilators and the expected quality of life if the child survives. Communicating in these situations can be difficult and parents may have trouble taking in what they are told at such an emotional time [22] . They may wish to discuss matters with the familiar face of their family doctor who is outside the hospital but who understands the issues involved.

Ethical issues

The success of improved survival in very premature infants has raised some serious ethical issues. It is now possible to save more, smaller and earlier babies. The difficult question is whether this is always in the best interest of the baby, their parents and society in general. Decisions pertaining to these sensitive issues are influenced by a number of factors, not least by parental views [23] .

- Such babies have a very high incidence of both physical and behavioural problems. There may be blindness, deafness, mental handicap or ADHD. The quality of life of the surviving child can be difficult to assess.
- The term bed-blockers is usually used pejoratively of the elderly; however, tiny, very early babies spend a very long time in SCBU cots that are in short supply. They may be depriving other babies of facilities from which they would extract greater benefit. The cost of SCBU care is also very high and finance is not a limitless resource.
- However, premature babies can become extremely productive, as shown by the list of famous premature babies on the premature babies UK website. It includes Albert Einstein, Isaac Newton and Charles Darwin.
- Who could ever make the decision that the quality of life salvaged is not worthy of the effort and cost? When would it be better to let tiny babies die? This is a very difficult question that will raise much passion and prejudice but it is an extremely important issue that does require sober assessment.
- The high survival rates that are achieved by some units for very premature babies have fuelled a debate about the upper limit for termination of pregnancy.

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