rupture and dissection has been described and was the probable cause of death in five of the 51 cases cited by Cruickshank and Marquis.⁴ It has been assumed that aneurysm of the ductus may resolve spontaneously as thrombus within it becomes organised and fibrosed, but there is no documented evidence for this. In view of the possible fatal complications, therefore, surgical treatment is advocated. Heikkinen and Simila were the first to describe successful elective resection of the aneurysm in two neonates.³

Greater awareness of the condition could have facilitated a preoperative diagnosis in case 1. It was impossible to achieve vascular control at left thoracotomy but the use of cardiopulmonary bypass, hypothermia, and circulatory arrest would certainly have helped in achieving haemostasis. Review of reported work showed only one successfully treated ruptured aneurysm.⁵ We recommend the use of cardiopulmonary bypass in suspected cases of aneurysmal rupture.

Because of our experience with case 1, the diagnosis was easily made with the use of echocardiography in case 2. The presence of a cystic mass in continuity with the left pulmonary artery and the aorta was unmistakable. Provided one maintains a high index of suspicion and includes aneurysm of the ductus in the differential of all mediastinal masses, the diagnosis can accurately and confidently be made on echocardiography. Further investigations, particularly angiography (which may jeopardise an already critically ill infant), are unnecessary.

In the second case the early natural history of the condition was documented. The rapid reduction in the size of the aneurysm led us to question the need for surgical intervention in all cases. A conservative policy of closely monitoring the clinical progress and

echocardiographic appearances was adopted. If the aneurysm had not undergone rapid resolution or had increased in size we would have resected it because of the risks of endocarditis, rupture, and compression of adjacent structures.

We recommend urgent operations using cardiopulmonary bypass if a ruptured aneurysm is suspected. If there is no evidence of rupture, however, we believe a conservative policy of monitoring the progress of the aneurysm by echocardiography is justified. If the aneurysm increases in size or does not undergo rapid resolution we recommend urgent resection.

Addendum

Since submitting this paper we have recognised two further cases. One resolved spontaneously and the other was corrected during cardiac surgery for pulmonary atresia.

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Ciprofloxacin in neonatal *Enterobacter cloacae* septicaemia

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SUMMARY Multiresistant *Enterobacter cloacae* infection in six premature infants was eradicated with intravenous ciprofloxacin (10 mg/kg/day). Bacterial resistance did not develop. Adequate plasma ciprofloxacin concentrations were achieved in all treated patients. No clinical evidence of side effects was observed.

Modi *et al* have documented an outbreak of multi-resistant *Enterobacter cloacae* infection that was observed in this regional intensive care unit between July 1985 and January 1987.¹ The organism was resistant not only to penicillins and aminoglycosides but also to third generation cephalosporins. Later in 1987 a further six infants developed septicaemia due to the same multiresistant strain of *E cloacae* that showed in vitro sensitivity to ciprofloxacin (Ciproxin,

Baypharm). Ciprofloxacin is a new synthetic fluoroquinolone with broad spectrum bactericidal activity and effective tissue penetration.² It has not been recommended for use in children as it has caused arthropathy in weight bearing joints of experimental animals. Chapman *et al* had previously treated *E cloacae* septicaemia with ciprofloxacin in a premature infant.³ We report our experience of treating the six infants in the second outbreak of *E cloacae* infection with ciprofloxacin.

Patients and methods

CLINICAL ASPECTS

The six infants were treated in the regional neonatal intensive care unit, Liverpool Maternity Hospital. All infants had received at least two courses of different antibiotics before the ciprofloxacin. These included ampicillin, gentamicin, netilmicin, cefotaxime, and chloramphenicol. Ciprofloxacin 10 mg/kg/day in two divided doses was given intravenously for 14 days to infants 2–5 and 21 days in the case of infant 1 who had ventriculitis. Patient 6 died nine days after ciprofloxacin was started.

Serum concentrations were estimated after the third dose in all cases, and in the cerebrospinal fluid on two occasions in one infant.

