ABC of preterm birth

Epidemiology of preterm birth

Janet Tucker, William McGuire

Preterm birth is a major challenge in perinatal health care. Most perinatal deaths occur in preterm infants, and preterm birth is an important risk factor for neurological impairment and disability. Preterm birth not only affects infants and their families—providing care for preterm infants, who may spend several months in hospital, has increasing cost implications for health services.

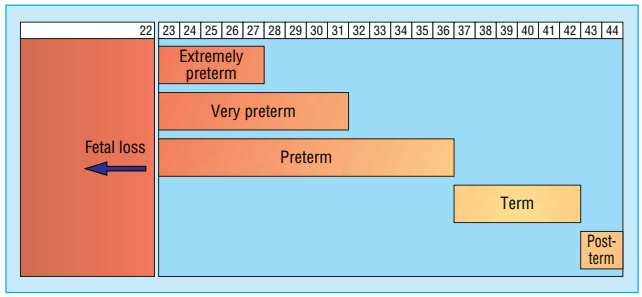
This is the first in a series of 12 articles

Extremely preterm infant born at 26 weeks' gestation

Definitions

Preterm birth is the delivery of a baby before 37 completed weeks' gestation. Most mortality and morbidity affects "very preterm" infants (those born before 32 weeks' gestation), and especially "extremely preterm" infants (those born before 28 weeks of gestation).

Over the past 20-30 years advances in perinatal care have improved outcomes for infants born after short gestations. The number of weeks of completed gestation that defines whether a birth is preterm rather than a fetal loss has become smaller. In 1992 the boundary that required registration as a preterm live birth in the United Kingdom was lowered from 28 completed weeks' gestation to 24 weeks' gestation. This boundary varies internationally, however, from about 20 to 24 weeks. Some classification of fetal loss, still birth, and early neonatal death for these very short gestations may be unreliable.



Definitions of preterm live births by completed weeks of gestation

Gestational age versus birth weight

Even in developed countries, there is often uncertainty and incomplete recording of estimates of gestation. In most of the United Kingdom data on birth weight data but not on gestational age are collected routinely.

Although some concordance exists between the categories of birth weight and gestational age, they are not interchangeable. The categories for birth weight are:

- Low birth weight (< 2500 g)
- Very low birth weight (< 1500 g)
- Extremely low birth weight (< 1000 g)

Only around two thirds of low birth weight infants are preterm. Term infants may be of low birth weight because they are "small for gestational age" or "light for date" infants. These infants are usually defined as below the 10th centile of the index population's distribution of birth weights by gestation—that is, in the lowest 10 per cent of birth weights.

Preterm infants may also be small for gestational age. They may have neonatal problems additional to those related to shortened gestation, particularly if they are small because of intrauterine growth restriction.

Perinatal problems related to intrauterine growth restriction include:

- Perinatal death
- Fetal distress
- Meconium aspiration syndrome
- Hypoglycaemia
- Polycythaemia or hyperviscosity
- Hypothermia.

Preterm infant born at 35 weeks' gestation

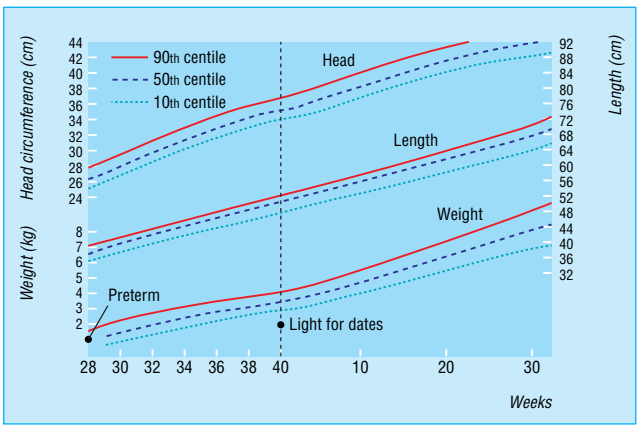


Chart for plotting progress of newborn infants' weight, head circumference, and length (with two examples)

Incidence

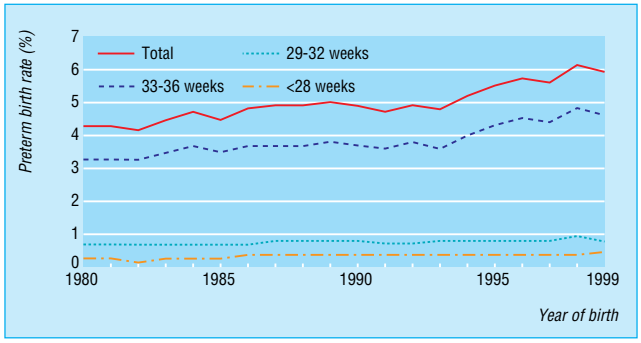
Over the past 20-30 years the incidence of preterm birth in most developed countries has been about 5-7% of live births. The incidence in the United States is higher, at about 12%. Some evidence shows that this incidence has increased slightly in the past few years, but the rate of birth before 32 weeks' gestation is almost unchanged, at 1-2%.

