

## ABC of preterm birth

# Neurodevelopmental outcomes after preterm birth

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The major clinical outcomes that are important to preterm infants and their families are survival and normal long term neurodevelopment. In developed countries over the past 30 years, better perinatal care has considerably improved these outcomes. This article covers the prevalence of neurodevelopmental problems and their types.

## Prevalence

For most preterm infants of > 32 weeks' gestation, survival and longer term neurodevelopment are similar to those of infants born at term. Overall, outcomes are also good for infants born after shorter gestations. Most infants survive without substantial neurodevelopmental problems and most go on to attend mainstream schools, ultimately living independent lives.

A few preterm babies, however, do develop important and lasting neurodevelopmental problems. The period between 20 and 32 weeks after conception is one of rapid brain growth and development. Illness, undernutrition, and infection during this time may compromise neurodevelopment. The clinical consequences can include serious neuromotor problems (principally cerebral palsy), visual and hearing impairments, learning difficulties, and psychological, behavioural, and social problems.

Most substantial impairment occurs in the 0.2% of infants born before 28 weeks' gestation, or with birth weights of < 1000 g (extremely low birth weight). The survival rate for extremely preterm infants has improved over the past decade, but the overall prevalence of neurodisability after preterm birth has not fallen. In a recent North American follow up study of extremely low birthweight infants, one quarter of the children had neurological abnormalities when examined at 18 to 22 months post term.

### Prevalence of neuromotor and sensory findings at 18 months in extremely low birthweight infants\*

#### Abnormal neurological examination—25%

- Cerebral palsy—17%
- Seizure disorder—5%
- Hydrocephalus with shunt—4%

#### Any vision impairment—9%

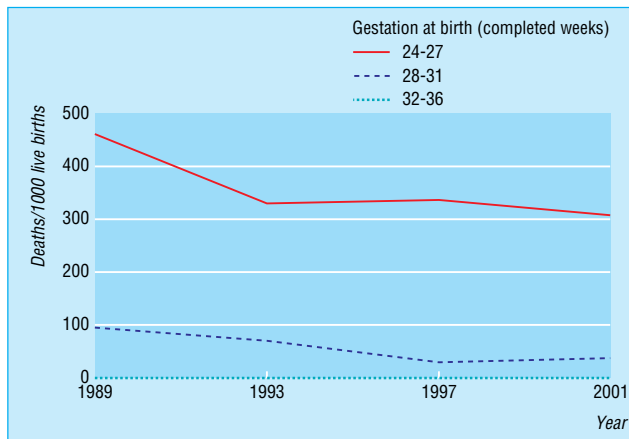
- Unilateral blindness—1%
- Bilateral blindness—2%

