three months. Closer follow-up might have reduced this number, but this is often difficult to achieve. Some relapses follow a single cigarette after months without, smoked either out of curiosity or as a result of some stress such as a car accident. The rule for the ex-cigarette smoker must be never to smoke another cigarette, whatever else he smokes. Patients are told to telephone the clinic immediately should they do so, and they are always welcomed back.

There remains a small hard-core of cigarette addicts who fail to respond initially to these methods and who probably need more intensive therapy, such as that described by Ejrup (1960) with use of lobeline injections.

Much research is needed to find the most effective methods for stopping smoking. Aversion therapy, either by drugs or by electric shock (McGuire and Vallance, 1964) needs further consideration. It may be that there are different kinds of smokers, each needing a different treatment, and in order to study this aspect of the problem we are now assessing the personality of our patients.

At present the combined pressures of society and the cigarette advertisers make some relapses inevitable. But as the force of public opinion progressively hardens against the cigarette, so will it become easier for our patients to rid themselves of this habit.

We are very grateful to Dr. C. H. Wood, Dr. M. W. McNicol, and Dr. A. S. Stevens for their help and advice in this clinic. Dr. Horace Joules provided much initial stimulus and help.

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Serum Creatine Kinase and Physical Exercise

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Studies on the effect of physical exercise on the levels of some serum enzymes in normal human subjects have yielded varying results (Tessari and Parrini, 1961 ; Critz and Merrick, 1962 ; Fowler *et al.*, 1962). Recently, determination of serum creatine kinase has been regarded by most workers in the field of muscle disorders to be superior to that of other enzymes, since the presence of creatine kinase in significant amounts is limited to skeletal and cardiac muscles and brain tissue. Hughes (1963) failed to show any consistent rise in the level of the serum enzyme in a normal subject after 15 minutes' stationary cycling in a laboratory. Using a somewhat similar procedure to that of Hughes for the enzyme estimation (modified Ennor and Rosenberg's method), Pearce *et al.* (1964) obtained similar results on three subjects exercised by running three times up and down two flights of stairs. Nor did Swaiman and Awad (1964), using the method of Kuby *et al.* (1954) for enzyme estimation, find any significant increase in the serum enzyme after 10 minutes of strenuous exertion, but they concluded that the exercise was insufficient in duration or severity.

The present study is concerned with the determination of the effect of strenuous physical exercise on the serum enzyme levels of 12 healthy young medical students or doctors. Six played rugby and six were oarsmen. Blood samples were taken from each subject half an hour before and half an hour after the exercise, which in each case was for about 80 minutes.

Level of Activity of Creatine Kinase Before and After Exercise

Subjects		Creatine Kinase Activity (Units)	
		Before	After
Rugby players	1	0·75	3·3
	2	1·8	2·8
	3	3·0	4·4
	4	6·2	11·0
	5	5·9	8·6
	6	2·9	6·8
Oarsmen	7	3·4	4·0
	8	1·6	2·5
	9	1·1	1·3
	10	12·7	18·0
	11	2·1	3·2
	12	1·7	6·2

Serum creatine kinase activity was determined in duplicate for each sample by the method used by Pearce *et al.* (1964). The results are shown in the Table.

The serum enzyme levels in normal human subjects expressed as micromoles of creatine formed per hour per millilitre at 37° C. ranged from 0.4 to 3.6, with a mean of 1.5 units (Pearce *et al.*, 1964).

In all but two of our subjects (Nos. 7 and 9) the serum enzyme levels after exercise exceeded the corresponding levels at rest by from 50% to 400%. Although the post-exertional levels were slightly raised in subjects 7 and 9 they were within the limit of experimental error. It is noteworthy that three subjects (Nos. 4, 5, and 10) had resting enzyme levels well above the accepted normal range, and in seven the enzyme levels after exercise reached levels generally regarded as pathological.

COMMENT

The present study reveals a consistent elevation of the serum creatine kinase level after severe physical exertion. The rise in the enzyme levels in rugby players was more striking than that in oarsmen. It may be that muscle trauma sometimes encountered during a rugby match may be partly responsible, though no significant bruising was present in any of our subjects. Alternatively, the amount of physical exertion in the two groups may be of a different order.

The abnormally high resting levels present in three normal subjects are of interest. The accepted range of normal levels was drawn from a very limited number of subjects (Hughes, 1962 ; Pearce *et al.*, 1964). Furthermore, Hughes (1963) found abnormally raised enzyme levels in two normal subjects who were manual labourers, and stressed that the time of collection of blood samples and the occupation of the subjects might have significant effects on these levels.

The present study raised two interesting points. Estimation of this serum enzyme is now widely employed in the investigation of muscle disorders, but if important issues such as those involved in diagnosis or genetic counselling are to depend on such estimations they should be made under defined basal conditions.

The reasons for increased serum creatine kinase activity after exercise are at present uncertain. Alteration in the permeability of the cell membrane may result from physical activity (Zierler, 1956). A further possible mechanism is release

of the enzyme into the circulation due to anoxia (Highman and Altland, 1960).

