

via syringes or infusion sets. Death occurred rapidly after the event but in three patients antemortem chest *x* radiography confirmed the diagnosis and lead to immediate cessation of attempts at resuscitation. Clinical features which alerted us to the diagnosis in the three last patients were the pallor of the infant,² the discrepancy between the state of the baby and the high readings of the continuous oxygen monitor, and finally the presence of air in the samples drawn from the umbilical artery catheter. The presence of supraventricular tachycardia in the fourth case is interesting and to our knowledge air embolism has not previously been recorded as a precipitating cause for this arrhythmia.

In the early reports of this complication the babies tended to be of longer gestation (range 25–34 weeks) and emphasis had been placed on the higher pressures (range 28–90 cm H₂O) that had been used.^{2,3} It is noteworthy that the pressures in the first four infants in this study (like those in a similar infant reported by Rudd and Wrigglesworth⁴) were lower (25–37 cm H₂O) although they were obviously much higher than we would like to use. Three of the babies had pulmonary interstitial emphysema in which it is thought high peak airways pressure used during ventilation for hyaline membrane disease plays a causative role.⁵ Four out of the five infants had proved difficult to oxygenate and the use of this high pressure was determined by the evidence of atelectasis on the chest *x* ray film.

Four of the five infants had an additional form of air leak to their air embolism and it seems likely that the air enters the circulation after rupturing out of the pulmonary air spaces. Whether this occurs at the site of weakness in the pericardial reflection near the ostia of the pulmonary veins is not clear.⁶ Two of the subjects had prolonged rupture of the membranes

(in one case four weeks) but there was no evidence that either pulmonary hypoplasia or infection played a role in the pathogenesis of their embolism, although congenital infection may have played a role in the fifth subject. There was no evidence of meconium aspiration or inappropriate resuscitation at birth that might have predisposed these infants to this disaster nor was there any evidence of accidental introduction of air through the peripheral or central cavities. All infants were appropriate for gestational age and there was no evidence of any underlying congenital disorder.

It is of interest that in the patients reported here death occurred at about 15 hours of age. In our experience this parallels the time course of the peak severity in the respiratory distress experienced by these very low birthweight immature babies. In our unit 42% of ventilated babies, <26 weeks' gestation, develop air leaks. It seems likely that air embolism represents the extreme end of the range of air leaks that occur in very immature lungs.

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Clostridium difficile and acute enterocolitis

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SUMMARY *Clostridium difficile* belonging to groups not normally detected in infancy was the only potential pathogen detected in the stools of two infants with severe enterocolitis. Further information regarding the virulence of this organism was obtained by use of a recently introduced typing scheme.

Clostridium difficile is not usually considered to be of clinical importance in stool specimens from infants because this organism can also be found as part of their normal gut flora.¹ In adults, *C difficile* is rarely isolated from normal faecal specimens and its overgrowth with production of toxin, secondary to antibiotic treatment, can result in the development of pseudomembranous colitis. In infancy there are only occasional reports of this condition.^{2,3} The

introduction of typing schemes for *C difficile* has provided evidence for the existence of different types of this organism with variable virulence.⁴⁻⁶

The two infants described below presented with severe enterocolitis and *C difficile* was the only potential pathogen found. It was possible to place the *C difficile* isolates into two unusual groups, not commonly found in young infants. This was established by the use of the typing scheme primarily used for epidemiological purposes, based on the incorporation of sulphur-35-labelled methionine into the cell proteins and their separation by gel electrophoresis.⁴

Case reports

Case 1. A 2 month old girl was referred from another hospital with a two day history of refusing feeds and 24 hour history of profuse non-bloody diarrhoea with one episode of vomiting. She was lethargic and tachypnoeic with a temperature of 40°C. No medicines had been given before the symptoms began but she had been started on benzylpenicillin and gentamicin at the referring hospital after the development of a noticeably distended abdomen.

Biochemical investigations gave normal results for urea and electrolytes. Her haemoglobin concentration was 95 g/l, white cell count $4.4 \times 10^9/l$, and platelets normal. A barium study showed no evidence of malrotation. There was no growth from blood culture, and cerebrospinal fluid showed no cells and no growth. Culture of her stools gave negative results for campylobacter, enteropathogenic *Escherichia coli*, salmonella, and shigella species. Five representative *E coli* cultures from the stool were sent to Dr B Rowe at the Enteric Reference Laboratory, Colindale and these were identified as *E coli* 013 (a non-enteropathogenic serotype) which did not produce heat stable or labile toxin, or verotoxin. No viruses were seen on electron microscopy or grown from faecal samples. Serology for *Yersinia enterocolitica* and *pseudotuberculosis* did not show raised titres. *C difficile* was grown from the infant's stools and was shown to be highly toxigenic for both the cytotoxin and the enterotoxin and further typing showed that it belonged to group X. Cytotoxin was also detected directly from the stool specimen.

