Her condition was stabilised with phenoxybenzamine, and at laparotomy a right suprarenal phaeochromocytoma was removed and cholecystectomy performed. An ampullary tumour (1·5 cm × 1·5 cm) was also resected. No metastases were found. After surgery her blood pressure returned to normal. Hypoglycaemia occurred in the early postoperative period, but subsequently the patient became normoglycaemic.

The ampullary tumour was examined by Professor N M Gibbs, St Luke's Hospital, Guildford, and reported as follows: "This is a tumour of carcinoid type and is strongly positive for argyrophil granules although the diazo is negative. Immunoperoxidase techniques using antibodies to insulin, glucagon, somatostatin and gastrin give the following results. The tumour shows a few positive insulin-reacting cells and large numbers of positive somatostatin-reacting cells, but there is no reaction with glucagon or gastrin. This tumour should, therefore be classified as a somatostatinoma with some insulin production."

Preparation and characterisation of antisera and validation of immunoassay technique were as described by Penman *et al.*[3]

## Comment

Eight cases of somatostatinoma have been described. The influence of somatostatin on the endocrine and digestive systems has been discussed by Krejs *et al.*[2] Cholelithiasis was found in five of six cases reviewed and was apparently due to depression of cholecystokinin-pancreozymin secretion. Diabetes was present in all patients, presumably because of inhibition of insulin activity. The postoperative hypoglycaemia in our patient was possibly due to removal of this inhibition. The presence of some insulin-reacting cells in the tumour suggests that the episodes of nocturnal hunger may have been due to transient hyperinsulinaemia. Hypoglycaemia was the presenting feature in the case reported by Wright *et al.*[4] Seven of the eight cases so far reported were malignant and in the present case the tumour was a carcinoid of low malignancy. The neurofibromatosis, although non-familial, was unlikely to be coincidental, and we regard this case as an unusual presentation of multiple endocrine adenomatosis type 2.

Our thanks are due to Professor Vincent Marks for his helpful correspondence and to Professor N M Gibbs for permission to quote his report.

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# Raised creatine kinase activity and presence of creatine kinase MB isoenzyme after exercise

The determination of serum creatine kinase activity is commonly used to aid in the diagnosis of myocardial infarction,[1] though its diagnostic value is lessened by its non-specificity. Moreover, exercise raises the serum creatine kinase activity in normal individuals.[2] Measurement of creatine kinase MB isoenzyme provides a more specific and sensitive indicator,[3] though it has been suggested that a raised value is not necessarily a reliable index of myocardial damage after strenuous exercise. We have investigated the relation between exercise, creatine kinase activity, and creatine kinase MB.

## Patients, methods, and results

A total of 335 male contenders for the 1980 British Olympic team were offered routine screening. In addition, 10 healthy male laboratory volunteers were studied before exercise and at six hours and 24 hours after a standardised exercise test.

Total creatine kinase activity was determined by the method of Forster *et al.*[4] In samples where the activity was above 150 U/l the isoenzyme composition was also determined. Isoenzyme composition was measured using an agarose electrophoresis system and the results expressed semi-quantitatively as: negative, trace, +, ++, or +++. A "trace" of creatine kinase MB is equivalent to 2-4 U/l, and "+" corresponds to an activity of 5-15 U/l.

Of the Olympic contenders, 85 (25%) had creatine kinase activities exceeding 150 U/l, and subsequent analysis showed the presence of MB isoenzyme in 52 cases (15·5% of the total, and 61·2% of those with raised creatine kinase values). Fifteen of these were + and 37 had a trace present. None was recorded as ++ or +++. The table shows the mean creatine kinase and aspartate transaminase activities for each exercise level in 278 of the Olympic men. (Exercise levels were not available for all subjects.) Values of both enzymes rose significantly with increasing exercise (F test, $p < 0·001$). The table also shows the proportion of subjects with creatine kinase MB present at each exercise level. In all 10 volunteers the activity of creatine kinase at six hours after exercise was higher than the pre-exercise value and remained raised 24 hours after exercise. The table shows the mean activities of creatine kinase and aspartate transaminase before and after exercise. There were no significant changes in aspartate transaminase. The MB isoenzyme (trace) was found after exercise in four of the volunteers.

