infusion suggesting that, though the oesophageal mucosa might have been stimulated, the pain produced was not epigastric.

We could not confirm that the cardiac sphincter pressure of those patients with epigastric pain was different from those without such pain. Moreover, radiological evidence of the capacity to herniate stomach, or of reflux of barium, as a measure of the incompetence of the anti-reflux mechanism, did not correspond with the incidence of epigastric pain.

Hence we find little support for Earlam's hypothesis that the epigastric pain of duodenal ulcer is caused by acid stimulation of the oesophageal mucosa.

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Intranasal Beclomethasone Dipropionate in Allergic Rhinitis

Beclomethasone dipropionate is a locally active corticosteroid of value in asthma in young people[1] and possibly also in hay fever[2] and perennial rhinitis.[3] We carried out double-blind clinical trials in 69 patients with seasonal and perennial rhinitis.

Methods and Results

Sixty-four patients were aged 8 to 16 years and five were over 16 years; 42 were male and 27 female. Forty-five had perennial rhinitis, clinically allergic, and all had large wealing skin reactions on prick testing to house dust extract and to extract of *Dermatophagoides pteronyssinus*. Twenty-eight of these patients had positive nasal provocation tests on challenge with the mite extract resulting in a fall of at least 50% in the "nasal FEV"—a simple practical,[4] but less accurate measure of nasal airways resistance than that developed by Taylor and Shivalkar.[5]

A double-blind cross-over trial of two weeks on beclomethasone dipropionate 50 μg in each nostril four times a day and two weeks on a similar placebo aerosol was carried out in the 45 patients with perennial rhinitis. Four weeks' treatment was given with beclomethasone dipropionate or with the placebo aerosol during the pollen season of 1974 to 24 patients with seasonal hay fever and large wealing reactions on prick testing with grass pollen extract. Treatment was allocated on a random basis with no cross-over.

Results were assessed by weekly clinical examination, the patients' subjective opinion, daily symptom record cards, and weekly measurements of "nasal FEV." Grass pollen counts were available from the Midlands Asthma and Allergy Research Association in Derby as a check on allergen challenge in the pollen season.

Assessment of 45 patients with perennial rhinitis showed that 29 improved on beclomethasone dipropionate, 11 improved on placebo aerosol, while five were unchanged throughout the trial. Statistically this result favours a beneficial effect of treatment ($P < 0.025$).

Among the 28 who had positive nasal challenge tests with mite extract 21 were improved when on beclomethasone dipropionate and only seven when on placebo ($P < 0.04$). Among the 17 patients with negative challenge tests to mite extract eight were assessed as better when on treatment, eight better on placebo, and one unchanged.

The results in the pollen-sensitive patients were that nine out of the 13 allocated to treatment with beclomethasone dipropionate were improved while only two of the 11 patients allocated to the placebo aerosol were improved. This difference is statistically indicative of a beneficial effect of the treatment in hay fever ($P < 0.05$). No toxic effects of any kind were noted during these trials.

Conclusion

Intranasal beclomethasone dipropionate is an effective treatment in allergic rhinitis. The best results were obtained in hay fever and in patients with perennial rhinitis shown to have positive nasal challenge test with extract of the mite, *Dermatophagoides pteronyssinus*. Though all the patients were considered to have typical allergic rhinitis, those who failed to give positive nasal challenge tests may have been the more chronic and intractable cases requiring longer treatment. Such simple measures as the "nasal FEV" may be of value in assessing results of clinical trials but no completely satisfactory and simple measure of changes in nasal airway is available.

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Generalized Pustular Psoriasis on Withdrawal of Clobetasol Propionate Ointment

Withdrawal of systemic corticosteroid treatment is a provocative factor in the development of generalized pustular psoriasis (G.P.P.) from chronic psoriasis.[1] The advent of a topical preparation more potent than previously available poses the question of whether a similar "rebound" effect might occur on reduction or withdrawal of its use. This is a report of two cases in which, after topical clobetasol propionate was withdrawn, G.P.P. developed for the first time in the patients' history.

Case Histories

A woman of 54 with chronic psoriasis for 40 years—treated recently with a proprietary tar-containing preparation—was started on clobetasol propionate ointment (Dermovate, Glaxo) by her doctor in August 1974. The schedule was designed to tail off the treatment as soon as a satisfactory response was obtained. Initially the response was excellent but plaques which had had no treatment for a week or two began to reappear, seemed more inflamed than usual, and had pustulation at the edges. At the outpatient clinic in December 1974 she had had no topical treatment for six weeks and her psoriasis showed widespread annular lesions with extensive pustulation (Lapière form of G.P.P.). She was admitted immediately; response to routine non-steroid treatment was poor though active pustulation stopped after two weeks. Extensive investigation showed no appreciable abnormality apart from a mild iron-deficiency anaemia, attributed to abstinence from meat. The deficiency responded to oral iron. In January 1975 she was started on methotrexate treatment to induce a remission and she has improved steadily ever since.

