vomiting in one (case 9). One patient (case 3) had abdominal pain; one (case 8) had intermittent claudication; two had hyperpigmentation, of the palms (case 2) and of the soles and palms (case 10); and six were mildly jaundiced.

Routine haematological investigations were performed using standard methods.¹ Serum vitamin B₁₂ and red cell folate concentrations were determined by microbiological methods, using *Lactobacillus leishmanii* and *L. casei*. In all but one case maximum reticulocyte response to 5 µg vitamin B₁₂ daily given parenterally (orally in case 2) was also measured. Absorption of B₁₂ was studied in six cases using the Schilling test² (with 1 µg radioactive B₁₂).

Clinical and haematological features of 10 men studied

Case No	Age	Haemoglobin concentration (g/dl)	Vegan diet (yr)	Serum B ₁₂ (ng/l)	Plasma folate (µg/l)	Red cell folate (µg/l)	Therapeutic response*	Result of Schilling test
1	23	13.7	2	40	3.7	87	ND	ND
2	19	6.3	3	70	4.8	ND	9%	ND
3	23	3.3	5	55	2.2	50	32%	Normal
4	40	13.3	5	10	2.4	112	2%	Normal
5	23	3.0	5	50	<1.0	ND	30%	ND
6	23	4.6	5	105	11.6	ND	3%	Normal
7	18	9.5	6½	75	12.5	176	32%	Normal
8	32	3.9	7	ND	2.4	45	17%	ND
9	22	4.7	9	10	18.0	ND	12%	Normal
10	37	3.9	20	130	15.7	ND	21%	Normal
Normal range		13.0-17.5		180-1000	2-20	80-470		

ND = Not done.

*Maximum reticulocyte count after parenteral vitamin B₁₂ treatment (see text) except case 2, where vitamin B₁₂ was given orally.

Eight patients were found to have moderate or severe macrocytic anaemia. Two of the three patients with subacute combined degeneration were not anaemic. The bone marrow was megoblastic in all patients, and all showed normal or increased iron stores. Vitamin B₁₂ deficiency was confirmed as the cause of megaloblastosis in all cases by low serum vitamin B₁₂ concentrations, reticulocyte response, or both. The reticulocyte response was poor in two patients; one was anaemic, but there was no clearly identifiable cause for the poor response in the other. Both patients had low serum vitamin B₁₂ concentrations and their haemoglobin concentrations rose after further vitamin B₁₂ treatment, reaching the normal range in the patient who was originally anaemic. Low plasma or red cell concentrations, detected in three of the patients described here, have been described in patients with vitamin B₁₂ deficiency.³

Onset of symptoms from two to 20 years after the start of the vegan diet suggests a dietary cause of vitamin B₁₂ deficiency. Vitamin B₁₂ absorption was normal in the six patients who underwent the Schilling test: more than 15% of the test dose appeared in the urine within 24 hours in all patients tested. Four patients did not undergo the Schilling test: in one case (2) the response to oral cyanocobalamin suggested that his vitamin B₁₂ absorption was also normal; in the other three cases (1, 5, and 8) other causes of vitamin B₁₂ deficiency were excluded by the clinical features and appropriate laboratory investigations.

There was complete haematological response to parenteral cyanocobalamin treatment in all patients. One of the three patients with subacute combined degeneration recovered completely and another showed considerable improvement but had residual motor defects after several months of treatment. The third patient died after a myocardial infarct 11 days after admission.

Comment

These patients were all members of the Rastafarian cult, a religious sect that started in Jamaica in the 1930s and has steadily increased in popularity, especially during the past decade. It has attracted young men in particular and the ages and sex of our patients are therefore not surprising. In contrast, most of the patients described in a report of vitamin B₁₂ deficiency in Hindus in Trinidad⁴—the only other territory in the region in which macrocytic megaloblastic anaemia due to dietary vitamin B₁₂ deficiency has been reported—were older, and women were also affected.

Rastafarians are now found in most of the English-speaking territories in the Caribbean and also in Europe (particularly Britain), Canada, and the United States of America. Most are easily recognisable because of their distinctive hairstyle. The continued growth of the cult indicates that increasing attention should be paid to the possibility of the vegans syndrome in young men presenting with neurological disease, overt megaloblastic anaemia, or both. Education of the public is also important, and members of the cult should be encouraged to include milk products in their diets. Our patients were not very co-operative in taking oral vitamin B₁₂ or attending the clinic for vitamin B₁₂ injections, and we have found it difficult to persuade them to eat meat.

Requests for reprints should be addressed to Dr W N Gibbs.

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Neurofibromatosis, phaeochromocytoma, and somatostatinoma

The tetradecapeptide, somatostatin, occurs in many tissues, including the upper gastrointestinal tract. In the pancreas it is found in the D cell of the Islets of Langerhans. Cells containing somatostatin have been found in various Islet-cell tumours. The first case of a tumour producing somatostatin-like immunoreactivity and bioactivity was discovered incidentally during cholecystectomy.¹ The first preoperative diagnosis of somatostatinoma was by Krejs *et al* in 1979² and was suggested by the combination of diabetes mellitus, cholelithiasis, steatorrhoea, and an ampullary tumour.

Case report

A 49-year-old unmarried woman was seen in July 1981 complaining of weight loss, exertional dyspnoea, and night sweats for 18 months. She had increased appetite and was often awakened during the night by a desire for food. She had widespread non-familial neurofibromatosis and had been hypertensive for 15 years. She had chronic dyspeptic symptoms, and partial gastrectomy had been performed for duodenal ulcer 21 years previously. On examination she had hepatomegaly, a right hypochondrial mass, tremor of the hands, and sinus tachycardia. Her blood pressure was 200/110 Hg mm. A provisional diagnosis of phaeochromocytoma was made.

INVESTIGATIONS

The 24-hour urinary 4-hydroxy-3-methoxymandelate concentration was 107 µmol (normal range 3-38 µmol). Liver function tests showed an obstructive pattern (serum alkaline phosphatase 3290 IU/l). Random blood sugar estimations were normal. Intravenous pyelography showed hydronephrosis of the left kidney and renal angiography left renal artery stenosis and a vascular mass above the right kidney. Ultrasonography indicated distension of the gall bladder, multiple gallstones, and dilatation of the biliary radicles. In addition, a computed tomography scan showed a right suprarenal mass with the characteristics of a phaeochromocytoma.

Her condition was stabilised with phenoxybenzamine, and at laparotomy a right suprarenal pheochromocytoma 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 immunocytochemistry 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

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	
<i>Olympic contenders</i>					
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)
<i>Laboratory volunteers</i>					
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.

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.

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.

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