

diuretics; three from progressive cholestasis (two of whom had ascites only in their final weeks of life); and one from chronic hepatic encephalopathy (without ascites) and bronchopneumonia. Six of the eight patients with a very high initial plasma methionine enkephalin concentration (530-1310 pmol/l) died compared with only one of the 26 patients with lower initial concentrations (50-365 pmol/l;  $p < 0.001$ , Fisher's exact test). In the six patients with a high initial concentration who died the concentration remained over 500 pmol/l ( $p < 0.05$ ) whereas in the two who survived it fell to less than 200 pmol/l. The two survivors had ascites when initially tested. They responded well to diuretics and remained free of fluid overload.

### Comment

Plasma methionine enkephalin concentration correlated strongly with plasma bilirubin concentration (the best available biochemical marker of severity in primary biliary cirrhosis<sup>2,3</sup>) and also correlated with alkaline phosphatase activity and plasma albumin concentration. Thus the methionine enkephalin concentration reflects the severity of the disease, and a high concentration, particularly if sustained, indicates a poor prognosis.

Advanced primary biliary cirrhosis is an important indication for liver transplantation.<sup>4</sup> Optimum timing of this operation is difficult.<sup>5</sup> Although a progressive rise in plasma bilirubin concentration is a useful guide to the need for transplantation, it does not occur in all cases (three of our patients died with a plasma bilirubin concentration below 100  $\mu\text{mol/l}$ ). All seven of our patients who died, however, had a plasma methionine enkephalin concentration greater than 500 pmol/l, and in six of them this was present a median of 10 months before death. This suggests that the plasma concentration of this peptide should be investigated further as a guide to the prognosis of primary biliary cirrhosis and to the timing of liver transplantation.

We thank Dr A D Clayden of the department of community medicine, University of Leeds, for statistical advice.

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(Accepted 19 July 1988)

## Bacteraemia in salmonellosis: a 15 year retrospective study from a regional infectious diseases unit

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The incidence of bacteraemia in non-typhoid salmonellosis is difficult to determine as many cases are never investigated and many patients are not admitted to hospital. In hospitals blood is not generally taken for culture unless septicaemia is suspected. Two large surveys in the United States, which reported incidences of 4.9%<sup>1</sup> and 2.9% (including enteric fever),<sup>2</sup> included patients managed in the community as well as in hospital. We present data from the regional infectious diseases unit in Manchester, where blood samples are cultured from all patients admitted with acute diarrhoea.

### Patients, methods, and results

We analysed the laboratory records of 1742 patients admitted during the 15 years 1969-83 with proved salmonella infections; 89 serotypes were found, of which 72 were identified. *Salmonella typhi* and *S paratyphi* types A and B were found in 213 patients, in whom the rates of bacteraemia were 63% (100/158), 71% (12/17), and 18% (7/38) respectively, whereas the rate was only 8% (124/1529) in the group with non-typhoid salmonellosis. *S typhimurium* was the commonest faecal and blood isolate, although the rate of bacteraemia associated with it (7.0%) ranked only tenth (table). Analysis of bacteraemia by age showed a rate of 4.3% in children aged <1; the rate changed little until age 40 but thereafter rose steadily to reach 17% in people aged  $\geq 70$ .

Clinical records were available for 67 patients with bacteraemia out of 966 with non-typhoid salmonellosis admitted during 1975-83. Seventeen of these died compared with 28 of the 899 patients without

bacteraemia ( $p < 0.00001$ ). Thirty six patients had fever and 18 had leucocytosis ( $> 14 \times 10^9/\text{l}$ ). Underlying conditions were identified in 39 patients: 17 had gastric disorders (surgery, pernicious anaemia, antiulcer treatment); three were taking corticosteroids; and 19, all elderly, had chronic conditions such as cardiorespiratory and cerebrovascular diseases and alcoholism.

Fifty nine patients presented with gastroenteritis. The illness was typhoidal in seven others, and four had focal manifestations (osteomyelitis, arthritis, lung abscess, and gluteal abscess; three also had acute diarrhoea). Thirty nine of the patients with gastroenteritis were aged  $\geq 60$  (36 of whom had moderate to severe dehydration), and all 17 deaths were in that age group. Of the 20 younger patients, eight were similarly

### Bacteraemia in relation to serotype and age of patient

|                             | No of patients | No (%) with bacteraemia |
|-----------------------------|----------------|-------------------------|
| Rate according to serotype* |                |                         |
| Serotypes:                  |                |                         |
| <i>S typhimurium</i>        | 540            | 38 (7.0)                |
| <i>S agona</i>              | 130            | 5 (3.8)                 |
| <i>S virchow</i>            | 115            | 19 (16.5)               |
| <i>S hadar</i>              | 74             | 6 (8.1)                 |
| <i>S enteritidis</i>        | 71             | 1 (1.4)                 |
| <i>S heidelberg</i>         | 69             | 7 (10.1)                |
| <i>S stanley</i>            | 58             | 9 (15.5)                |
| <i>S newport</i>            | 38             | 5 (13.2)                |
| <i>S indiana</i>            | 36             |                         |
| <i>S infantis</i>           | 32             | 7 (21.9)                |
| <i>S saint paul</i>         | 24             | 1 (4.2)                 |
| <i>S kedougou</i>           | 23             | 2 (8.7)                 |
| <i>S panama</i>             | 22             | 3 (13.6)                |
| <i>S montevideo</i>         | 15             |                         |
| <i>S dublin</i>             | 13             | 5 (38.5)                |
| Age specific rates          |                |                         |
| Age (years):                |                |                         |
| <1                          | 230            | 10 (4.3)                |
| 1-                          | 172            | 7 (4.1)                 |
| 5-                          | 66             | 5 (7.6)                 |
| 10-                         | 100            | 5 (5.0)                 |
| 20-                         | 356            | 15 (4.2)                |
| 40-                         | 191            | 16 (8.4)                |
| 60-                         | 114            | 15 (13.2)               |
| $\geq 70$                   | 300            | 51 (17.0)               |
| Total                       | 1529           | 124 (8.1)               |

\*Fifteen most common isolates.

dehydrated (five had had gastric surgery, one was taking H<sub>2</sub> receptor blockers) while the others generally had a milder illness and were often recovering by the time the results of blood cultures were available.

