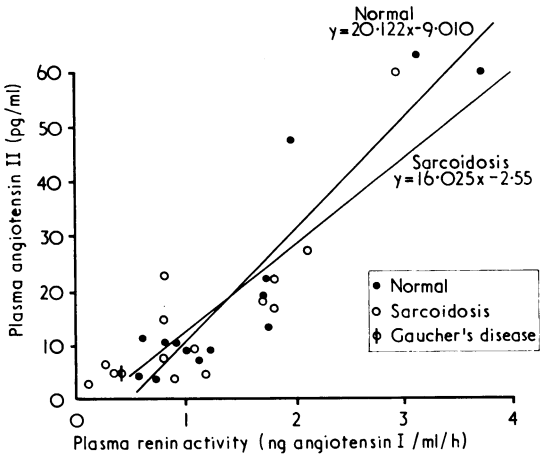

Regressions of concentrations of angiotensin II on plasma renin activity in normal subjects and patients with sarcoidosis are also shown for one patient with Gaucher's disease.

between these two variables for the two groups might be expected if the conversion of angiotensin I to angiotensin II was a rate-limiting step. The absence of any difference in the correlations in patients with sarcoidosis and in normal subjects reported here suggests that converting enzyme does not have a regulatory role in the renin-angiotensin system. Increased concentrations of angiotensin-converting enzyme therefore have no apparent physiological consequences, although when the enzyme is inhibited a fall in blood pressure may occur.

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Specific IgM responses after rubella vaccination; potential application following inadvertent vaccination during pregnancy

Despite recommendations from the DHSS that pregnancy should be excluded at the time of rubella vaccination and prevented for two months thereafter,[1] at least 120 terminations of pregnancy were reported in England and Wales between 1972 and 1975 after inadvertent vaccination during pregnancy or the eight weeks before estimated conception.[2] This figure almost certainly represents a considerable underestimate. Although the immune state of women of childbearing age should always be established before vaccination, a study in the USA reported that the immune state of 259 of 343 (70%) women inadvertently vaccinated during pregnancy was unknown[3]; probably a similar proportion of women whose pregnancies were terminated in England and Wales were not tested for rubella antibodies. Since roughly 80% of women of childbearing age are already immune, many pregnancies may have been terminated unnecessarily, for the risk of giving rubella vaccine to a woman who is immune is negligible.

It may be difficult to determine whether a woman vaccinated without previous antibody screening was indeed susceptible unless she has virological investigation shortly after vaccination. Detection of rubella-specific IgM may be useful, for it is usually present for up to six weeks after naturally acquired primary infections, but in some cases it may persist much longer.[4] In our experience, however, pregnant women who have been inadvertently vaccinated may not have virological investigations for some 8-12 weeks after vaccination. But less is known of the reliability of detecting rubella-specific IgM responses and their duration after rubella vaccination, since the number of specimens so far examined at varying intervals after vaccination with different vaccines is small.[4] We have therefore tried to determine how consistently rubella-specific IgM may be detected in people given either of the two currently licensed vaccines in Britain, RA 27/3 or Cendehill. Results were compared with those obtained from patients who had acquired the disease naturally at similar times.

Materials and methods

Sera were collected from 40 susceptible nurses and female medical students who had been given RA 27/3 or Cendehill vaccines and 16 women who had acquired the infection naturally. Rubella-specific IgM was detected by serum fractionation on sucrose density gradients, the sensitivity of the haemagglutination-inhibition (HAI) test being enhanced by incubating serum fractions with rubella antigen overnight at 4°C, as described.[4] Instead of using day-old chick erythrocytes, however, we used trypsinised, human O erythrocytes.[5] Because it has been suggested that IgM titres may decline if sera are kept at ambient temperature during transport, two serum samples from vaccinated women which were known to contain high and low rubella-specific IgM titres were sent to the laboratory by second-class mail. Their virus-specific IgM titres were compared with aliquots of the same samples kept at −20°C.

Results and comment

Eight weeks after vaccination rubella-specific IgM was detected in the sera of all 16 patients with naturally acquired infection, all 20 women given RA 27/3, and 16 of the 20 given Cendehill vaccine (see table). Among women given Cendehill, three of the four in whom rubella-specific IgM was not detected had low total HAI antibody titres (≤1/16). Among those given RA 27/3, however, rubella-specific IgM could be detected in the sera with low HAI titres (table).

Number of subjects found to be positive for rubella-specific IgM six weeks after naturally acquired infection and eight weeks after vaccination with RA 27/3 and Cendehill vaccines. Results expressed as proportions of number tested*

HAI titre 1 in:	8	16	32	≥64	Total (%)
Natural infection				16/16	16/16 (100)
RA 27/3	1/1	1/1	5/5	13/13	20/20 (100)
Cendehill	1/2	3/5	6/7	6/6	16/20 (80)
Total:	2/3	4/6	11/12	35/35	52/56 (92)

HAI = haemagglutination-inhibition.
*Six weeks after naturally acquired infection and eight weeks after vaccination represent comparable periods, as there is a delay of approximately two weeks before symptoms may occur and antibodies develop after vaccination.

By 12 weeks, rubella-specific IgM was detected less consistently: thus it was present in 10 of the 14 women given RA 27/3, four of the five given Cendehill, and three of the five who had had the natural disease. Since the results of testing at this time were apparently less reliable no further samples were tested. No difference in the IgM titres was observed in the two serum samples that had been posted, although they had been two days in the post, and had been held for five days at 4°C before being tested.

