Severe apnoeas following immunisation in premature infants

M H Slack, D Schapira

Abstract
Four premature infants developed apnoeas severe enough to warrant resuscitation after immunisation with diphtheria, pertussis, and tetanus (DPT), and Haemophilus influenzae B (Hib). One required re-intubation and ventilation.

Although apnoeas after immunisation are recognised, they are not well documented. It is time for further research to elucidate the best time to immunise such infants.

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Case reports
Four previously stable premature infants, born under 30 weeks of gestation, developed profound apnoeic and bradycardic episodes within 24 hours of being immunised with diphtheria/tetanus/pertussis and Haemophilus influenzae B vaccines.

Case 1 was a boy born at 29 weeks of gestation, weighing 1070 g, and ventilated for three days. His cerebral ultrasound scans were normal and his course unremarkable. He had no apnoeas and bradycardias for 13 days before immunisation. He received his first course of DTP and Hib at a corrected age of 36+4 weeks. Within a few hours of immunisation he had multiple profound apnoeas and bradycardias and required intubation and ventilation. He quickly improved and was extubated after 36 hours. A full septic screen including a nasopharyngeal aspirate for respiratory syncytial virus was negative. He underwent his second and third course at term and 6 weeks without event.

Case 2 was a girl born at 26 weeks of gestation, weighing 740 g, and ventilated for 20 days. She sustained a pulmonary haemorrhage and required ligation of a patent ductus arteriosus (PDA). Her cerebral ultrasound scans were normal. Before vaccination she had only the occasional apnoea and bradycardia that required stimulation. At a corrected gestational age of 40 weeks she was immunised with her first course of DPT and Hib. Within 24 hours she was having multiple profound apnoeic episodes requiring resuscitation with bag and mask ventilation. These settled the following day. Six weeks later she received his second course of DTP and Hib without any adverse effect.

Discussion
It is common practice in neonatal units to immunise premature infants with DTP and Hib. Although the occurrence of apnoeic episodes in premature babies immunised at eight weeks is recognised, it has not been well documented in the UK. Indeed, the most recent UK study did not look at apnoea as an adverse event.1 In Australia and North America one retrospective and two prospective studies,2–4 estimated the risk of apnoea after immunisation in premature infants at between 17–23%. Most episodes were clinically insignificant. Some episodes, however, may be profound enough to require respiratory support. The presumed cause is the pertussis component.

Two studies4 suggested that those infants more at risk of apnoea tend to be of a lower gestation and birthweight, require ventilation for longer, and are more likely to have chronic lung disease. One study7 showed no significant difference between those infants who had apnoeas and those who did not.

It is clear from our experience that some premature infants are at risk of life threatening apnoea after immunisation. During the period in which these cases occurred, we immunised a total of 51 infants of a similar gestational age. The risk of severe apnoea may, therefore, be as high as 8% in those infants born at less than 30 weeks of gestation. We believe that further, larger studies are needed to show the exact risk to these smaller infants. It would be interesting to know if the risk could be reduced by using the...
acellular pertussis vaccine. Depending on the outcome of these trials, it may be necessary to delay immunisation in extremely low birthweight infants.