### Comment

The American studies were based on data from patients in the community as well as in hospitals<sup>1,2</sup> and thus are not strictly comparable with our study, which found a higher rate of bacteraemia among patients with salmonellosis in hospital. Two factors influenced this rate: the serotype and age. The rates varied widely with serotype, with *S dublin*, *S infantis*, *S virchow*, *S panama*, and *S newport* being the five most invasive strains; the invasiveness of *S dublin* and *S virchow* has been reported before.<sup>2,4</sup> The vulnerability of elderly patients to bacteraemia and to severe dehydration and often fatal illness was highlighted. Associated debilitating states and the decline in cell mediated immunity with age are probably important in the pathogenesis of bacteraemia in the elderly. In the absence of comparable clinical data on patients with

non-bacteraemic salmonellosis we cannot comment on whether patients with bacteraemia have a more severe illness. The mortality statistics, however, suggest that this may be so.

Antibiotics are not generally advocated in salmonella gastroenteritis unless there is associated septicaemia, but this is difficult to determine clinically during the early stages of the illness, when the antibiotics will be most successful. Delaying treatment until results of blood culture are available may result in dehydration related to septicaemia and renal failure. Fever and leucocytosis are unreliable indicators of bacteraemia. Perhaps a lower threshold is needed for early use of antibiotics in elderly patients with severe diarrhoea.

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(Accepted 1 September 1988)

## Metatarsal periosteal reactions: a common non-specific finding in radiographs of the diabetic foot

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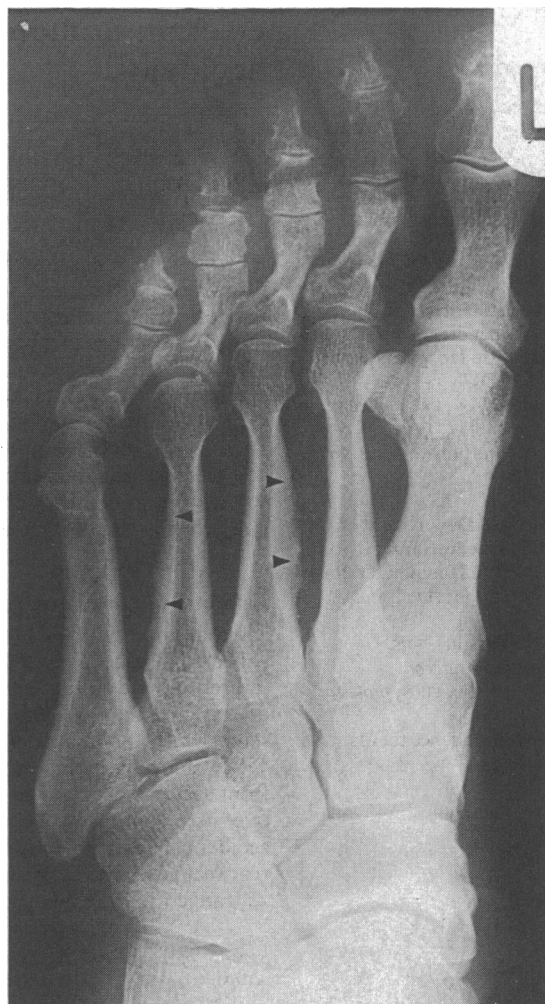
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Periosteal reaction, when evident in a radiograph of a diabetic foot, is generally considered to indicate osteomyelitis. We have, however, observed metatarsal periosteal reactions in radiographs of the feet of diabetic patients without other evidence of osteomyelitis whose foot problems have subsequently resolved with local treatments alone—that is, without systematic antibiotics. We reviewed a large representative group of diabetic patients and determined the prevalence of metatarsal periosteal reactions.

### Patients, methods, and results

Radiographs of the feet were obtained for the first 195 diabetic patients (50 with type I diabetes and 145 with type II; median age 65 (range 19-87); 99 men and 96 women) attending a foot screening clinic. All radiographs were reviewed independently by two radiologists without knowledge of clinical findings. Any radiographs over which they disagreed were not included in the results. A control group, individually matched for age and sex, was compiled from patients attending the casualty department who required foot radiographs for what proved to be unimportant soft tissue injuries. Films were assessed for the presence of periosteal reaction, subluxation, fractures, and vascular calcification. Statistical analyses were performed by McNemar's test for paired samples and  $\chi^2$  and Mann-Whitney U tests for unpaired samples.

Periosteal reactions were found in 42 diabetic patients (21 men) but only seven controls (four men), ( $p < 0.001$ ). Disagreement over the radiological interpretation excluded a further five patients and one control from the study. The periosteal reaction was on both sides of the metatarsal shaft in 11 of the 21 women and six of the 21 men and was generally thick and without demarcation from the cortex (figure). Second, third, and fourth metatarsals were most commonly



Radiograph of left foot showing thick periosteal reactions along shafts of third and fourth metatarsals

affected and more often in combination than individually. None of the patients had trophic ulcers or clinical evidence of infection or fracture. The presence of periosteal reaction was not associated with other radiological abnormalities, age, duration of diabetes (perhaps because of the preponderance of patients with type II diabetes), or clinical neuropathy (absence of