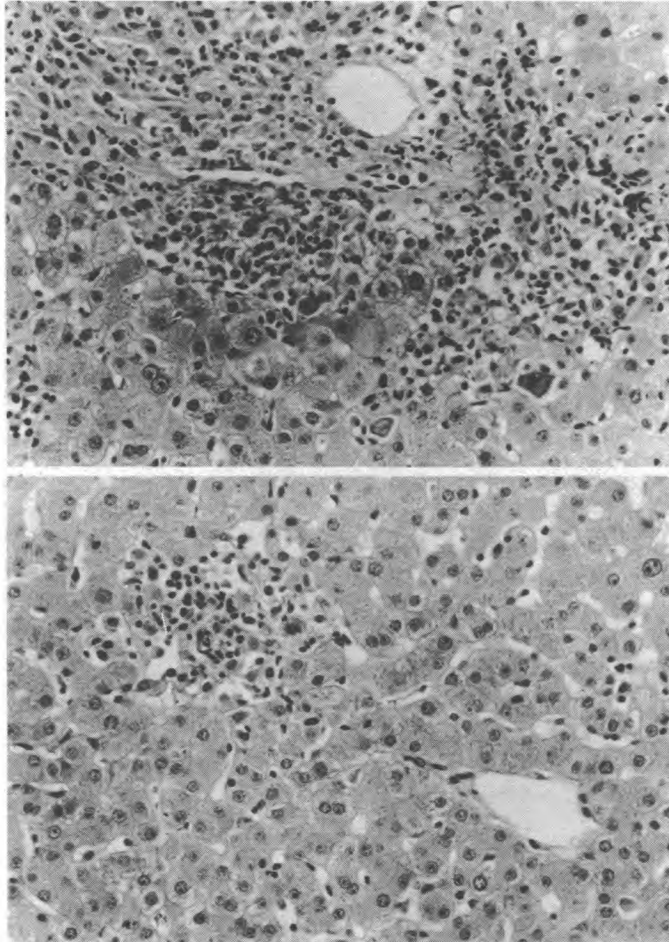


three Fansidar tablets. She was advised to end her holiday after only two weeks. She had no history of contact with jaundice, and the other members of her party were well.

Her gastrointestinal upset had settled by the time she arrived in Nottingham. On admission to hospital she was not jaundiced but was dehydrated with a temperature of 38.5°C. Analysis of her urine showed a trace of albumin and microscopic haematuria. Investigations showed creatinine concentration 83  $\mu\text{mol/l}$  (0.94 mg/100 ml), alkaline phosphatase activity 809 IU/l, bilirubin concentration 11  $\mu\text{mol/l}$  (0.64 mg/100 ml), alanine aminotransferase activity 89 IU/l, and prothrombin time 14 seconds. She developed progressive jaundice during the first week (bilirubin concentration increased to 385  $\mu\text{mol/l}$  (22.5 mg/100 ml)), results of the tests of her liver enzymes deteriorated (alkaline phosphatase activity increased to 1468 IU/l,



Liver biopsy specimen showing inflamed portal tract (top) and well preserved centrilobular zone (bottom). Haematoxylin and eosin  $\times 315$  (original magnification).

and alanine aminotransferase activity to 560 IU/l), and prothrombin time increased to 255 s. She had evidence of pancreatic dysfunction (blood glucose concentration was 70 mmol/l (1261 mg/100 ml)), and deteriorating biochemical renal function (creatinine concentration 242  $\mu\text{mol/l}$  (2.7 mg/100 ml)), and a spreading maculopapular skin eruption.

During the next week she was delirious and had hepatic and oliguric renal failure. The skin eruption progressed to a bullous epidermal necrolysis affecting the whole body and was associated with oral and genital ulceration. Cultures of blood, urine, faeces, liver, and bone marrow yielded negative results; microscopical examination of faeces, sputum, and blood films was not helpful; and serological investigations for viruses, bacteria, and parasites also yielded negative results. Histological examination of a needle biopsy specimen of her liver (figure) showed preserved lobular architecture with a portal infiltrate of inflammatory cells containing an excess of eosinophils and extensive focal hepatocyte necrosis. Skin biopsy showed all the histological features of the subepidermal type of Lyell's syndrome (toxic epidermal necrolysis).