*Effect of exercise on mean creatine kinase and aspartate transaminase activities in 278 Olympic contenders and 10 laboratory volunteers*

| | Creatine kinase | | Aspartate transaminase | | No (%) of subjects with creatine kinase MB |
|---|---|---|---|---|---|
| | Mean ± SD (U/l) | No of subjects | Mean ± SD (U/l) | No of subjects | |
| | *Olympic contenders* | | | | |
| Hours of exercise/day: | | | | | |
| <2 | 109·7 ± 117·9 | 120 | 24·2 ± 10·6 | 120 | 12 (10·0) |
| 2– | 101·5 ± 73·6 | 91 | 24·4 ± 7·5 | 91 | 6 (6·6) |
| 4– | 166·4 ± 99·9 | 50 | 31·6 ± 12·0 | 50 | 11 (22·0) |
| ≥6 | 322·2 ± 288·3 | 17 | 45·1 ± 25·3 | 17 | 5 (29·4) |
| | *Laboratory volunteers* | | | | |
| Before exercise | 53·2 ± 20·4 | 10 | 21·8 ± 5·7 | 10 | |
| 6 hours after exercise | 118·7 ± 59·2** | 10 | 22·9 ± 6·7 (NS) | 9 | |
| 24 hours after exercise | 108·9 ± 66·8* | 9 | 23·7 ± 7·6 (NS) | 9 | |

Significance of difference from values before exercise in laboratory volunteers (paired *t* tests): *$0·005 < p < 0·025$; **$p < 0·005$; NS = $p > 0·05$.

## Comment

Our results indicate that as many as 15% of highly exercised men with no apparent myocardial damage may have increased amounts of creatine kinase MB isoenzyme. These changes occur not only in athletes undergoing persistent and prolonged exercise but also in non-athletes undergoing acute strenuous exercise. The relation between duration of exercise and creatine kinase activity is controversial.[5] Our findings suggest that there is a significant positive correlation, even at low exercise rates. Thus even in those sportsmen exercising for less than two hours a day the mean creatine kinase activity was above normal, and as many as 10% had creatine kinase MB present. All the volunteers showed significant increases in creatine kinase activity after short-term exercise.

Serum aspartate transaminase activity is less sensitive to the effects of exercise than the activity of creatine kinase and as such provides a valuable adjunct in the differential diagnosis of myocardial infarction. Moreover, in none of our subjects did the creatine kinase MB value exceed +, even in extreme periods of exercise. A creatine kinase MB value above 15 U/l is highly unlikely to be due to exercise.

In a clinical setting where acute chest pain of unknown origin is the diagnostic problem, it is generally accepted that detection of the MB isoenzyme supports a diagnosis of myocardial infarction. In the light of our findings the significance of a moderately raised value should not be overestimated, and a careful history concerning physical activity before the onset of chest pain should always be taken.

We thank Professor T P Whitehead for helpful advice.

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# Rheumatoid arthritis developing after plant thorn synovitis

Sporadic cases of monoarticular synovitis after penetrating injury by plant thorns have been described over the past two decades. In 1966 Kelly[1] reviewed 24 patients with chronic articular or periarticular inflammation secondary to injury by thorns of the blackthorn or sloe (*Prunus spinosa*). In all cases the inflammation was localised at the site of injury.

We describe a patient who presented with seropositive polyarthritis shortly after developing a monoarticular synovitis secondary to a penetrating wound by a rose thorn. Some additional results are reported to support this temporal relationship.

