CURRENT OPINION

Pertussis is increasing in unimmunised infants: is a change in policy needed?

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Abstract

The proportion and trend in absolute number of pertussis notifications in young infants has increased each year in England and Wales since the accelerated immunisation schedule was introduced. We report five infants all less than 3 months of age admitted with life threatening pertussis infection to two paediatric intensive care units. Despite aggressive cardiorespiratory support measures, three of the infants died. Pertussis remains a significant cause of morbidity and mortality in unimmunised infants. In this age group presentation is likely to be atypical and infection more severe. Public health measures to prevent the disease could be strengthened. Chemoprophylaxis should be offered to susceptible contacts and booster vaccinations against pertussis considered.

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Although the current rate of immunisation uptake is high (estimated at about 93%),[1] *Bordetella pertussis* continues to cause significant morbidity and mortality.[2] Pertussis is frequently underreported as although culture is very specific it is at best 80% sensitive.[3] The total morbidity and mortality from infection with this organism may be greatly underestimated.

Infants below the age of vaccination are now the population most at risk in countries with high uptake of pertussis vaccine.[4] We report five consecutive infants less than 3 months of age admitted with pertussis to two paediatric intensive care units between October 1996 and May 1997.

Case reports

Table 1 summarises the clinical features of the five cases. Cases 1 and 4 were in contact with children who had culture positive pertussis. Family members of cases 3 and 5 had concurrent, paroxysmal cough. In these four cases chemoprophylaxis had not been given and unvaccinated, susceptible infants were exposed. Despite the use of advanced cardiorespiratory support measures, which included surfactant, high frequency oscillatory ventilation, nitric oxide, and extracorporeal membrane oxygenation, three infants died suggesting that if infants require mechanical ventilation for severe lung disease following pertussis infection then the mortality is high.

Discussion

The age distribution of infection with *B pertussis* has changed as vaccine coverage has risen since the late 1970s.[1] The proportion and

Table 1 Clinical details of five infants presenting with pertussis

Case	*Age (weeks)*	*Presentation*	*Relevant history*	*Antibiotic prophylaxis to close contacts*	*Blood leucocytes (lymphocytes) × 10^9/l*	*Duration of endotracheal intubation, mode of respiratory support & outcome*	*B pertussis cultured from*
1	3	Fever, cough, poor feeding, cyanosis	In household contact with cousin with a culture positive pertussis infection	Not given	70.7 (27.3)	18 hours Mechanical ventilation, HFOV & NO Died	Nasal swab in cousin
2	5	Apnoeas No cough/whoop	Born prematurely at 34 weeks' gestation	Not given	26 (18.72)	2 days Mechanical ventilation, nasal CPAP (3 weeks) Survived	Nasal swab
3	2	Cough, apnoea, vomiting, hypoxia, bradycardia	Concurrent, paroxysmal cough in parents	Not given	18.1 (11.8)	9 days Mechanical ventilation Survived	Nasal swab
4	4	Cough, poor feeding	2 patients on ward with culture positive pertussis	Not given	81.0 (36.5)	36 days Mechanical ventilation HFOV, ECMO Died	Tracheal secretions
5	4	Cough, hypoxia	Concurrent, paroxysmal cough in 2 older sibs	Not given	63.0 (23.0)	33 days Mechanical ventilation, ECMO Died	Nasal swab

HFOV, High frequency oscillatory ventilation; NO, nitric oxide; ECMO, extracorporeal membrane oxygenation.

absolute number of cases in infants under 3 months of age is increasing. In 1991, 121 of 5201 (2.3%) cases of *B pertussis* notified in England and Wales were under 3 months of age compared to 92 of 2309 (4%) in 1992, 186 of 4091 (4.5%) in 1993, 203 of 3964 (5.1%) in 1994, 146 of 1869 (7.8%) in 1995, 204 of 2387 (8.5%) in 1996,[5] and 344 of 2989 (11.5%) in 1997 (Harding D, Communicable Diseases Surveillance Centre, personal communication, 1998). There is a rising trend in absolute numbers of cases in infants less than 3 months ($p < 0.00001$, χ^2 test for trend). Between 1995 and 1997 there were at least 18 deaths from pertussis in the UK, and 15 (83%) of these were in infants less than 3 months (Miller E, personal communication, 1998).