Several factors have contributed to the overall rise in the incidence of preterm birth. These factors include increasing rates of multiple births, greater use of assisted reproduction techniques, and more obstetric intervention.

Part of the apparent rise in the incidence of preterm birth, however, may reflect changes in clinical practice. Increasingly, ultrasonography rather than the last menstrual period date is used to estimate gestational age. The rise in incidence may also be caused by inconsistent classification of fetal loss, still birth, and early neonatal death. In some countries, infants who are born after very short gestations (less than 24 weeks) are more likely to be categorised as live births.

With the limited provision of antenatal or perinatal care in developing countries, there are difficulties with population based data. Registration of births is incomplete and information is lacking on gestational age, especially outside hospital settings. Data that are collected tend to give only estimates of perinatal outcomes that are specific to birth weight. These data show that the incidence of low birth weight is much higher in developing countries than in developed countries with good care services.

In developing countries, low birth weight is probably caused by intrauterine growth restriction. Maternal undernutrition and chronic infection in pregnancy are the main factors that cause intrauterine growth restriction. Although the technical advances in the care of preterm infants have improved outcomes in developed countries with well resourced care services, they have not influenced neonatal morbidity and mortality in countries that lack basic midwifery and obstetric care. In these developing countries, the priorities are to reduce infection associated with delivery, identify and manage pregnancies of women who are at risk, and provide basic neonatal resuscitation.



Rates of preterm birth, by gestational age, in singleton live births in New Zealand, 1980-99

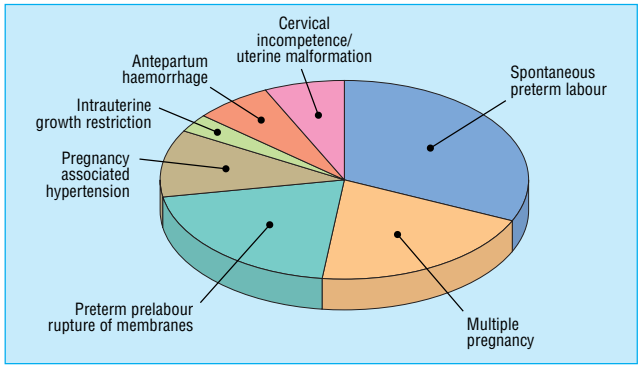
Percentage of preterm births in United States*

Year	Gestational age <37 weeks	Gestational age <32 weeks
1981	9.4	1.81
1990	10.6	1.92
2000	11.6	1.93

*Adapted from MacDorman MF et al. *Pediatrics* 2002;110: 1037-52

Risk factors for babies with low birth weight in developing countries

- Infection, especially malaria
- Poor maternal nutrition
- Maternal anaemia
- Low maternal body mass index before pregnancy
- Short interval between pregnancies



Causes of preterm birth

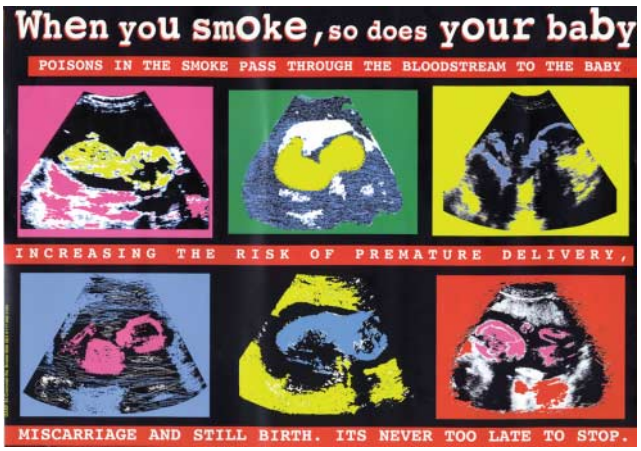
Causes of preterm birth

Spontaneous preterm labour and rupture of membranes
Most preterm births follow spontaneous, unexplained preterm labour, or spontaneous preterm prelabour rupture of the amniotic membranes. The most important predictors of spontaneous preterm delivery are a history of preterm birth and poor socioeconomic background of the mother.

