should be aware that oesophageal stricture is a possible late complication of endoscopy, particularly in the elderly.

¹ Schiller, K F R, and Prout, B J, *Modern Topics in Gastrointestinal Endoscopy*, p 147-165. London, Heinemann, 1976.

(Accepted 5 January 1978)

Department of Gastroenterology, Royal Victoria Hospital, Bournemouth

G E HOLDSTOCK, MB, MRCP, medical registrar
M J WISEMAN, MB, MRCP, senior house officer
C A LOEHRY, MD, FRCP, consultant physician

Sodium cromoglycate in intrinsic asthma

Sodium cromoglycate (SCG) gives prophylactic benefit in many patients with extrinsic asthma, but its value in intrinsic asthma, where no allergic mechanisms can be shown, is not clear.¹ Using a clinical trial we attempted to answer the following questions: (a) what proportion of intrinsic asthmatics respond to SCG? (b) over what time period does a response take place? (c) do responders have any identifying clinical characteristics?

Study and results

We studied 20 patients (10 of each sex), average age 57. None had a personal or family history of atopy. All had negative skin-prick tests to 18 common allergens; 10 had chronic cough with sputum. Since SCG is an inhaled powder which may cause immediate bronchoconstriction by direct irritation, a truly matching placebo cannot be prepared. Therefore lung function measurements made when the subject was taking SCG (contents of 1 capsule inhaled four times daily) were compared with control measurements, both before and after treatment. Initially, after a two-week control period, patients received SCG for four to eight weeks followed by a second control period of two weeks. Experience with the first 10 patients showed that when a response was seen it was detectable at the end of two weeks, though further response might occur over the next four weeks, and that when no response was seen in the first two weeks no response occurred subsequently. Therefore, the second 10 patients received SCG for two weeks only. Other necessary treatment for asthma, including oral prednisone 5 mg/day in four patients and beclomethasone inhalations in five, continued throughout.

Peak expiratory flow rate (PEFR) was measured as the best of three attempts with a Wright peak flow meter four times daily. The highest and lowest readings for each day were plotted as in the figure. The highest PEFRs during the last seven days of the treatment period were compared by unpaired *t* tests with the highest PEFRs of the last seven days of both control periods, with $P < 0.05$ as the level of significance. Two similar comparisons were made for the lowest PEFRs, making four comparisons for each patient. Forced expiratory volumes (using a dry spirometer), absolute lung volumes, and airways resistance (using a body plethysmograph) were measured at the end of treatment and both control periods.

Three patients showed a significant beneficial response for all four comparisons (figure). The significance levels achieved were always greater for the lowest as opposed to the highest PEFRs. Three patients showed a significant deterioration in PEFRs (and symptoms) requiring termination of the trial. The remaining 14 showed no significant change. The three patients responding positively were not detected by the infrequent comprehensive lung function testing. Although all three responders had a relatively short history of asthma (<1 year) and had not received treatment with corticosteroids, four other patients with both these criteria failed to respond. We examined also the blood eosinophil counts, immunoglobulin concentrations, presence of autoantibodies, and degree of lung hyperinflation for prognostic significance without success.

Conclusions

We draw five conclusions from this study. Firstly, only three of 20 patients with intrinsic asthma showed benefit from SCG, and three got worse, presumably from the direct irritant effect. Secondly, two weeks is an adequate trial period. Thirdly, we could find no clinical features which predicted a positive or negative response. Fourthly, the true effect of this mast-cell stabiliser cannot be assessed with this preparation, for there may have been patients who responded but

A beneficial response to SCG. Each pair of points represents highest and lowest PEFRs on a given day. Improvement is seen mainly in the lowest readings and appears to occur progressively over two months. Salbutamol could be discontinued.

in whom the benefit was cancelled by direct irritant bronchoconstriction. Fifthly, infrequent (even if comprehensive) lung function testing is useless in detecting drug response over days or weeks in asthmatic patients. Frequent simple measurements such as PEFR are essential.

¹ Rawlins, M D, *British Medical Journal*, 1977, 2, 701.

