florid pseudomembranous colitis throughout the colon. Histological examination confirmed the diagnosis and showed superadded ischaemic necrosis.

Discussion

This patient developed pseudomembranous colitis within seven days of starting antibiotics. Despite adequate doses of vancomycin and clearance of both the organism and its toxin from the faeces he did not improve clinically or histologically. The reason for this is not clear, but possibly the underlying disease process or the corticosteroid treatment may have modified the therapeutic response.

Price and Davies⁵ divided the histological appearances of pseudomembranous colitis into three categories: type 1 is characterised by the "summit" lesion; type 2 by the pseudomembrane; and type 3, the most severe and advanced lesion, by structural necrosis and disease of the lamina propria. They suggested that the type 3 lesion may be due to a Shwartzman reaction with localised intravascular coagulation and microthrombosis leading to ischaemic necrosis. Our patient developed the type 3 lesion before vancomycin was started, and we suggest that by this stage the disease may be irreversible and unaffected by a bacteriological response. If this is so we think that in pseudomembranous colitis, especially in the presence of other serious disease, treatment with vancomycin should not be delayed.

¹ Larson HE, Price AB, Honour P, Borriello SP. *Clostridium difficile* and the aetiology of pseudomembranous colitis. *Lancet* 1978;ii:1063-6.

² Bartlett JG, Chang TW, Gurwith M, Gorbach S, Onderdonk AB. Antibiotic-associated pseudomembranous colitis due to toxic-producing clostridia. *N Engl J Med* 1978;298:531-4.

³ Keighley MRB, Burdon DW, Arabi Y, et al. Randomised controlled trial of vancomycin for pseudomembranous colitis and postoperative diarrhoea. *Br Med J* 1978;iii:1667-9.

⁴ Bartlett JG, Tedesco FJ, Shull S, Lowe B, Chang T. Symptomatic relapse after oral vancomycin therapy of antibiotic-associated pseudomembranous colitis. *Gastroenterology* 1980;78:431-4.

⁵ Price AB, Davies DR. Pseudomembranous colitis. *J Clin Pathol* 1977;30:1-12.

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General Hospital, Birmingham B4 6NH

P C HAWKER, MD, MRCP, senior medical registrar
K R HINE, MB, MRCP, research fellow (present appointment: senior medical registrar, Derbyshire Royal Infirmary, Derby)
D W BURDON, MB, MRCPATH, consultant microbiologist
H THOMPSON, MB, FRCPATH, reader in pathology
M R B KEIGHLEY, MS, FRCS, reader in surgery

Sulphasalazine desensitisation

Sulphasalazine is extremely valuable in ulcerative colitis, particularly when used as maintenance treatment.¹ Rash, often associated with fever, occurs as a side effect in 1-5% of patients in different series. Svartz, who introduced sulphasalazine into therapeutics, indicated that some patients who experienced such a reaction could be desensitised,² but this observation has been forgotten or ignored, and most authorities state firmly that development of a rash is a contraindication to further use of the drug.³ I report that most patients who have had a rash or fever after taking sulphasalazine may be easily desensitised.

Methods and results

With the precedent of desensitisation regimens to penicillin,⁴ treatment was started in eight patients at one-thousandth of the normal therapeutic dose. Capsules were prepared containing 1 mg, 10 mg, and 100 mg of sulphasalazine. All patients started with 1 mg daily and the dose was progressively doubled; pauses in this dose increase occurred when 10 mg and 100 mg daily were achieved, each of these doses being taken for one week before doubling began again. The precise rate of increase varied, but 100 mg was never reached before 14 days and the normal tablet strength of 500 mg was never reached before 23 days. Patients were instructed that should any reaction develop, such as fever or skin eruption, the dose should not be increased further but should be continued until the reaction had settled down.

The table shows that of the eight patients studied, six had previously had a

rash, sometimes associated with fever, and two fever alone, as a reaction to treatment with the drug. In five patients the reaction had occurred while they were under observation as inpatients and was well documented. In the three others (cases 3, 5, 6) there was clear evidence of a reaction in the history. Desensitisation failed only one patient (case 8), who developed permanent light sensitivity, a rare, though well-recognised, reaction after treatment with sulphonamides.⁵ All other patients are now taking a normal maintenance dose of 2 g or 3 g daily.

Desensitisation was also tried in two patients whose reactions to sulphasalazine were abdominal pain, headache, and diarrhoea, rather than fever or rash. In both it was unsuccessful, diarrhoea and headache developing when 20 mg and 500 mg daily were reached.

Original reaction and duration of associated treatment and reaction on desensitisation. (Statements in quotation marks are summaries of patients' own descriptions)

Case No	Age (years)	Sex	Original reaction and duration of associated treatment	Reaction on desensitisation
1	21	F	Rash 7 days	
2	32	F	Fever 15 days; rash 26 days	
3	36	M	"Rash and fever" about 7 days	
4	40	F	Fever 8 days	
5	65	F	"Face swollen every time Salazopyrine taken"	
6	39	F	"Came out in blotches" about 7 days	
7	28	F	Abdominal pain and fever about 7 days	
8	11	M	Rash, fever, oedema, lymphadenopathy Residual permanent light sensitivity	Rash and vomiting at 100 mg daily Later reaction at 10 mg thrice daily

Comment

Desensitisation was successful in all except one of the patients who had previously developed rash or fever when taking the drug and were thought to be still likely to benefit from the drug for maintenance treatment. It is likely that the sensitivity is due to the sulphapyridine component of sulphasalazine; similar ease of desensitisation, except in patients with light sensitivity, has been recorded in patients sensitised to sulphonamides.⁵ Desensitisation is an easy outpatient procedure and requires only the co-operation of the hospital pharmacy to prepare capsules of appropriate strength. Corticosteroid cover is not needed: none of the patients who were successfully desensitised were taking steroids at the time, though several had been taking large doses when they developed their initial reaction.

Extrapolation from this study in one clinic suggests that there may be several hundred patients in Great Britain alone who are currently denied treatment with sulphasalazine in the mistaken belief that it is permanently contraindicated because of an initial skin eruption or drug fever. The only cautionary note is that should the drug be stopped in such patients, sudden readministration at full dosage would probably again be followed by an adverse reaction. Furthermore, desensitisation is not worth attempting for the more common side effects of sulphasalazine such as headaches, nausea, and abdominal discomfort.

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³ Goodman MJ, Sparberg M. *Ulcerative colitis*. New York, Chichester, Brisbane, Toronto: John Wiley and Sons, 1978:123.

⁴ Peck SM, Siegel S, Gliok AW, Kurtin A. Clinical problems in penicillin sensitivity. *JAMA* 1948;138:631-40.

⁵ Peterkin GAG. Sulphonamide rashes. *Br Med J* 1945;iii:1-6.

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Gastroenterology Unit, Royal Hallamshire Hospital, Sheffield S10 2JF

C D HOLDSWORTH, MD, FRCP, consultant physician