



### CHANGING OUTCOMES OF INFANTS BORN AT 22 AND 23 WEEKS IN SWEDEN 2004-19

Aijaz Farooqi *et al* report survival and morbidity outcomes of infants born at 22-23 weeks of gestation in Sweden in three time windows, from 2004 to 2019. They relate these outcomes to the perinatal activity that was provided. A perinatal activity score was based on indicators of obstetric care (delivery at level III/IV hospital, any antenatal steroids, caesarean delivery) and neonatal care (intubation at birth, surfactant administration <2 hours of birth, delivery attended by a neonatologist and admission to a neonatal intensive care unit (NICU) of infants alive at 30 min of life). In the three time windows there were 977 infants (567 live births and 410 stillbirths). Birth rates did not change over time. Measures of perinatal activity increased significantly over time. Stillbirths fell from 65% to 35% at 22 weeks. The percentage of live-born infants admitted to a NICU increased from 39% to 84% at 22 weeks and from 80% to 96% at 23 weeks. One year survival after live birth at 22 weeks increased from 10% to 39%. Survival at 22 weeks was higher in regions with above-average perinatal activity scores than in those with below-average scores (48% vs 20%,  $p < 0.001$ ). Rates of severe BPD, ROP stage 3-5, IVH grade 3-4 and surgically treated NEC did not differ significantly over time as survival increased and were not different between infants born at 22 and 23 weeks. These data show how much survival at these gestations depends on whether the baby is born in an environment where survival focussed care is usual. The fall in stillbirth rates and sharp rise in the proportion of liveborn infants admitted to a neonatal unit are dramatic. The differences in survival curves between more active centres and less active centres show that the differences in survival are largely attributable to the effects of active perinatal care on the day of birth. It is important to recognise that the attitude of the clinicians determines survival at these gestations as much as the characteristics of the baby. *See page F10*

### HYPOGLYCAEMIA AND HYPERGLYCAEMIA IN ENCEPHALOPATHY

Simona Puzone *et al* report a systematic review and meta-analysis of studies reporting the association between neonatal hypoglycaemia/hyperglycaemia and outcome in infants with neonatal encephalopathy. The studies are observational, so mechanisms and therapeutic implications cannot be determined. Both phenomena were common. There were clear associations between both hypoglycaemia (6 studies, 685 infants; 40.6% vs 25.4%; OR=2.17,  $p = 0.0001$ ) and hyperglycaemia (7 studies, 807 infants; 46.1% vs 28.0%; OR=3.07,  $p < 0.00001$ ) and the composite of death or neurodevelopmental impairment at 18 months. These associations remained when data were restricted to infants who received therapeutic hypothermia. There was an association between hypoglycaemia and risk of white matter injury but not other MRI injury patterns. The association between hyperglycaemia and risk of injury on MRI was observed in all patterns of injury. Both hyperglycaemia and hypoglycaemia can be modified and represent targets for study. It is tempting to speculate that the association between hyperglycaemia and increased risk of injury to all areas reflects the degree of stress response to the hypoxic ischaemic insult and may be a proxy for the severity of the prior insult. An association between hypoglycaemia and risk of white matter injury is already recognised in infants without encephalopathy and could represent an avoidable second hit. There is a widespread practice of initial fluid restriction in infants with HIE, to avoid fluid and electrolyte balance problems, that may restrict substrate as an unintended consequence. *See page F18*

### SWITCH FROM INTRAVENOUS TO ORAL ANTIBIOTICS IN NEONATAL PROBABLE AND PROVEN EARLY-ONSET INFECTION

Emma Louise Malchau Carsen *et al* report the outcomes of a national change in antibiotic practice in Denmark in 2018. The data reported span the 2 years following the start of the new policy and provide information on term infants who were started on intravenous penicillin and

gentamicin due to suspicion of early onset neonatal sepsis. Infants who were clinically well 48 hours after starting antibiotics but had raised CRP, were switched from intravenous antibiotics to oral amoxicillin. During the 2 years of study 835 infants were included. There were 554 who received at least 5 days of antibiotics and 489/554 (88%) underwent switch therapy. None of the infants who were switched to oral antibiotics required readmission to hospital due to infection. The median duration of hospitalisation was 3.0 days (IQR 2.5-3.5) and 7.4 days (IQR 7.0-7.5) in the switch and intravenous therapy groups. This post-implementation evaluation is a welcome addition to the literature in an area where practice is based on habit rather than evidence. It appears that these habits resulted in a well-intentioned but unnecessary prolongation of hospitalisation. *See page F34*

### PREDICTIVE PERFORMANCE OF MULTIPLE ORGAN DYSFUNCTION ON LONG TERM OUTCOME OF ASPHYXIATED NEWBORNS TREATED WITH THERAPEUTIC HYPOTHERMIA

Juliet Langeslag *et al* studied the predictive value for death or severe neurodevelopmental impairment at 24 months of measures of multiple organ dysfunction (MOD) in asphyxiated infants treated with therapeutic hypothermia. MOD was considered to be present when it affected the brain and 2 other organs, with inclusion criteria defined for each organ. They studied 189 infants and found that MOD was poor at predicting later outcome. There are lots of reasons why this might be, including a modifying effect of hypothermia, a wide variation in the duration and severity of hypoxia and fetal circulatory adaptation, at least in prolonged partial hypoxia, that may protect the brain at the expense of other organs. The bottom line is that clinical assessments of prognosis should be focussed on the brain and not influenced by the function of other organs unless the degree of organ dysfunction is severe enough to be a direct threat to survival. *See page F41*