(Accepted 20 January 1978)

Departments of Medicine and Immunology, The Middlesex Hospital Medical School, London W1

KENNETH B SAUNDERS, MD, MRCP, senior lecturer
MICHAEL RUDOLF, MB, MRCP, Jules Thorn research fellow
JONATHAN BROSTOFF, MB, MRCP, senior lecturer

Associated clinical syndromes in a patient homozygous for HLA B27

Several diseases are associated with the expression of certain HLA antigens,¹ the strongest being that between ankylosing spondylitis and HLA B27. About 90% of the patients with this disease possess the B27 antigen compared with only 6% of the general population.^{2,3} Other syndromes associated with HLA B27 include Reiter's disease, anterior uveitis, Still's disease, psoriatic arthropathy, and various reactive arthropathies such as salmonella and Yersinia arthropathy. The clinical features of these syndromes show considerable overlap but the pathological mechanisms remain a puzzle. We report a patient who presented with features of several of these syndromes concurrently. Tissue typing revealed the expression of HLA A2, B27, and a subsequent family study suggested that the patient was homozygous at the HLA A and B loci, but not at the D locus.

Case report

A 64-year-old man was referred to the medical clinic because of progressive stiffening and pain in the joints of his hands together with increasing low back pain developing over several months. He had also noted a persistent dry cough, urinary frequency, and dysuria. Six weeks before referral he had

been treated for an acute episode of anterior uveitis with atropine and prednisolone eye drops. There was no relevant history or family history. He was married with three children and had retired from grocery work three years before presentation. He was a non-smoker. He showed appreciable soft tissue swelling and deformity of his distal interphalangeal joints together with dystrophic, pitted nails. Some of his toes were swollen and sausage-shaped but his toe nails were normal. His sacroiliac joints were tender to percussion and he could get within only 15 cm of his toes on bending forward. His spine was stiff. Elbows, shoulders, knees, and ankle joints appeared unaffected. There were no rheumatoid nodules, gouty tophi, or neurological abnormalities. His right eye showed changes consistent with healing anterior uveitis. His glans penis was ulcerated with patches of keratinisation. There was no other rash. Skeletal x-ray films showed an erosive bilateral distal interphalangeal arthropathy with no osteoporosis and normal joints of his feet, although a calcaneal spur was visible. Both sacroiliac joints were eroded with underlying sclerosis. His sedimentation rate was persistently raised at 40–50 mm in first hour. There was no anaemia, and the results of tests for rheumatoid factor (Rose Waaler); antinuclear factor; antibodies to mitochondria, smooth muscle, parietal cells, and thyroid microsomes and colloid were all negative. His serum uric acid concentration was 0.41 mmol/l.

He was treated conservatively with indomethacin, 25 mg thrice daily, which rapidly improved his joint symptoms. Six months after presentation he could stop taking regular indomethacin, and two years later he noted only occasional joint pains. His finger swelling had disappeared and his nails were now normal. There were no changes in the x-ray appearances of his interphalangeal or sacroiliac joints and no new erosions could be seen. There was no recurrence of his urinary symptoms, genital ulceration, or eye problems.

Tissue typing—The family was tested for all antigens designated at the WHO Nomenclature Meeting after the VII Histocompatibility Workshop. The patient was A2, B27, CW3; his mother A2, B27, CW3/AX(2), BW39; and his three offspring A2, B27, CW3/A1, B7 (see figure). Since his father was

at the D locus. It is intriguing to speculate that the pathogenetic mechanisms in these related diseases were triggered by the interaction of an external factor, such as infection with a common virus, and his immunogenetic background.

We thank Dr Eva Wolf and Janet Pritchard for the HLA serological studies and the patient and his family for their co-operation.

¹ *HLA and Disease*, ed J Dausset and A Svejgaard. Copenhagen, Munksgaard, 1977.

² Brewerton, D A, *et al*, *Lancet*, 1973, **1**, 907.

³ Schlosstein, L, *et al*, *New England Journal of Medicine*, 1973, **288**, 704.