#### Hearing impairment—11%

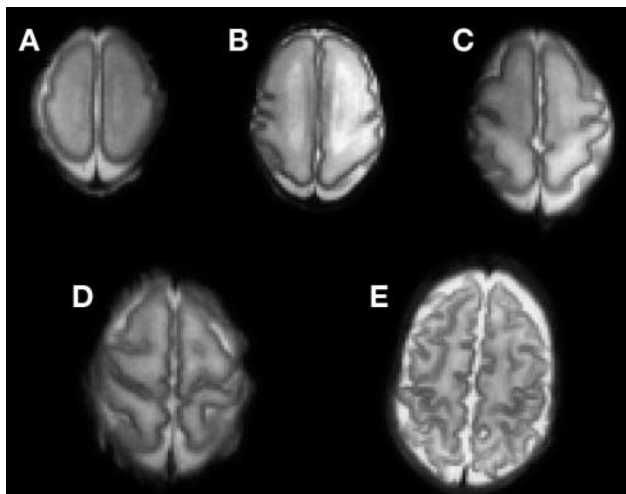
- Wears hearing aids—3%

\*Adapted from Vohr BR et al. *Paediatrics* 2000;105:1216-26

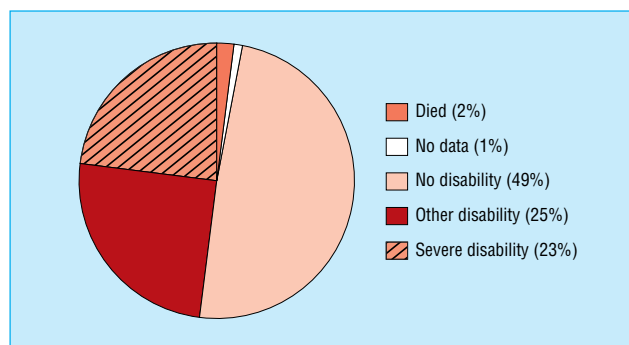
In the United Kingdom, the EPICure Study Group has evaluated outcomes for surviving infants born before 26 weeks' gestation. At a median age of 30 months (corrected for gestational age), about half the children had disability and about half of these children had severe disability. Severe disability is defined as impairments that will probably put the child in need of assistance to perform daily activities. The prevalence of disability remained high when the children were reassessed at 6 years, with less than half of them having no evidence of impairment.



Neonatal death rate for preterm infants in Scotland since 1989 (deaths per 1000 live births by gestational age band). Adapted from Scottish perinatal and infant mortality and morbidity report, 2001



Brain growth and development of sulcation and gyration with increasing gestational age. Magnetic resonance images at the level of the central sulcus at: (A) 25 weeks; (B) 28 weeks; (C) 30 weeks; (D) 33 weeks; and (E) 39 weeks. With permission from Counsell SJ et al. *Arch Dis Child* 2003;88:269-74



Outcomes for surviving infants born before 26 weeks' gestation when assessed at 30 months. Adapted from Wood NS et al. *N Engl J Med* 2000;343:378-84

## Cerebral palsy

Most children with cerebral palsy were not born preterm. However, preterm infants, particularly those born after very short gestations, are at increased risk of cerebral palsy. Additional specific perinatal risk factors for cerebral palsy in preterm infants include fetomaternal infection, neonatal sepsis, and other severe illness in the newborn period.

Brain damage related to periventricular haemorrhage, particularly periventricular cystic leucomalacia and posthaemorrhagic hydrocephalus are strong predictors of future neurodevelopmental problems, especially cerebral palsy.

The most common forms of cerebral palsy in children who have been born preterm are spastic hemiplegia (unilateral) or quadriplegia (bilateral). The functional consequences can vary from abnormalities of muscle tone or power that do not cause serious problems, to severe impairments that result in considerable lifelong disability and handicap, such as being unable to walk or to feed independently.

## Visual impairment

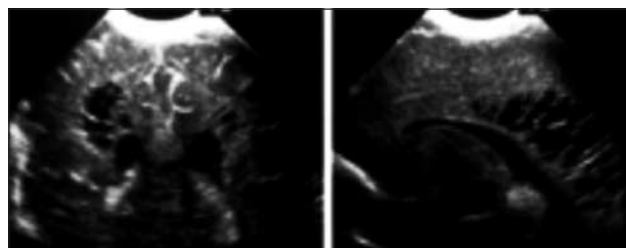
Most visual impairment in very preterm infants is secondary to retinopathy of prematurity, although some cases are caused by cortical damage. Retinopathy of prematurity affects infants born at < 32 weeks' gestation. The incidence and severity is inversely related to gestational age. The risk seems to be directly related to the concentration and the duration of oxygen treatment to which the very preterm infant is exposed. Relative hyperoxia (compared with the hypoxic intrauterine environment) disturbs normal retinal vascular development in preterm infants. Careful use of supplemental oxygen treatment, with monitoring of the blood oxygen saturation and partial pressure, may prevent severe retinopathy in many infants. The ideal target range of saturation or partial pressure of oxygen in very preterm infants is unclear.