Over the next 24 hours the child's haemoglobin dropped to 78 g/l and an emergency laparotomy was carried out. Intravenous metronidazole was added to the antibiotic treatment preoperatively. Large quantities of clear yellow peritoneal fluid were found but no organisms were seen on Gram stain and no growth was obtained from culture. Dilated

loops of ileum were noted and the distal half of the ileum was oedematous with the terminal 2 cm appearing to be bruised. No evidence of appendicitis or intussusception was found. The patient's condition improved dramatically after the operation. She was maintained on antibiotics and her diarrhoea diminished gradually over the next few days.

Case 2. A 3 week old girl was admitted with a 24 hour history of profuse watery, offensive, but non-bloody diarrhoea. She had no history of vomiting. Four days before admission she had been given an anticholinergic drug, pipenzolate bromide, which was initially prescribed at twice the normal dose for her age and weight. This was given at double the prescribed dose by her parents and the diarrhoea had started 24 hours after stopping this drug.

Biochemical investigations gave normal results for urea and electrolytes. Her haemoglobin was 143 g/l, white cell count $20.5 \times 10^9/l$, neutrophils 28%, platelets $25\,000 \times 10^9/l$. There was no growth from blood culture, and cerebrospinal fluid showed no cells and no growth. Numerous stool cultures gave negative results for enteropathogenic *E coli*, salmonella, shigella, and campylobacter species. No antibodies were detected against yersinia species and no stool viruses were seen on electron microscopy or grown from tissue culture. *C difficile* was cultured from stool specimens and its cytotoxin was also identified directly from one stool. The organism was a potent producer of enterotoxin and cytotoxin and further typing showed that it belonged to group W.

Thirty six hours after admission the child developed abdominal distension. Moderate gaseous distension of large and small bowel was noted with occasional fluid levels apparent. She was given intravenous benzylpenicillin, gentamicin and metronidazole, and oral feeding was completely stopped. Her abdominal wall became distended and oedematous; she passed blood in her stools and 'coffee ground' fluid was aspirated through her nasogastric tube. Her white cell count rose to $38\,000 \times 10^9/l$ (47% neutrophils) and bowel sounds could not be heard. She was given nine days total parenteral nutrition; her general condition slowly improved and the diarrhoea gradually stopped.

Discussion

Both these infants were seriously ill and none of the pathogens normally associated with diarrhoea in infancy were found. Neither of the children had been given antibiotics before onset of symptoms but one of them had been given an inappropriate dose of an anticholinergic drug. The advisability of giving

infants drugs that may interfere with gut motility and indirectly influence the composition of the gut flora should be questioned.

The renal function in both infants remained normal and excluded haemolytic uraemic syndrome. *E coli* isolates from one of the infant's stools were further investigated for production of toxins, including verotoxin, but these were not detected. Neither child had a colonoscopy performed and biopsy specimens for histological examination were therefore not available.

One of the infants had group X *C difficile* identified and the organism was a potent producer of both enterotoxin and cytotoxin. This group has caused an outbreak of antibiotic associated colitis in patients on oncology wards.⁴ The other infant had a highly toxigenic group W *C difficile* identified—the usual groups found in newborn infants are A–D.⁴ Group W has been isolated from an adult with pseudomembranous colitis (unpublished data) and this organism was also found to be a high producer of toxins A and B.⁶

It seems probable that *C difficile* had clinical importance in these two infants. Both children appeared to respond to treatment with intravenous antibiotics, including metronidazole, which is effective against the organism. Possible pathogenic significance of *C difficile* in the gut of infants with severe enterocolitis should not be discounted on the

basis that this organism may also be found in stools of normal children in this age group. The use of typing schemes, often used for epidemiological purposes, may help elucidate the potential pathogenic role of *C difficile* in individual patients and also determine whether specific antimicrobial treatment should be urgently instituted.

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AIDS encephalopathy with response to treatment

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SUMMARY A 3 year old boy who had acquired HIV infection transplacentally developed the classical features of AIDS encephalopathy, spastic diplegia and expressive aphasia. His computed tomogram showed cerebral atrophy. Treatment with zidovudine and weekly infusions of gammaglobulin led to considerable clinical improvement and an almost normal computed tomogram nine weeks later.

A boy was identified as HIV antibody positive at the age of 21 months after his mother presented and died of pneumonia due to *Pneumocystis carinii*. She was HIV antibody positive and had received two units of blood after the birth of her first child. The source of her infection remains unclear. The first

child is well at age 6 and has no detectable HIV antibody. Our patient, the second child, is thought to have acquired HIV transplacentally.

The boy was born after a full term normal delivery, birth weight 3150 g, and he received all conventional immunisations, including measles, without problem. His head circumference, weight, and length had grown along the 50th, 10th, and 10th centiles, respectively. His development was normal, and he had been walking normally since age 13 months and, aged 21 months, was starting to join words. The only clinical abnormality was moderate inguinal lymphadenopathy.

Initial investigation showed normal T lymphocyte subsets (fig 1) and a normal number of T helper cells. He had a grossly raised IgG (37 g/l) concentration but no IgG virus antibodies (including measles