Interaction of the many factors that contribute to the association of preterm birth with socioeconomic status is complex. Mothers who smoke cigarettes are twice as likely as non-smoking mothers to deliver before 32 weeks of gestation, although this effect does not explain all the risk associated with social disadvantage.

Evidence from meta-analysis of randomised controlled trials shows that antenatal smoking cessation programmes can lower the incidence of preterm birth. Women from poorer socioeconomic backgrounds, however, are least likely to stop smoking in pregnancy although they are most at risk of preterm delivery.

No studies have shown that other interventions, such as better antenatal care, dietary advice, or increased social support during pregnancy, improve perinatal outcomes or reduce the social inequalities in the incidence of preterm delivery.



Smoking cessation programmes can lower the incidence of preterm birth

The rate of preterm birth varies between ethnic groups. In the United Kingdom, and even more markedly in the United States, the incidence of preterm birth in black women is higher than that in white women of similar age. The reason for this variation is unclear because differences remain after taking into account socioeconomic risk factors.

Multiple pregnancy and assisted reproduction

Multifetal pregnancy increases the risk of preterm delivery. About one quarter of preterm births occur in multiple pregnancies. Half of all twins and most triplets are born preterm. Multiple pregnancy is more likely than singleton pregnancy to be associated with spontaneous preterm labour and with preterm obstetric interventions, such as induction of labour or delivery by caesarean section.

The incidence of multiple pregnancies in developed countries has increased over the past 20-30 years. This rise is mainly because of the increased use of assisted reproduction techniques, such as drugs that induce ovulation and in vitro fertilisation. For example, the birth rate of twins in the United States has increased by 55% since 1980. The rate of higher order multiple births increased fourfold between 1980 and 1998, although this rate has decreased slightly over the past five years. In some countries two embryos only are allowed to be placed in the uterus after in vitro fertilisation to limit the incidence of higher order pregnancy.

Singleton pregnancies that follow assisted reproduction are at a considerable increased risk of preterm delivery, probably because of factors such as cervical trauma, the higher incidence of uterine problems, and possibly because of the increased risk of infection.

Maternal and fetal complications

About 15% to 25% of preterm infants are delivered because of maternal or fetal complications of pregnancy. The principal causes are hypertensive disorders of pregnancy and severe intrauterine growth restriction, which is often associated with hypertensive disorders. The decision to deliver these infants is informed by balancing the risks of preterm birth for the infant against the consequence of continued pregnancy for the mother and fetus. Over the past two decades improved antenatal and perinatal care has increased the rate of iatrogenic preterm delivery. During that time the incidence of still birth in the third trimester has fallen.

Outcomes after preterm birth

Broadly, outcomes improve with increasing gestational age, although for any given length of gestation survival varies with birth weight. Other factors, including ethnicity and gender also influence survival and the risk of neurological impairment.

The outcomes for preterm infants born at or after 32 weeks of gestation are similar to those for term infants. Most serious problems associated with preterm birth occur in the 1% to 2% of infants who are born before 32 completed weeks' gestation, and particularly the 0.4% of infants born before 28 weeks' gestation. Modern perinatal care and specific interventions, such as prophylactic antenatal steroids and exogenous surfactants, have contributed to some improved outcomes for very preterm infants. The overall prognosis remains poor, however, particularly for infants who are born before 26 weeks' gestation.

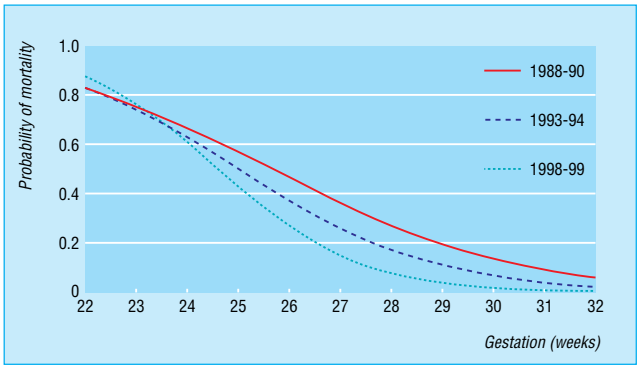
The outcome for preterm infants of multiple pregnancies can be better than that of singleton pregnancies of the same gestation. In term infants the situation is reversed. The improved outcome for preterm infants of multiple pregnancies has been attributed to closer surveillance of the mother and

Preterm births by ethnic group in United States 2000*

- Black—17.3%
- Hispanic—11.2%
- Non-Hispanic white—10.4%

*Adapted from MacDorman MF et al. *Pediatrics* 2002;110:1037-52

Twin pregnancy increases the risk of preterm birth



Mortality in UK neonatal intensive care cohorts of infants born before 32 weeks' gestation. Adapted from Parry G, et al. *Lancet* 2003;361:1789-91

Outcomes for infants live born before 26 weeks' gestation in British Isles*

Gestation (weeks)	Survival to discharge (%)	Survival without handicap at 30 months (%)
22	1	0.7
23	11	5
24	26	12
25	44	23

*Adapted from Wood NS et al. *New Engl J Med* 2000;343:378-84

preterm obstetric intervention. As preterm multiple births are more likely to follow spontaneous preterm labour, the frequency of adverse factors—for example, severe intrauterine growth restriction, placental abruption, and fetomaternal infection—is lower than for preterm singletons.