Most infants born at < 28 weeks' gestation will develop some form of retinopathy. In most cases this is mild and regresses spontaneously. Some infants, however, develop progressive retinopathy with abnormal vessel growth, retinal haemorrhage, scarring, and detachment. As outcome is improved with early treatment, infants born at < 32 weeks' gestation or with birth weights of < 1500 g should be screened for early signs of the disease by an ophthalmologist. Screening should continue at least fortnightly until vascularisation has progressed to the outer retina, with progressive retinopathy being treated with either cryotherapy or laser photocoagulation.

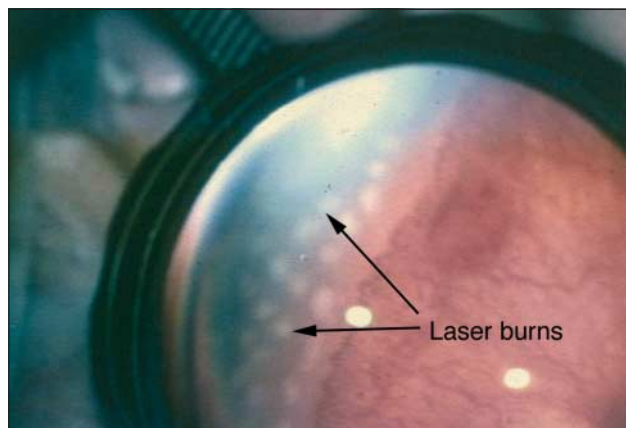
Although the incidence and severity of retinopathy of prematurity has fallen in developed countries over the past 20 years, it remains one of the commonest causes of childhood blindness, visual field defects, and refractive errors. Despite screening and treatment, about 2% of extremely low birthweight infants are blind as a result of retinopathy of prematurity. The incidence is increasing in some countries, especially "middle income" countries in Latin America, Eastern Europe, and South East Asia that have introduced neonatal intensive care services for preterm infants.

## Hearing impairment

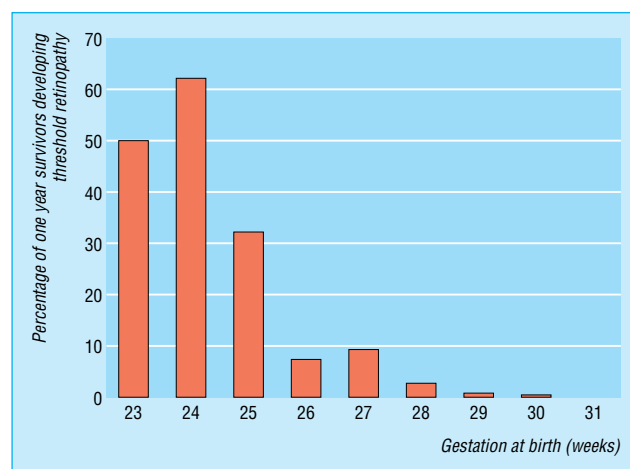
About 3% of infants born at < 28 weeks' gestation require hearing aids, though more infants have milder hearing impairment or high frequency hearing loss. The aetiology of sensorineural hearing loss is probably multifactorial, with a variety of interacting factors that are related to illness severity



Cranial ultrasonography: (left) coronal and (right) parasagittal views on day 24 in an infant born at 28 weeks' gestation, showing extensive periventricular cysts. With permission from Pierrat V et al. *Arch Dis Child* 2001;84:151-6



Magnified view of laser treatment of retinopathy of prematurity



Incidence of severe retinopathy and its relation to gestation at birth. Adapted from Pennefather PM et al. *Eye* 1995;9:26-30



Screening for retinopathy of prematurity

contributing. Hearing impairment is associated with delayed language development, although very preterm infants with normal hearing may also develop speech and language problems. Early use of hearing aids plus support from audiology services can improve language development in infants with sensorineural hearing loss.