SURVEILLANCE AND TREATMENT

Prevention practices and antibiotic treatment of babies in this nursery have been described previously.¹ The combination of ampicillin and gentamicin was used as a standard initial treatment of suspected infection.

LABORATORY METHODS

Isolation and identification of organisms as well as

the breakpoint technique for determination of antibiotic sensitivities were used.¹ The breakpoints for ciprofloxacin were 0.5 mg/l (low) and 2.0 mg/l (high). The sensitivity of the strains of *E cloacae* isolated initially were tested by Stokes disc method¹ with disc concentration of 5 mg. For selected strains, the minimum inhibitory concentration of ciprofloxacin was determined. For this Adatabs (Mast House, Bootle) were used to make twofold dilutions ranging from 2 mg/l to 0.015 mg/l, a technique similar to the breakpoint method.¹

Ciprofloxacin serum concentrations were measured by high performance liquid chromatography. Trough and peak plasma concentrations were measured, taking blood 30 minutes after intravenous injection for the latter.

Results

CLINICAL ASPECTS

All six infants were premature and of very low birth weight (see table 1). All infants were ventilated for chronic lung disease. Three infants had periventricular haemorrhages and two developed necrotising enterocolitis before the institution of ciprofloxacin treatment. The initial sites of colonisation with *E cloacae* are shown in table 1. There was a short interval between colonisation and the onset of systemic infection in the majority. Although *E cloacae* was eradicated in every case, three of the six infants died. The causes of death were necrotising enterocolitis and bronchopulmonary dysplasia in infant 3, bronchopulmonary dysplasia in infant 4, and necrotising enterocolitis in infant 6. In all infants *E cloacae* had been eradicated four to five days after starting ciprofloxacin.

Table 1 Patient details

Patient No	Gestation (weeks)	Birth weight (g)	Site of isolation of <i>E cloacae</i>	Age at time of isolation (days)	Outcome and cause of death
1	28	1200	Pharyngeal aspirate Blood Cerebrospinal fluid	16 24 26	Survived
2	28	800	Throat swab Blood	29 29	Survived
3	24	800	Throat swab Blood	25 30	Died aged 81 days of necrotising enterocolitis and bronchopulmonary dysplasia
4	26	900	Pharyngeal aspirate Blood	6 6	Died aged 66 days of bronchopulmonary dysplasia
5	26	1000	Pharyngeal aspirate Blood	5 5	Survived
6	29	700	Throat swab Blood	6 7	Died aged 19 days of necrotising enterocolitis

Table 2 Ciprofloxacin treatment

Patient No	Age at start of ciprofloxacin (days)	Ciprofloxacin concentration (mg/l)		Time for eradication of <i>E cloacae</i> at all sites with ciprofloxacin (days)
		Plasma	Cerebrospinal fluid	
1	35	3rd dose	0.88	4
		Pre 0.04		
		Post 1.45		
		5th dose	1.45	
		Pre 0.57		
		Post 1.77		
2	42	14th dose		2
		Pre 0.52		
		Post 2.15		
3	49	3rd dose		5
		Pre 1.0		
4	9	Post 3.1		4
		3rd dose		
5	21	Pre 0.6		5
		Post 3.3		
6	10	3rd dose		4
		Pre 2.6		
		Post 5.7		
		3rd dose		
		Pre 1.1		
		Post 2.9		

MICROBIOLOGICAL ASPECTS

Ciprofloxacin concentrations in serum and cerebrospinal fluid are shown in table 2. The mean concentration in the cerebrospinal fluid was 64% of the corresponding post dose concentration in the serum.

At the beginning of this outbreak two babies were colonised and infected with strains sensitive to cefotaxime and ceftazidime. Later, isolates from various sites became resistant to these antibiotics. The isolates of *E cloacae* that subsequently colonised and infected other babies were resistant to cefotaxime and ceftazidime. The biotypes of all these *E cloacae* isolates were identical—that is, resistant to ampicillin, augmentin, trimethoprim, and cefuroxime. They had reduced sensitivities to aminoglycosides as shown by high breakpoints to gentamicin (4 mg/l), netilmicin (4 mg/l), and amikacin (16 mg/l). All isolates of *E cloacae* tested both by the disc and breakpoint method were sensitive to ciprofloxacin. The minimum inhibitory concentration for ciprofloxacin was 0.03 mg/l in four infants and 0.06 mg/l in two infants. There was no change in minimum inhibitory concentration during treatment with ciprofloxacin.