All five patients in our series were less than 3 months of age. There is still significant morbidity and mortality in the younger age group.[2 6] There is little placentally transferred passive immunity to pertussis, and as accelerated primary vaccination is not complete until 4 months of age, young infants are highly susceptible to pertussis if exposed.[7] In addition these children are much more likely to require hospitalisation (82%) and intensive care.[6] The highest rates of major complications such as pneumonia (25%), apnoea, seizures (4%), and encephalopathy (1%) are also found in children younger than 2 months, as is the highest mortality.[2 6] None of the five infants in our series presented with the characteristic whoop or paroxysmal cough seen in older children, indeed case 2 presented with frequent apnoeas and no cough. At this age the presentation of pertussis tends to be with apnoea or similar to other respiratory tract infections, either of which could result in the diagnosis of pertussis not being considered and treatment being delayed.[8 9]

Pertussis is an occasional cause of sudden infant death. Polymerase chain reaction analysis identified *B pertussis* in 18% of nasopharyngeal specimens taken from 51 children who died suddenly.[10]

Susceptibility of older children and adults to infection with *B pertussis* and their role in its transmission to younger, unvaccinated infants has been well documented.[11] Family members of cases 3 and 5 had concurrent, paroxysmal cough. More cases of pertussis occur in infants whose mothers have themselves had cough of at least seven days duration during the infant's incubation period than those without this family history, suggesting that mothers are a source of infection to their babies.[11] Could a reduction in cases in infants under 3 months of age be brought about by the use of booster doses of pertussis? Since 1990 the accelerated immunisation schedule has been employed in the UK. Three doses of diphtheria, tetanus, and pertussis (DTP) vaccine are given at 2, 3, and 4 months. In the UK, in several other European countries (Ireland, Denmark, Spain), and in most developing countries no further booster doses are recommended after 1 year old. Without booster doses vaccine derived immunity declines over 6–10 years[12] and is unmeasurable by 12 years of age.[13] Preschool booster doses of pertussis in this country could protect children during their ensuing school age years and more importantly reduce transmission of the disease to younger unvaccinated siblings.[14] There may be a case for considering a pertussis booster for young teenagers when they normally receive diphtheria, tetanus, and polio. Because *B pertussis* infection in adults is common and endemic some authors have advocated boosting adults.[15] However, the side effect rates of whole cell vaccine in older children and adults are unacceptably high. In the UK an acellular preparation (acellular pertussis vaccine, Acel-B; Wyeth Laboratories, Maidenhead, Berks, UK) is available presently only on a named patient basis. A recently reported trial found that the efficacy of certain acellular vaccines was similar to that of the UK whole cell vaccine. Further, although there were no significant differences between the vaccine groups for serious adverse events, high fever and seizures were less frequent after acellular vaccines than the UK whole cell vaccine.[16] Acellular pertussis vaccine (APV) was safe with good immunogenicity when administered to preschool children.[17] In the United States, the American Committee on Immunisation Practices recommends primary immunisation at 2, 4, and 6 months of age, with two further boosters of DTP using APV at 12–18 months and 4–6 years of age.[18]

Although our case 1 had been in contact with a cousin with culture positive pertussis infection and case 4 had been in contact with two patients on the same ward with culture positive infection, neither case had been given pertussis chemoprophylaxis. Delay in administering erythromycin as chemoprophylaxis to household contacts is known to be associated with an increased rate of secondary infection.[19] Erythromycin protected newborn babies when pertussis was serologically confirmed or culture positive in their mothers.[20] There are no controlled trials demonstrating that prompt treatment of the index case will result in decreased transmission to close contacts. However, while erythromycin treatment of cases has little effect on the clinical course of illness, it does render the individual culture negative.[21] There are analytical studies that support the use of erythromycin treatment with prophylaxis. Sprauer *et al* found an association with delay beyond two weeks in initiation of treatment and prophylaxis and secondary spread to household contacts.[22] Erythromycin administered as chemoprophylaxis before the first secondary case significantly reduced the rate of secondary transmission within families in one study.[23] In view of high secondary attack rates of up to 80–100% in families,[22] we believe that erythromycin treatment and prophylaxis should be given to the index case and close contacts in all households where there are unimmunised or partially immunised children. This should be given before 21 days of onset of a primary case.[24] Doses of erythromycin used have been 40–50 mg/kg/day for children and 250–500 mg/day for adults in three divided doses for 10–14 days.[24] Seven days' of erythromycin

treatment has been shown to be as effective as 14 days' at eradicating carriage in cases.[25] This shorter course may be especially attractive in adult contacts, in whom erythromycin is more likely to cause unpleasant side effects.[25] However, blinded, randomised controlled trials are needed before erythromycin prophylaxis can be recommended for all contacts irrespective of their vaccination status, as is the current practice in the USA and Canada.[26 27] Future trials should consider the newer macrolide antibiotics as these have fewer gastrointestinal adverse effects and may decrease the risk:benefit ratio of prophylaxis. The use of shorter courses of erythromycin also needs to be evaluated.

In summary, the proportion of pertussis notifications in infants less than 3 months of age has increased each year in England and Wales since the accelerated immunisation schedule was introduced, and the absolute number in 1997 was the highest this decade. Young infants are particularly vulnerable to infection resulting in small but significant morbidity and mortality. In this age group presentation is likely to be atypical. Consideration should be given to the introduction of preschool booster vaccinations against pertussis in the UK to reduce transmission to younger unvaccinated siblings. We suggest prompt treatment of the index case and that chemoprophylaxis be administered to all household contacts where there are unimmunised or partially immunised children.

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