## Learning difficulties

At school age, up to 50% of infants born before 28 weeks' gestation need some form of additional educational support. A recent systematic review found that the IQ of extremely low birthweight children is on average 10 points lower than in children who were born at term. Learning difficulties are often associated with problems such as visual or hearing impairment, but children can have isolated cognitive problems. Very preterm children of normal intelligence may have specific learning difficulties, commonly with mathematics or reading. Confounding social factors (for example, mother's educational status) may have a greater influence on educational outcome than extremely preterm birth.

## Social development, behaviour, and psychological problems

Early social development—for example, responsive smiling and recognising family members—may be delayed in preterm infants. Interactive and imaginative play may also be delayed. Investigators from several countries have noted a higher incidence of behavioural problems in extremely low birthweight children of school age, with attention, social, and thought processing problems the most commonly detected. As behavioural problems can adversely affect school performance and development of social relations, these are important long term effects of preterm birth.

## Quality of life

In the last decade, data from cohort studies have indicated that quality of life related to health (measured using validated tools) is considerably lower in surviving extremely low birthweight children than in children born at term. Evidence exists, however, that most children do not perceive their quality of life as being substantially different from that of their peers born at term.

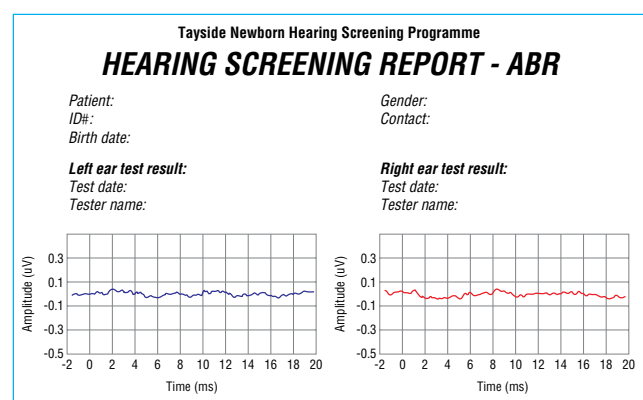
## Neurodevelopmental follow up

Regular follow up assessments of children at risk of neurodevelopmental impairment may allow the early detection of problems and the provision of medical, social, and educational support if required. Many signs of neurodevelopmental impairment are evident only after infancy, and follow up should continue until the child is at least 18-24 months old, corrected for gestation. Standardised, validated assessment tools to monitor developmental progress are available. Ideally, these follow up data should be included in the annual audit of activity and outcomes of neonatal units. Even in well resourced centres, it is often difficult to undertake comprehensive follow up programmes.

Data on the longer term neurodevelopmental outcomes are important for informing the antenatal counselling of mothers who may deliver preterm, especially at the limits of viability (< 26 weeks' gestation). National, population-based data are most valid. The number of extremely preterm infants cared for



Preterm infants at risk of hearing loss should be screened, usually with brainstem auditory evoked responses, before discharge from the neonatal unit



Screening audiogram that indicates possible hearing impairment and referral for further assessment

**Children, their parents, other parents and, importantly, healthcare workers may all view similar health states differently**

### Benefits of neurodevelopmental follow up

- Early detection of problems in individual children
- Prognostic information for families can be provided
- Allows audit of outcomes for neonatal units and health services

### Further reading

- Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR. Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. *N Engl J Med* 2000;343:378-84
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- Donohue PK. Health-related quality of life of preterm children and their caregivers. *Ment Retard Dev Disabil Res Rev* 2002;8:293-7
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in each unit is small, and estimates of the incidence of outcomes are often imprecise. At present, such population-based data are mainly available through research studies, such as the EPICure study. In some countries routine collection and synthesis of such data is being attempted—for example, using nationally agreed minimum datasets reporting standardised assessments.

## Conclusion

Most preterm infants have good neurodevelopmental outcomes and cannot readily be distinguished from term infants. As survival rates for extremely preterm infants have improved, however, the overall number of preterm infants with disability and handicap has not fallen as might have been expected. These impairments may have an adverse effect on family life as well as having an important impact on social, education, and health service resources. The longer term neurodevelopmental outcomes must be considered when reviewing the impact of neonatal intensive care for preterm infants.