## Patients, methods, and results

### CASE REPORT

A 55-year-old woman (case 1) was pruning a rose when a thorn penetrated the lateral aspect of her second metacarpophalangeal joint. Within 24 hours the joint had become hot, red, and swollen and the inflammation persisted. Just under a month later she developed swelling over all the metacarpophalangeal joints and of the third and fourth proximal interphalangeal joints of both hands, together with pain and tenderness in the right foot. At this point, she presented to us together with part of the offending rose bush. On examination she had active synovitis of the joints as described and tenderness across the right metatarsophalangeal joints.

### INVESTIGATIONS

*X*-ray films of hands, feet, and chest showed no abnormalities; haemoglobin concentration was 13·4 g/dl; white cell count $6·0 \times 10^9$/l, plasma viscosity 1·85 (normal range 1·5-1·72); immunoglobulin concentrations normal; rheumatoid arthritis latex fixation test positive (differential agglutination titre 1/256 later rising to 1/2048); antinuclear factor negative; tissue type HLA A2, B8, B27, DR1, DR3, CW1. A surgical synovectomy of the second metacarpophalangeal joint showed no histological evidence of retained thorn fragments. Culture of synovium and synovial fluid showed no growth. The synovial histology was consistent with rheumatoid arthritis. Subsequently the disease has progressed to definite rheumatoid arthritis (American Rheumatism Association criteria).

To investigate this phenomenon further thorn tips from the rose bush (*Rosa sp*), blackthorn (*Prunus spinosa*), and gooseberry (*Ribes grossularia*) were tested for their capacity to stimulate lymphocyte blastogenesis in a small group of patients. The lymphocytes were labelled with $^3$H-thymidine and the results expressed as: stimulated counts per minute minus background counts per minute. The findings in our patient (case 1) together with those in a healthy volunteer and a patient with established rheumatoid arthritis (case 2) are shown in the table, as are the results of a later identical experiment on four more subjects: with a monoarticular plant thorn synovitis (cases 3 and 4), a healthy volunteer, and a further patient with rheumatoid arthritis (case 5). Lymphocytes from all of the patients responded normally to the three mitogens, concanavalin A, phytohaemagglutinin, and pokeweed mitogen.

*Results of stimulated lymphocyte blastogenesis in five patients and two healthy volunteers*

| Subject | Diagnosis | Background cpm | Cpm (stimulated − background) | | |
|---|---|---|---|---|---|
| | | | Rose | Blackthorn | Gooseberry |
| Case 1 | Monoarticular plant-thorn synovitis | 1004 | 3225 | 633 | 922 |
| Healthy volunteer | | 1640 | − | 142 | − |
| Case 2 | Rheumatoid arthritis | 860 | 140 | − | − |
| Case 3 | Monoarticular plant-thorn synovitis | 97 | 52 | 130 | 194 |
| Case 4 | Monoarticular plant-thorn synovitis | 215 | − | − | 208 |
| Healthy volunteer | | 163 | 225 | 79 | 111 |
| Case 5 | Rheumatoid arthritis | 316 | 85 | − | − |

Cpm = counts per minute; − = negative.

## Comment

Only the lymphocytes in our patient (case 1) responded convincingly to the rose-thorn extract, when related to the background counts per minute, which infers that she may have been sensitised by earlier rose-pruning mishaps. There is some evidence from animal experiments that previous immunisation to an antigen may prolong its retention in a joint,[2 3] while Sugarman *et al*[4] suggested that plant-thorn synovitis is nearly always associated with the retention of microscopical thorn fragments in the affected joint, although these may be difficult to find even after synovectomy.

Recent hypotheses on the aetiology of rheumatoid arthritis have included the possibility that retention of antigen in a joint may set up chronic inflammation in genetically susceptible individuals, leading ultimately to a self-perpetuating process, perhaps by the exposure of autogenous antigens or even by way of an immune response to components of the inflammatory exudate.[5] The HLA genotype in our patient (case 1) included the HLA B8 and DR3 antigens, which have been associated with an exaggerated immune response. It is tempting to speculate that an abnormal immune reaction to retained plant-thorn fragments may have played a part in the precipitation of this patient's seropositive polyarthritis.

We thank Pauline Bigelow for her work on lymphocyte responses.

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