Conclusion

The outcomes for preterm infants have improved greatly over the past 20-30 years in developed countries. Continued research is needed, however, to define the aetiology of preterm birth and identify interventions that will reduce its incidence.

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The ABC of preterm birth is edited by William McGuire, senior lecturer in neonatal medicine, Tayside Institute of Child Health, Ninewells Hospital and Medical School, University of Dundee; and Peter W Fowlie, consultant paediatrician, Perth Royal Infirmary and Ninewells Hospital and Medical School, Dundee. The series will be published as a book in spring 2005.

Competing interests: WMcG received a grant from Pfizer UK for a national study of fungal infection in preterm infants.

Further reading

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The figure showing the definition of live births is adapted from Dunn PM, McIllwaine G, eds. *Perinatal audit: a report for the European Association of Perinatal Medicine*. London: Parthenon, 1996. The graph showing rates of preterm birth by gestational age group is adapted from Craig ED et al. *Arch Dis Child* 2002;86:142-6. The poster promoting smoking cessation in pregnancy is reproduced with permission from Group Against Smoking in Public, Bristol.

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Down the cascade

When Dan's wife called on Monday morning—my busiest day—and asked if I could see Dan urgently, I mentally said no but found myself telling her to come. She was impossible to refuse; Dan was one of those favourite patients who remind you how successful (and lucky) you both were.

Eight years ago, at the age of 70, he came to me complaining of weight loss and anorexia, certain that he has incurable cancer. When coeliac disease was diagnosed and responded completely to a gluten-free diet, his relief was touching. Later, he needed cardiac surgery and came again to get my blessing. Examination revealed high grade carotid artery stenosis, and a search of the evidence led me to recommend carotid endarterectomy preceding cardiac surgery by two teams on the same operation. This was something of a novelty at the time, and when it was completed Dan was ecstatic and continued to come to me, regular as clockwork. We were happy to see each other on those occasions, particularly as there was nothing much to do.

Now was different: Dan had had a sleepless night with abdominal pain of sudden onset. When I saw Dan he looked ill and worried. Faithful to my credo that taking a good history was the most important test, I listened, rarely intervening. Even before I touched him, my opinion was made: I was getting a classic history of biliary colic, and finding right upper quadrant tenderness supported it. I reassured Dan, explaining that he probably had acute cholecystitis, and sent him for further evaluation by a surgeon.

That was a fateful turning point. The irony is that everyone did what they should have done. Each and every decision was sensible by itself and justified according to the latest evidence. Yet the end result was a total disaster.

The surgeon confirmed my diagnosis. The patient was comfortable by now, without fever and with normal blood test results and an innocent looking common bile duct on ultrasound. He wanted to go home, but he was admitted and given parenteral antibiotics. When, on the third day in hospital, a single spike of fever was recorded, the patient had an endoscopic retrograde cholangiopancreatography performed almost at once. No significant obstruction was identified, but sphincterotomy followed, extracting some small stones.

The next day Dan had more abdominal pain and vomiting. A nasogastric tube was inserted. Dan became more cachectic and hypoalbuminaemic each day, and his temperature and white blood cell count rose markedly. Soon he had most of Ranson's or Glasgow criteria predicting a patient at a high risk of death from necrotising pancreatitis. The fever persisted despite massive antibiotics. Protocol demanded a guided pancreatic aspiration, and when that yielded bacteria Dan had surgery. It was remarkable that his diseased heart had held up so far. Intubated and ventilated in the intensive care unit, he was to remain there for more than a fortnight, undergo another laparotomy to debride necrotic tissue and leave the abdomen open for further manipulations, undergo tracheostomy, and remain in limbo hanging on to his life by a thread.

I have often told my students and residents about cascades in medicine. Never before have I seen one that was so correct in each step, yet so inevitably doomed. At first I blamed the sphincterotomy, then the cholangiopancreatography. Now, I feel that, had I given Dan an injection of ketorolac on that busy Monday morning and sent him home to take a nap and return in four weeks' time for a cholecystectomy, things might have been radically different for all of us.

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