⁴ Robinette, M, *et al*, *Histocompatibility Testing*, p 482. Copenhagen, Munksgaard, 1975

(Accepted 5 January 1978)

Department of Medicine, Addenbrooke's Hospital, Cambridge

KAROL SIKORA, PHD, MRCP, honorary registrar and MRC Research Fellow, MRC Laboratory for Molecular Biology (at present clinical fellow in medical oncology, Stanford University Hospital, Stanford, California 94305, USA)

STEPHEN WEBSTER, MD, MRCP, consultant physician

Department of Immunology, London Hospital Medical College, London E1 2AD

JOHN SACHS, MB, PHD, senior lecturer

HILLIARD FESTENSTEIN, MRCPATH, professor

Family tree of patient showing the relatives studied and their HLA A + B locus antigens determined serologically. The patient is represented by the crossed square.

dead it was not possible to establish definitely that he was homozygous for A2, B27, CW3 on serological typing, although the likelihood of having an unidentified antigen at both the A and B locus is very small. If the three offspring who had inherited the same haplotype from the mother had also inherited the same haplotype from the father, their cells should not have stimulated each other in culture.⁴ Two of the siblings did not reciprocally stimulate each other but were strongly stimulated by the third. This suggested that the latter had inherited a different paternal haplotype from the other two siblings, consistent with the view that the daughter had inherited one A3, B27, CW3 haplotype and her two siblings had inherited the other A3, B27, CW3 haplotype with a different D-locus specificity. This view was confirmed by the observation that the father's cells were *not* homozygous for the D-locus as they stimulated his offsprings' cells. Possibly, however, the positive MLC test result among the siblings could be due to the fact that all the offspring had inherited the same paternal haplotype but that a cross-over between HLA-B and D had occurred in the one offspring, who would then differ for a D locus antigen from the other two. From these results it was concluded that the patient was homozygous for A2, B27, and CW3 and heterozygous at the D locus.

Discussion

This patient presented with several of the syndromes known to be associated with HLA B27 (anterior uveitis, ankylosing spondylitis, psoriatic arthropathy with nail changes and features of Reiter's syndrome (urethritis and a keratinising balanitis)). In addition, he had linear shadows in his chest x-ray film and reduced gas transfer suggesting pulmonary alveolitis. These syndromes appeared over a short time and resolved within a year after symptomatic treatment alone. The patient was HLA A2 B27 homozygous but heterozygous

Mononeuritis multiplex due to haemorrhage

Congenital, acquired, and iatrogenic haemorrhagic disorders may cause bleeding into and around peripheral nerves.¹ This case shows the role of a haemorrhagic diathesis in the development of complications of bony and soft tissue injuries.

Case report

A 57-year-old man was admitted after a road traffic accident, in which he had sustained multiple rib fractures, a fractured right clavicle, and a mild head injury. He had been found to have a prolonged clotting time at the age of 15 after a tonsillectomy. In 1962 he had had a factor XI result assay of 12%, and his last episode of bleeding had been a haematoma in the left thigh in 1965. On admission he was bleeding from the right ear; the facial nerve and other cranial nerves were intact, and x-ray films of the skull, including tomography, showed no fracture. Further x-ray films confirmed fractures of several ribs on the right side with a pneumothorax and a fracture of the right clavicle. Soft tissue bruising was also present behind both knees. On the second day he complained of paraesthesiae in the right arm in the distribution of the C7, C8, and T1 dermatomes and later had detectable sensory alteration over this distribution with sensory loss over C8. On the fourth day he developed a right sided lower motor neurone facial weakness, which became complete over the next 24 hours. The threshold to stimulation of the facial nerve remained the same as that on the unaffected side when tested three, five, and 13 days after the onset of the facial weakness. Electromyography on days 5 and 13 showed no evidence of denervation, and on day 5 a single unit firing in isolation showed that the lesion was incomplete. Facial movements were improving within two weeks and had recovered fully within four weeks. As he was mobilised he developed a bilateral foot drop, due to lateral popliteal nerve lesions. Nerve conduction studies showed evidence of a 50% conduction block at the neck of the fibula. Recovery was complete within three months.

Discussion

After bony and soft tissue injuries this patient developed traumatic facial palsy, evidence of damage to the brachial plexus on the side of the fractured clavicle, and bilateral lateral popliteal nerve lesions at the site of extensive bruising.

Potter and Braakman² considered that the aetiology of delayed traumatic facial palsy might be delayed swelling of the nerve within its perineurium; ischaemia; external compression from progressive oedema within the bony canal; or pressure on the nerve due to an expanding haematoma, which in turn might be intraneural or between