Supportive treatment was given including high dose steroids, but her deterioration continued and she died two weeks after admission, four weeks after becoming ill. A postmortem examination showed confluent skin bullae, liver histology as described, oedematous kidneys, and fibrinous pericarditis. Further viral, serological, and microbiological investigations yielded negative results.

## Comment

This patient suffered a short fatal illness that was related to prophylactic use of Fansidar. An extensive search while she was alive and after death failed to find an aetiology other than this drug.

Skin, liver, and renal toxicity with fever are well known idiosyncratic reactions to sulphonamides. They have occurred separately in patients after use of Fansidar<sup>3,4</sup> and are presumably due to the sulphadoxine (a long acting sulphonamide). No other cases have been reported in which all these toxic manifestations have occurred in the same patient. We have reported this case to the Committee on the Safety of Medicines and to the manufacturer.

We thank Professor J R Hampton for permission to report his case and Mr Bill Brackenbury for the photography.

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## Cryptosporidiosis in Bangladesh

Despite the large number of enteropathogens identified in recent years the cause of many episodes of diarrhoea remain undetermined. The protozoan *Cryptosporidium* was first described as a pathogen causing diarrhoea in animals in 1907, and in man in 1976.<sup>1</sup> We were able to identify the cause for diarrhoea in only two thirds of patients coming to our clinic.<sup>2</sup> Cryptosporidiosis is an emerging zoonotic disease, and we therefore began screening for cryptosporidial oocysts in stools of patients visiting our clinic as part of a surveillance programme.<sup>2</sup>

### Methods and results

At the Dacca clinic we screened 4% of patients with diarrhoea for cryptosporidial oocysts, using Giemsa stain on faecal smears.<sup>3</sup> All specimens were examined for other common enteropathogens. Thirty eight of 578 smears collected from 1 January to 31 May 1984 were judged to be positive, based on the finding of characteristic oocysts—that is, "holes" in the stained background. These unstained areas sometimes have a faint blue centre with fine red or purple corpuscles.<sup>3</sup> Replicate smears made from refrigerated faeces were stained by a modified acid fast technique<sup>4</sup>; 25 were found to be positive (4.3% of 578 samples).

Eighteen of the 25 patients with cryptosporidiosis were children aged under 2. The disease was found in both sexes and in 21 patients who were moderately to well nourished. *Cryptosporidium* was the only pathogen in 20 of the 25 patients. Twenty four of them had watery diarrhoea, and 18 were either mildly dehydrated or not dehydrated at all three days after the start of diarrhoea. Six of the 18 children under 2 were moderately dehydrated. Twenty two patients suffered from vomiting and three from mild fever. There was a sudden increase in cases of cryptosporidiosis during the hot, humid weather in March.

In most stool samples we found few segmented leukocytes, no other inflammatory cells, and no red blood cells. All dehydrated patients were successfully rehydrated orally with a rice based solution, and 18 were discharged within 16 hours of admission. A cough was present in six of the patients under 2.

### Comment

By studying a small sample of patients we have established that *Cryptosporidium* exists in Bangladesh. As the sole pathogen it seems to cause a mild, transient, easily managed form of diarrhoea, particularly among young children; only four (16%) of the 25 patients studied were malnourished. The presence of cough in some of the

children raises the possibility of respiratory infection, as previously reported in man and birds. The oocyst is small enough to be carried by dust. Much of the inhaled dust (possibly in the form of dried poultry litter) is undoubtedly cleared from the tracheobronchial mucosa by the cilia. It is then swallowed and enters the gastrointestinal tract. Many families in Bangladesh keep their poultry and cattle within their premises. *Cryptosporidium* was recently detected in 14% of calves with diarrhoea and 1% of calves without diarrhoea at a dairy farm in Bangladesh, as well as in 8.5% of their handlers with diarrhoea. *Cryptosporidium* was not, however, found in healthy people.<sup>5</sup>

We are now carrying out more extensive studies.

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## Relation between dentition and dyspeptic disorders

There is a dearth of information relating the state of the teeth to dyspepsia. This study examined a theory that a disproportionately high number of patients with gastric ulcer and gastric cancer were edentulous.