We are grateful to Professor Henry Miller for his advice and support. We wish to thank Dr. R. J. Pennington for allowing one of us (A. V.) to use facilities in his laboratory at the Regional Neurological Centre, Newcastle General Hospital, and for his helpful criticism; and also our medical colleagues who generously gave their blood for the present study.

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Biochemical Findings in Suprarenal Adenoma

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It is often believed that in cases of Cushing's syndrome due to suprarenal adenoma the levels of excretion of adrenal steroids are unaffected by the administration both of corticotrophin and dexamethasone. Exceptions to this rule have been reported but are extremely rare.

CASE REPORT

A woman aged 47 was referred to the out-patient department by her general practitioner as a case of Cushing's syndrome. She complained of lack of energy for three years, gain of a stone (6.3 kg.) in weight, and increasing fine hirsutism of the face. She had noticed that she bruised easily, and a recent wound on her leg had had to be skin-grafted as there was delayed healing. In 1958 she had had a hysterectomy for menorrhagia, and in 1960 she was treated by a psychiatrist for depression. For one year she had had numbness and tingling in the thumb and index finger of the right hand.

On examination she presented the classical features of Cushing's syndrome, with moon facies, high colour, and fine hirsutism. There was marked increase in body fat with slim arms and legs. There were no striae, but she had several bruises on her legs.

Her blood-pressure was 170/100 mm. Hg, and the only other abnormal finding was sensory loss of the distribution found in the carpal-tunnel syndrome. Visual fields were probably normal.

Investigations gave the following results: Hb 94%, W.B.C. 9,400/c.mm., eosinophils 60/c.mm., P.C.V. 51%. Bleeding and clotting times were normal. Glucose-tolerance test showed a "lag" curve. Serum sodium 139 mEq/l. Potassium 3.76 mEq/l.

A radiograph of the chest showed slight cardiac enlargement, but a radiograph of the spine did not show osteoporosis. A radiograph of the pituitary fossa was normal.

Twenty-four Hour Urinary Output of 17-Oxysteroids and 17-Oxygenic Steroids

Treatment		Volume of Specimen (ml.)	17-Oxysteroids		17-Oxygenic Steroids		Total Creatinine
			mg./24 Hours	mg./g. Creatinine	mg./24 Hours	mg./g. Creatinine	
None	Basal levels 1	2,235	29·5	19·9	32·9	22·0	1·48
	Basal levels 2	1,550	12·9	9·6	19·2	14·2	1·35
40 Units of A.C.T.H. for 2 days	1st day	1,670	25·5	18·6	85·0	62·0	1·37
	3rd „	2,300	33·8	20·7	114·0	68·8	1·66
None (4 days after A.C.T.H. treatment)		1,460	14·2	12·5	33·0	29·0	1·15
Dexamethasone	1st day	1,400	12·8	10·8	23·7	20·1	1·18
	2nd „	1,660	11·2	9·8	24·4	21·2	1·15
	3rd „	1,390	13·6	10·9	42·1	34·9	1·25
	4th „	1,800	15·5	11·5	20·2	14·9	1·35

A 24-hour urinary output of 17-oxysteroids and 17-oxygenic steroids are seen in the Table. Basal levels were estimated and repeated after (1) an infusion of 40 units of adrenocorticotrophic hormone (A.C.T.H.) given over a period of eight hours on two consecutive days, and (2) dexamethasone 2 mg. six-hourly for four days.

A report on radiography with presacral air insufflation (CO_2) read as follows: "Gas passed almost entirely into the left peri-renal region. Tomography showed good outlining of the left kidney and suprarenal, and the latter was considered to be within normal limits. Repeat examination demonstrated only the right kidney. The gas did not appear to pass between the latter and the suprarenal" (Dr. A. H. Isaacson).

On 5 May 1964 a right adrenalectomy was performed by Mr. A. J. Heriot through the bed of the eleventh rib. He found a small tumour of the suprarenal gland and a small accessory suprarenal which he also removed.

The pathology report was as follows: "Adrenal gland measures 6 by 3 by 2 cm. within which is a small tumour 1 cm. diameter. Gland weighs 12 g. Sections show the presence of a cortical adenoma composed of cells of the middle zone of the cortex zona fasciculata. There may be some hyperplasia also of the inner zona reticularis" (Dr. F. E. Dische).

COMMENT

Stimulation with A.C.T.H. in cases of adrenal hyperplasia causes considerable rise in glucocorticoid excretion. It has been suggested that stimulation of adrenal tumours with A.C.T.H. causes little or no rise (Bayliss, 1957).

However, Soffer *et al.* (1957) reviewed the literature and found six cases of adenoma, in four of which the response to A.C.T.H. was indistinguishable from that seen in adrenal hyperplasia. In the other two cases and in their own two cases there was little or no response to A.C.T.H. They concluded that a failure of the plasma 17-hydroxycorticoid level to rise strongly suggested a tumour, but the presence of an augmented response was not of diagnostic significance. Since then other cases have been described (Scott *et al.*, 1962); these included four cases of adenomas that gave no response to A.C.T.H. and one in which there was a good response. The case here reported is a further example of the latter.

I am grateful to Dr. B. J. Freedman for permission to publish this case, and to Dr. Raymond Greene, who first suggested that I should do so.

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