The second patient was a 45-year-old man with a seven-year history of chronic psoriasis. Since coming under our department's care he had had two periods of inpatient treatment with tar preparations supplemented by betamethasone valerate ointment. His psoriasis had tended to relapse within a few weeks of discharge, but had always shown itself as chronic scaly plaques. In June 1974 he was admitted during a phase of worsening psoriasis which was treated with tar and salicylic acid ointment supplemented with the new preparation clobetasol propionate ointment; there was some improvement and the steroid preparation was diluted. Because his psoriasis was recalcitrant full-scale investigation was arranged, including liver biopsy, to prepare him for methotrexate treatment. This was started, but produced a dramatic fall in his platelet count so it was decided that he was not suitable for long-term methotrexate. When discharged in October 1974 he was treating his trunk and limbs with one-tenth strength clobetasol propionate cream. Nevertheless, he did not use the ointment on his thighs and, within two weeks of discharge, stopped using it altogether. When seen for follow-up in November he had widespread psoriasis with numerous flaccid pustules over whole plaques on his trunk and legs (incipient Zumbusch type of G.P.P.). He was admitted immediately and improved somewhat with the reintroduction of clobetasol propionate ointment, but after a month pustulation was still present on the thighs (the first site from which clobetasol had been withdrawn completely) and it was decided to treat him with azathioprine. He improved slowly over three weeks and all pustulation stopped.

Conclusion

While "rebound" after topical steroid treatment of psoriasis is recognized, hitherto we have not had a topical preparation potent

enough to produce conversion to the generalized pustular form, with its attendant risks of severe systemic illness. We think that our experience should sound a note of caution in the prescribing and withdrawal of such a potent preparation.

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Costing Cryoprecipitate for Haemophilia

Though haemophilia is rare, affecting two to three males per 100 000 of the population, the management of patients presents a continuing problem. The only effective treatment is replacement of the anti-haemophilic factor (A.H.F. factor VIII) which the patient lacks. There are two main sources of this material—cryoprecipitate, which can be made in regional blood transfusion laboratories, or A.H.F. concentrates which may be bought from commercial sources or made in national blood products laboratories. Nationally-made A.H.F. concentrates are not yet made in sufficient quantity to meet the haemophilic needs of all regions. Hence in most haemophilic centres they have to decide between using cryoprecipitate or commercial A.H.F. concentrates. We present here a study of the cost of cryoprecipitate production in the West of Scotland Regional Blood Transfusion Laboratory, Carluke.

Methods and Results

Cryoprecipitate is prepared here by a slight modification of the original method of Pool *et al.*[1] Occasionally blood platelets may also be produced by addition of a centrifugation step before freezing the plasma. About half of the cryoprecipitate used in the west of Scotland is prepared in the blood transfusion centre in West Regent Street, Glasgow, which is what we costed (see table). As cryoprecipitate is an additional product, the cost of collecting blood is immaterial. Only the extra costs incurred in preparing cryoprecipitate need be assessed—including wages and salaries, materials, equipment, and overheads.

In 1973 8680 packs of cryoprecipitate out of a regional total of 20 000 were prepared at the centre. Of these about 3000 were produced jointly with platelets. The average yield of A.H.F. units per pack was 80. A total annual cost of £14 658 gives a cost per pack of cryoprecipitate of about £1·69 and a cost per unit of A.H.F. of just over 2p.

Breakdown of total annual cost of preparing cryoprecipitates

Item		Annual cost	%
		£	
Wages and Salaries		6901	47·1
Materials	(i) transfusion packs	4411	30·1
	(ii) other materials	1056	7·2
Equipment	(i) capital cost	1095	7·5
	(ii) maintenance	170	1·1
Overheads		1025	7·0
Total		14 658	100·0

Discussion

Though replacement of antihaemophilic factor will rapidly control haemophilic bleeding, only about 10% of haemophilic patients receive optimum treatment for their disease.[2]

The major disadvantages of cryoprecipitate are (*a*) the factor VIII level is not known, (*b*) recovery is variable and unpredictable, (*c*) reconstitution is time-consuming and tiresome, (*d*) it must be stored in a deep freeze, and (*e*) there is an appreciable incidence of allergic reactions. Hence much effort has gone into the search for a more potent concentrate of A.H.F. and the U.K. now has three commercial sources of such concentrates. Their advantages are that the material is preassayed and a predicted dose can be given to the patient; it is freeze-dried and, therefore, much more stable; and because of the high concentration, the predicted dose can be injected by syringe in a small volume. This makes concentrates very suitable for self-administration and hence for home treatment. Perhaps the major disadvantage is cost (about 10p per A.H.F. unit), which is about five times our estimate for cryoprecipitate.

There are no accurate figures available for the cost of treating all haemophilics in the United Kingdom. In our region we have 232 patients with a diagnosis of haemophilia. Nevertheless, 80% of the 20 000 packs of cryoprecipitate are needed for only 40 of the regular attenders—that is, the more severely affected patients. Ninety-five per cent. of the material used in the period surveyed was cryoprecipitate (cost £33 800). If commercial concentrate had been used exclusively the cost would have been £160 000. If these figures are projected to national requirements the cost of cryoprecipitate would be £676 000, compared with £3·2m for commercial concentrates. But this level of treatment is unsatisfactory in at least 90% of patients.

In the current financial climate we must strike a compromise and use commercial A.H.F. concentrates for home treatment where it is most effective, and use the very much cheaper cryoprecipitate in the haemophilia centres where some of its main disadvantages may be overcome.

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An appendix with detailed notes of the figures used in the costing is available from the authors.

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