### Patients, methods, and results

From a consecutive series of 400 patients undergoing endoscopy 291 patients fell into the four categories of normal endoscopic findings, gastric ulcer, duodenal ulcer, and gastric cancer; their ages and dentition were recorded. By a subsequent questionnaire to 100 of the patients selected at random we determined the chronological relation between total loss of natural teeth and onset of dyspepsia and whether the patients wore dentures at meal times. To investigate the association of each category with dentition, allowing for age, we divided the patients into age groups of five years. Within each group we constructed a contingency table of dyspepsia against dentition. From each of these tables the expected number of patients with dentures within each category of dyspepsia was calculated under the null hypothesis that dentition and disease were unrelated. Finally, we summed the expected numbers of patients with dentures within the categories of dyspepsia over all ages and compared them with the observed numbers. We assessed the significance of the association with a  $\chi^2$  test based on the expected and observed numbers in this pooled contingency table.<sup>1</sup>

The table shows the use of dentures by the patients in the four categories and their mean ages: lack of natural teeth was commonest among the patients with gastric ulcer and gastric cancer. These patients were also older. When the observed numbers of patients with and without dentures were compared with the expected numbers there was no significant

Cross tabulation of endoscopic findings with dentition in patients with dyspepsia, after allowing for age

	Normal findings (n = 85)	Duodenal ulcer (n = 133)	Gastric ulcer (n = 59)	Gastric cancer (n = 14)
With dentures	Observed 38 (45%)	79 (59%)	46 (78%)	12 (86%)
	Expected 43.9	76.7	41.9	12.4
With only natural teeth	Observed 47	54	13	2
	Expected 41.1	56.3	17.1	1.6
Mean (SD) age (years)	52.0 (17.7)	54.2 (15.1)	62.2 (12.8)	75.2 (12.0)

association between dentition and category of dyspepsia after allowing for age ( $\chi^2 = 3.3$ ,  $df = 3$ ,  $0.3 < p < 0.4$ ).

The chronological relation between onset of dyspepsia and total loss of natural teeth could be clearly defined in 89 patients. Sixty three had lost their teeth before the onset of dyspepsia. This was true for all categories. No difference was found in the duration of dyspepsia before endoscopy between patients with only natural teeth and those with dentures. Only six patients admitted to removing their dentures before a meal.

### Comment

There have been few reports in the past 50 years of a relation between diseases of the upper alimentary tract and dentition. In 1929 Hurst and Stewart attributed peptic ulcer of the stomach and duodenum to carious teeth and apical abscesses, based on an increased prevalence of caries in patients with ulcers compared with normal controls<sup>2</sup>: "sound" teeth were present in 19% of patients with ulcers compared with 48% of controls. These observations have not been confirmed. Draper *et al*, from anthropometric measurements, identified a jaw shape and disposition of teeth that they regarded as being of "ulcer type,"<sup>3</sup> but they did not provide any data to substantiate this. Differences in the prevalence of peptic ulcer in various regions of India have been attributed to differences in the demand for mastication by the type of food eaten and in the quantity and content of saliva, but the dental state was not reported.<sup>4</sup> In a survey of dental health in Scotland 45% of subjects aged 35-54 and 83% of those aged 55 plus had lost all their teeth.<sup>5</sup> The ratio of full to partial dentures in our patients was 4:1, and 67% had no natural teeth. The theory that most patients with gastric ulcer and gastric cancer are edentulous was confirmed, but this would be expected from their age.

In conclusion, loss of teeth generally precedes dyspepsia and was observed in all clinical categories including patients with normal endoscopic findings. Though lack of teeth may have a role in some cases of dyspepsia, it can be only a minimal one.

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## Vascular occlusion and disseminated intravascular coagulation in falciparum malaria

Disseminated intravascular coagulation is the probable cause of the renal, pulmonary, and cerebral complications seen in falciparum but not in benign tertian or quartan malaria,<sup>1</sup> but how the abnormality in coagulation is produced is not known. We suspected that the red blood cells containing parasites might be responsible for initiating disseminated intravascular coagulation in falciparum malaria, and so we compared the procoagulant activity in red blood cells from control patients and from patients infected with *Plasmodium falciparum* and *P. vivax*.

### Patients, methods, and results

Shortening of the one stage plasma recalcification time of normal plasma was taken as an index of red cell procoagulant activity.<sup>2</sup> The plasma recalcification time of normal pooled plasma (pool of six samples) obtained on each day of the study was taken as 100% in the calculation of the effect