E cloacae was eradicated from all infants treated with ciprofloxacin. The median time for eradication was four days with a range of two to five days. After

the use of ciprofloxacin, *E cloacae* has not been isolated again from infants at this hospital.

Discussion

As in previously reported outbreaks of *E cloacae* infection,¹ the strains causing neonatal infections were multiresistant. In this new outbreak the isolates of *E cloacae* were initially sensitive to third generation cephalosporins. Subsequent isolates, however, became resistant to cephalosporins, confirming our previous findings and supporting the possibility of a spread of a derepressed mutant.¹ These resistant strains of *E cloacae* were eradicated with ciprofloxacin treatment, previous courses of other antibiotics having failed. Resistance to ciprofloxacin was not encountered in our series, although Scully *et al* have described the development of resistance to ciprofloxacin in pseudomonas infection.⁴

By acting directly on the DNA gyrase enzyme that is present in many Gram negative bacteria, cell division is inhibited and plasmid mediated resistance is thus prevented.² Resistance to ciprofloxacin can only develop by bacterial mutation.

Eradication of the organism was achieved with a mean post dose concentration of 3.1 mg/l. We aimed for post dose concentrations below 7.0 mg/l.

Ciprofloxacin penetrates tissues well and therapeutic concentrations in the cerebrospinal fluid have been achieved even in subjects without inflammation of the meninges.⁵ Isaacs *et al* have already reported the successful treatment of ventriculitis caused by a multiresistant *Pseudomonas aeruginosa* strain.⁶ Concentrations of ciprofloxacin in the cerebrospinal fluid have been reported to be 40% of concentrations in serum in meningitis.⁵ In our patients 60–70% of peak plasma concentrations were achieved in the cerebrospinal fluid—14 times the minimum inhibitory concentration of the organism. The ventriculitis was effectively treated with intravenous ciprofloxacin.

Unwanted effects of ciprofloxacin include damage to weight bearing joints, hepatic and renal impairment, interaction with DNA of lymphocytes and with theophylline. No side effects were observed in our patients.

The high mortality in this series was disappointing, although the delay between eradication of the organism and death suggested that death was not directly related to *E cloacae* infection. Despite the relatively late introduction of ciprofloxacin during the course of the infection the organism was eradicated in all cases.

With the benefit of this experience we would now use ciprofloxacin at a much earlier stage of the infective process, but only when our usual first line

antibiotics are ineffective. We would advise caution when considering its use, however, and suggest that it should be prescribed only in instances of proved infection with multiresistant organisms.

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Fetal ascites: an unusual presentation of Niemann-Pick disease type C

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SUMMARY Two infants were seen with severe ascites detected before birth, a previously unreported presentation of Niemann-Pick disease type C. In the second infant no diagnostic storage cells were present in bone marrow. Confirmatory investigations were prompted by experience of the first case.

Niemann-Pick disease type C is a heterogeneous neurovisceral storage disorder inherited in an autosomal recessive fashion. A defect in cholesterol esterification has been identified, so that antenatal diagnosis is possible.¹

Three presentations have been described. Some patients present with jaundice and hepatosplenomegaly in the first two months of life, most of whom become symptom free, though a few die of liver failure by the age of 6 months. Others have asymptomatic splenomegaly in the first six years of life, and yet others develop progressive neurological dysfunction or psychosis, with or without splenomegaly, between the ages of 2 and 59 years.

Progressive neurological deterioration occurs in all cases, often causing death by the third decade. Diagnosis is suspected on identifying typical storage cells in bone marrow and confirmed by electron microscopy of neural tissue; in addition a laboratory test has recently been described.¹