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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 Fowle, 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: For WMcG's competing interests see first article in the series.

The magnified view of laser treatment of retinopathy of prematurity is with permission from Nick George, Ninewells Hospital, Dundee. The chart showing neonatal death rate for preterm infants in Scotland since 1989 is adapted from the Scottish perinatal and infant mortality and morbidity report 2001, which can be found on the website [www.isdscotland.org](http://www.isdscotland.org)

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## French lessons

"Aren't you going to give me something for my nose?"

It was the end of a busy weekend on call; I was hungry and tired, and this was not what I wanted to hear. I had been called out to see a man with a cough, which I had diagnosed as asthma due to a cold. He had all sorts of treatments at home for asthma, which I encouraged him to take regularly. The attack was not severe, and he was quite well apart from the slight cough and a runny nose. I prepared to leave, not before collecting my €42.60 (£29.89; \$56.56) cheque and giving him his form for reimbursement.

"And my cough?" he asked. I explained again, as patiently as I could given my weakened state, that treating the asthma would stop the cough and that symptomatic treatment was unhelpful.

"My tiredness?" Once more, I related this to his condition, said that this couldn't be treated *per se*, and explained that, as his asthma improved, all his other symptoms would get better.

"Aren't you going to give me something for my nose?" finally floored me. He emphasised, slightly belligerently and in minute detail, how being at work was incompatible with a runny nose and that his life would be impossible without treatment for this.

I gave up, too tired to argue. "What do you normally have?" I asked lamely.

"I don't remember. Don't you know what to give?" He had won hands down.

"Not really—in Britain we don't give symptomatic treatment much."

His eyes lit up with comprehension: this was the explanation for the doctor's intransigence in the face of extreme suffering. "Un médecin anglais—oh là!" Of course, all was now clear—the weakened state of the NHS, endless waiting lists, cancelled operations, no trains, bad food, rain. Triumphant, he suddenly became friendly, slightly patronising, almost apologetic. Well, of course, an English doctor wouldn't prescribe; what could you expect? "Les britanniques" were used to suffering uncomplainingly; and so he carefully explained, as though to a child, how one medicine was for a cough, another for the fatigue, yet another for the runny nose, and an antibiotic for the infection.

There you had it—four items on the prescription, at last. God was in his firmament, watching over the land of *liberté, égalité, et fraternité*, and the English doctor had at last understood that medicine in *la belle France* was different and incomparably better. I left gratefully, my tail between my legs, hoping to get home for dinner before the next batch of visits. I had a lot to learn.

Speaking the language and knowing the names of the medicines, of which only 5% are prescribed generically, are the least of the problems for an English doctor in France. Patient expectations are cultural, and what we take for granted as "good medicine" is nothing of the sort here. The right to treatment and to call a doctor out for what in Britain would be seen as trivial symptoms is enshrined in the national consciousness in France.

Doctors are paid only when they see patients—€20 per consultation in surgery and €30 per home visit, rising to €42.60 at weekends and €63.50 at night. Patients are reimbursed at least 70% by the state and the rest by top up insurance, usually paid for by their employer. This has sometimes encouraged an unholy alliance between patient and doctor. However, there are now less doctors, who all want more time at home, and they are reaping the whirlwind of excess demand which is proving difficult to control.

The French government, faced with massive overspend on the social security budget, is trying various measures to reduce demand. Home visits now have to be "justifiées," and in theory a medically unjustified visit will not be fully reimbursed. It is understandably difficult for doctors to see their patients' reimbursements reduced, especially as patients may move freely between doctors—for the moment. Further proposals are to require a patient contribution of €1 per consultation and, much more controversially, to ask patients to state a preferred general practitioner to claim full reimbursement and, even worse, to limit access to specialists except by referral from a general practitioner.

Sacré bleu! Pardieu! Just like in Britain.

Peter Turkie *locum general practitioner, Perpignan, France*