The risk of damaging the fetus when rubella vaccines are given in early pregnancy appears to be less than after naturally acquired disease, for no defects have so far been detected in 38 American babies born to rubella-susceptible mothers vaccinated in early pregnancy who chose to go to term.[3] Nevertheless, it would be premature to conclude that rubella vaccination during pregnancy is without risk, since relatively few patients have been studied, and follow-up studies are too short to exclude the possibility that defects will subsequently be revealed. Furthermore, rubella virus has been recovered from the products of conception of susceptible women inadvertently vaccinated

during pregnancy, and histological changes in the decidua and fetal organs resemble those present after naturally acquired maternal disease.[3] Until more information has been collected, pregnancy must remain a contraindication to rubella vaccination. Nevertheless, inadvertent vaccination during pregnancy will undoubtedly still occur, and unfortunately many who have not been screened for rubella antibodies will be advised to have their pregnancies terminated. We think that this fetal wastage could be considerably reduced, since our results show that if patients not screened for rubella antibodies before vaccination have virological assessment within eight weeks of receiving RA 27/3 vaccine, it is possible to determine whether their antibody results from recent vaccination or from past infection. Results after vaccination with Cendehill vaccine are somewhat less reliable, however, unless the vaccine has induced a reasonably high HAI antibody response (for example, $\geqslant 1/32$ in our study).

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Sulphasalazine rectal enemas: topical method of inducing remission of active ulcerative colitis affecting rectum and descending colon

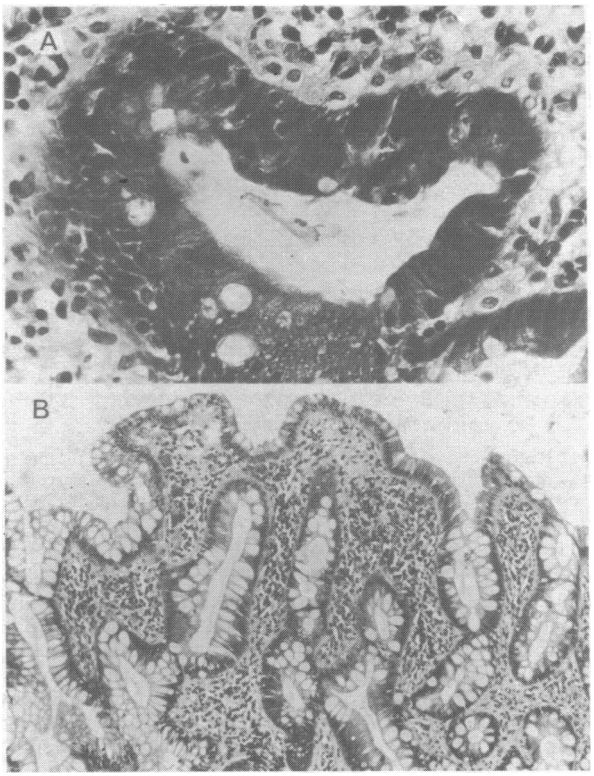
The Truelove regimen, which includes prednisolone and sulphasalazine by mouth, is an effective treatment for acute active ulcerative colitis with total colonic involvement,[1-3] though relapse may occur and the steroid component may aggravate underlying disorders such as diabetes mellitus. Intolerance to sulphasalazine by mouth is common, with rash, haemolytic anaemia, nausea, and vomiting.[4] Suppositories of sulphasalazine have been used in ulcerative colitis,[5] but we report for the first time the use of sulphasalazine enemas.

Patients, methods, and results

We selected 10 patients with acute ulcerative colitis (five male, and five female), of whom five were in relapse and five had not previously been treated. All had severe clinical disease with loss of the normal mucosal vascular pattern and friability of the mucosa on light swabbing. Sigmoidoscopy and rectal biopsy were performed in all cases before and after introduction of the enemas. Multiple rectal biopsy specimens were taken to obviate sampling errors. All pretreatment specimens showed acute active ulcerative colitis. Multiple post-treatment biopsies were performed on days 8-213. Enemas were prepared by dissolving two sulphasalazine tablets (1 g sulphasalazine) in a glass of water and administered twice daily with a bulb enema syringe. All patients found the treatment acceptable.

Five patients in relapse after treatment with the Truelove regimen or maintenance doses of sulphasalazine by mouth or both entered a period of maintained clinical remission of 11 months with sulphasalazine enemas. In one of these patients steroids had greatly aggravated an underlying diabetes mellitus, necessitating insulin treatment. Of the patients who had not been treated previously, four became asymptomatic after receiving sulphasalazine enemas as the initial treatment. The remaining patient was severely ill on admission and was started on the Truelove regimen together with sulphasalazine enemas. There was a remarkable clinical and sigmoidoscopic improvement, and after 10 days he was discharged on maintenance treatment with sulphasalazine enemas and sulphasalazine and steroids by mouth. He relapsed after four months but again responded rapidly to the Truelove regimen and sulphasalazine enemas. He continued in remission for three months and gained 13·6 kg.

Only one patient, in whom biopsy was carried out nine days after treatment, showed no histological evidence of improvement. The other nine patients showed remarkable improvement, which began as early as eight days after treatment and was maintained for up to 11 months (see figure).



Rectal biopsy appearances before and after treatment with Truelove regimen and sulphasalazine enemas. Top: Before treatment. Gland showing severe borderline dysplasia. (Haematoxylin and eosin. ×233.) Bottom: Fifteen days after treatment. Return of normal pattern with no dysplasia (H and E. ×60.)

Comment

The mechanism by which sulphasalazine enemas exert an effect extending back to the splenic flexure is not understood, though in patients with generalised ulcerative colitis steroid enemas mixed with contrast material have been shown to reach the hepatic flexure. Our results suggest that the topical application of sulphasalazine to rectal and colonic mucosa in acute ulcerative colitis is highly effective, and thus sulphasalazine enemas are a useful adjunct to the Truelove regimen. The method is cheap and well tolerated.

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