Maloprim by the patient who had near fatal results. Pyrimethamine was taken by all four patients, suggesting that this may have been the toxic agent.

Previous workers assumed that the sulphonamide component of Fansidar was responsible for the pulmonary toxicity. In one report a lymphocyte transformation test yielded positive results in the presence of sulfadoxine but also with pyrimethamine, perhaps suggesting that non-specific cell activation had occurred. We were unable to show lymphocyte activation with either dapsone or pyrimethamine, but this was assessed in only one patient and then only after she had recovered and taken steroids. Dapsone, the other constituent of Maloprim, is structurally related to the sulphonamides. Nevertheless, despite its widespread use it has not been reported to cause pulmonary eosinophilia. Similarly there are no reports of pulmonary toxicity with chloroquine. Three further cases of pulmonary eosinophilia, one confirmed by lung biopsy, have been reported to Wellcome Research Laboratories in patients who had taken Maloprim, and two cases of pulmonary toxicity with systemic features have been reported in patients who had taken pyrimethamine-chloroquine (L. Maskell, personal communication). We therefore believe that pyrimethamine may cause pulmonary eosinophilia.

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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) 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.

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% and 2.9% (including enteric fever), 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 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 >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<0.0001). Thirty six patients had fever and 18 had leucocytosis (>14×109/l). Underlying conditions were identified in 39 patients: 17 had gastric disorders (surgery, pernicious anaemia, antilucer treatment); three were taking corticosteroids; and 19, all elderly, had chronic conditions such as cardiovascular 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 gastro-enteritis were aged ≥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 advanced primary biliary cirrhosis is an important indication for liver transplantation. Optimum timing of this operation is difficult. 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 µmol/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.

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