Resuscitation at birth and long-term follow-up

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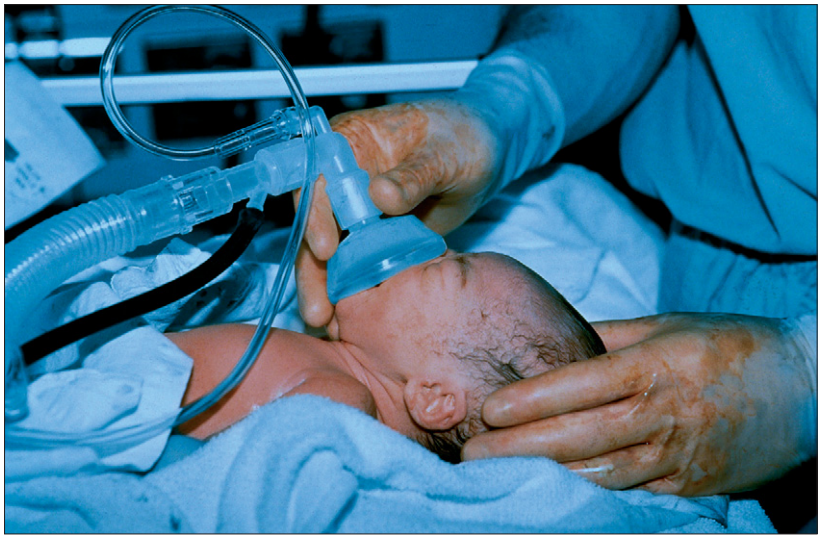
In 1995, WHO estimated that perinatal asphyxia accounted for almost a fifth of global neonatal deaths.[1] However, the number of children who survive, but whose later development is affected, is unknown. Perinatal asphyxia impairs gas exchange during or soon after labour, which leads to hypoxia and hypercapnoea. Hypoxic–ischaemic encephalopathy is the neonatal neurological syndrome that results from a hypoxic or ischaemic event.[2] This syndrome was defined by Sarnat in 1976 and classified as mild, moderate, or severe dependent on neurological behavioural symptoms.[3] The mild state includes hyperalertness or hyperexcitability, but normal muscle tone and no seizures. The moderate state includes hypotonia and often seizures. The severe state includes a stuporous flaccidity with absent primitive reflexes and is associated with high rates of death or major neurodevelopmental impairment. Children who survive the moderate syndrome have lower rates of sequelae than do those with the severe state, but are at higher risk of complications than are normal infants. By contrast, children who present with the mild syndrome have no major disabilities.[3-6] Follow-up studies confirmed the belief that, after a hypoxic event, neonates who are asymptomatic or have the mild neurological syndrome do not differ at school age from a normal comparison group.[3-6]

In *The Lancet* today, David Odd and colleagues[7] report their follow-up of more than 11 000 babies born at or after 36 weeks' gestation from the Avon Longitudinal Study. 815 (7·1%) infants were resuscitated at birth but were asymptomatic for encephalopathy and needed no additional neonatal care. 58 (0·5%) other resuscitated infants needed neonatal care for encephalopathy. The infants who needed resuscitation were at significantly higher risk than the 10 609 infants who did not: they had lower birthweights, were born at an earlier gestational age, and had significantly lower Apgar scores at birth. Their mothers were also less educated and more had hypertension or fever in pregnancy.

Follow-up cognitive assessments of nearly 5900 children (51% of the original population) at age 8 years showed that, as would be expected, children who needed resuscitation and developed neonatal signs of hypoxic–ischaemic encephalopathy fared significantly worse than children who did not require resuscitation. The surprising finding was that rate of a low intelligence quotient—defined as a Wechsler Intelligence Scale for Children III score of less than 80—was significantly higher in the children who required resuscitation but were asymptomatic during the neonatal period than in the non-resuscitated infants (9·8% *vs* 6·5%; odds ratio 1·65, 95% CI 1·13–2·43, adjusted for confounding factors). These results are consistent with Odd and colleagues' previous 18-year follow-up of male Swedish conscripts who had low Apgar scores.[8] These researchers suggest a continuum of risk after perinatal hypoxia which might range from severe neurodevelopmental impairment in children who present with abnormal neurological symptoms after birth, to a low intelligence quotient at school age for those who are asymptomatic. Their results suggest that, because most infants who require resuscitation are asymptomatic, the numbers of surviving children with a low intelligence quotient could have a greater effect on society than would symptomatic infants.

There are, however, some considerations in the evaluation of Odd and colleagues' findings. No evidence was presented of signs of fetal distress before delivery. The study's definition of a potential hypoxic–ischaemic event was made on the basis of need to resuscitate infants who presented with respiratory depression; however, respiratory depression at birth can result from other causes, such as maternal use of drugs. Only 51% of the birth cohort were followed up to school age



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and, although comparison between groups of rates of intelligence quotient less than 80 proved statistically significant, mean scores of the asymptomatic resuscitated children and controls did not differ.

Assessment of a perinatal hypoxic event and its prognosis needs an objective measure other than the neonatal neurological presentation alone. Future studies should include biochemical markers of the degree of metabolic acidosis, which reflects the primary hypoxic insult, electroencephalography including amplitude-integrated recordings,[2,5] neuroimaging including MRI,[9,10] and evidence of multiorgan dysfunction.[5] Information from such studies could lend support to Odd and colleagues' findings, and contribute to understanding of the pathophysiology associated with asymptomatic neonatal hypoxic–ischaemic encephalopathy.

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Home-based management of malaria in the era of urbanisation

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Exactly 1 year remains to the Abuja target of having 80% of patients with malaria treated early and effectively.[1] Yet, in 2008, only 19% of febrile children in malarious areas received prompt antimalarial treatment, and merely 3% got the recommended artemisinin combinations.[2] WHO now advocates for home management of fever/malaria to increase early recognition, physical access to and affordability of drugs, and use of preventive methods.[3] The official endorsement for such home management was given initially for chloroquine, but with widespread resistance to this drug, home management is now being promoted for artemisinin combinations. The debate on use of combination therapy for home management continues, with the pendulum swinging between safeguarding this expensive drug and the ethical issue of using "poor medicines for the poor".[4,5]

Uganda was among the first to take home management for malaria to scale through free distribution of prepacked sulphadoxine–pyrimethamine plus chloroquine through distributors in the community who classify, treat, and refer sick children. Many have looked at the implications of this strategy but no one has managed to answer whether such home management should be extended to the urban setting. Although home management of malaria in rural areas can reduce mortality and morbidity in children,[6] strategies for rural areas might not be directly transferable to urban settings.[7] This view is supported by Sarah Staedke and colleagues who, in *The Lancet* today, report on the merits of home delivery of artemether–lumefantrine for febrile illnesses in a low-transmission area in urban Uganda.[8] In a randomised trial, the authors compared stocking households with free artemether–lumefantrine to standard care and to a concurrent clinical cohort in the same area, and evaluated the effects on anaemia, parasitaemia, and the innovative measure of treatment-incidence density. They found increased prompt effective malaria treatment for febrile children; the effect on clinical outcomes was moderate and obtained at the cost of substantial overtreatment. Whereas the intervention is not home management for malaria per definition, this study is the first to evaluate the implications of presumptive home treatment of fevers with artemisinin combinations in a low-transmission urban setting.