A case of recurrent salmonella septicaemia in an infant

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Summary
A 6-month-old girl was admitted with a febrile illness. *Salmonella eastbourne* was isolated from the stool and blood cultures. Septicaemia was treated with antibiotics but recurred twice on cessation of therapy. The only focus of infection found was the gut itself. Septicaemia did not recur following loss of the pathogen from the gut.

KEY WORDS: salmonellosis, septicaemia, IgA deficiency.

Introduction
Salmonella septicaemia occurs in about 1-1% of reported cases of salmonellosis (Hyams et al., 1980; Cherubin et al., 1974). In the U.K. in 1980 one-third of those reported occurred in children under 14 years of age and 71% of these occurred in infants under 1 year of age giving a much higher incidence in this age group (PHLS, 1980). This report describes a case of salmonella septicaemia in an infant, recurrent in spite of antibiotic therapy, and highlights the possible sequelae of infectious diarrhoea in infants, some difficulties of treatment, and the particular importance of adequate bacteriological investigation especially blood cultures.

Case report
A female Sudanese infant, aged 6 months, was admitted with a 2-day history of fever, nasal discharge, cough and diarrhoea. She had arrived in this country from the Sudan 8 days earlier. The parents gave a history of unconfirmed dysentery, 'malaria' and 'giardiasis'.

On examination the child was febrile (41°C) and moderately dehydrated. There was hepatosplenomegaly. Initial investigations revealed a haemoglobin of 10.4 g/dl, white cell count of 12.6 x 10^9/L with 37% band forms. Sickledex was negative and blood urea was 22.3 mmol/l. Malaria parasites were not seen in thick blood films. Faeces contained a large amount of pus cells but no parasites. Urine and cerebro-spinal fluid analyses were normal.

After admission profuse diarrhoea developed and the patient was treated with intravenous fluids. Following an initial improvement there was rapid deterioration with increased diarrhoea, pyrexia and convulsions. In order to control the fits, high dose phenobarbitone, curare and intermittent positive pressure ventilation were required.

*Salmonella* sp. was isolated on faecal culture and treatment with gentamicin and chloramphenicol was begun. This organism was isolated from further blood cultures and stool specimens. It was sensitive to gentamicin, cefuroxime, chloramphenicol and cotrimoxazole, and was identified as *Salmonella eastbourne*. Antibiotic therapy was changed to chloramphenicol (100 mg/kg) alone. Recovery was uneventful. After 12 days' treatment and negative blood cultures, therapy was stopped although *Salmonella eastbourne* was still being excreted in the faeces. Faecal specimens from the family proved negative.

After 36 hr the patient again became clinically septicaemic. *Salmonella eastbourne* was isolated from blood cultures with unchanged sensitivity. Treatment was commenced with intravenous cefuroxime 100 mg/kg for 9 days and then reduced to 30 mg/kg intramuscularly for a further 12 days. Treatment was discontinued after repeatedly negative blood cultures although the organism persisted in the faeces. After 36 hr septicaemia once again became apparent. *Salmonella eastbourne* was isolated once more from blood culture and treatment with cefuroxime 100 mg/kg was re-started.

After the third episode of septicaemia the dosage of cefuroxime was increased to 150 mg/kg. Seven days later *Salmonella eastbourne* ceased to be isolated from the faeces. Therapy was changed after 10 days to cotrimoxazole orally 80 mg/b.d., and continued for 3 months. Since then the patient has remained well.

Following the first relapse a variety of investiga-
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tions were undertaken to determine a reason for the failure of therapy.

A covert focus of infection was sought by abdominal ultrasonography, radionucleotide imaging of bone and brain, and culture of bile, marrow and liver. Pyelography revealed renal medullary tubular ectasia. There was good renal function and no renal or urinary infection was found.

Investigation of immunoglobulin and complement levels and lymphocyte numbers and function tests showed a low level of immunoglobulin A on two testings: the levels being 0·18 and 0·12 g/l with a normal range of 0·5-4·0 g/l and a mean of 0·6 g/l for this age group. These measurements were obtained by radioimmunoassay techniques.

Minimum inhibitory concentrations (MIC) were found to be ampicillin 2·0 mg/l; gentamicin 0·5 mg/l; chloramphenicol 40 mg/l; cefuroxime 40 mg/l; cotrimoxazole 0·5-9·5 mg/l and with the exception of chloramphenicol all are below normally attainable serum levels. This may explain the first recurrence. However, the second occurred in spite of adequate levels of a further apparently appropriate antibiotic. The patients' serum level 3 hr after dosage was 8 mg/l whilst on 100 mg/kg cefuroxime.

Discussion

Salmonella eastbourne is an uncommon isolate in the U.K. Only 13 isolates were reported in 1980. This case is the only report with septicaemia in the U.K. in 1980. No source was found in the family and no other cases were reported concurrently in the same area. It seems probable that this infection was acquired in the Sudan.

The high incidence of salmonella septicaemia in infants may be due to the low levels of IgA as the serum level at 6 months of age are only a quarter of the normal adult value (Tomasi, 1976). Studies with gnotobiotic animals have shown that the normal microbial flora is the major stimulus for the production of intraluminal IgA (Crabbe et al., 1968). These observations may explain the high incidence of salmonella septicaemia in infants and has led to suggestions that antibiotic therapy should be considered for infants of less than 3 months in the hope of keeping the organism confined to the gastrointestinal tract until the protective immune response of secretory IgA develops due to stimulation by the pathogen (Davis, 1981). However, relapse following cessation of therapy may occur (Nelson, 1981).

In the present case several factors may have predisposed to the recurrence of the septicaemia. The IgA levels were low even after correction for age. IgA deficiency occurs in 1/522 of the population (Holt, Tandy and Anstee, 1977), but is usually asymptomatic unless there is a concomitant T cell dysfunction.

Although this patient has definite IgA deficiency this alone is unlikely to explain repeated septicaemia in the presence of normal lymphocyte function.

The finding of renal medullary tubular ectasia, often associated with hepatic fibrosis (Kerr et al., 1961), present in this case gave two likely foci for infection but in spite of a careful search no infection was found.

Cefuroxime has previously been used successfully in the treatment of salmonella septicaemia, but it has been shown to have low cellular association (Percival et al., 1981), and there is a possibility of organisms remaining viable intracellularly which could lead to reinfection on cessation of therapy. This observation suggests limitations to in vitro sensitivity testing. Antibiotics with low cellular penetration may fail to eliminate sensitive organisms in spite of serum levels in excess of the MIC.

It is difficult to make clear recommendations for antibiotic therapy because of the high incidence of plasmid mediated resistance amongst Enterobacteriaceae (Gill and Hook, 1966; Barros et al., 1977; Bissett, Abbot and Wood, 1974).

Although initial therapy must often be blind, it should take account of known possible resistance. Final choice of antibiotic can only be made after careful appraisal of laboratory findings.

The incidence of salmonella septicaemia in infants and its associated mortality has been well documented (Hyams et al., 1980; Cherubin et al., 1974; Davis, 1981), and although this case is unusual it demonstrates the general principle that the illness may be dangerous and prolonged and therapeutic response unpredictable even with full bacteriological information.

Extreme difficulties may be encountered if the likelihood of septicaemia is overlooked and therapy postponed or blind therapy begun before appropriate investigation. We recommend early and repeated blood cultures in any febrile infant with infective diarrhoea.

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References


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