(Pasteels, 1969; Friesen *et al.*, 1970), as well as measurements of plasma growth hormone and prolactin levels in galactorrhoeic patients (Frantz and Kleinberg 1970; Forsyth *et al.*, 1971), suggests the separate existence of prolactin in man.

As has been described in other cases of hypothyroidism (Havard *et al.*, 1970) there was pronounced insulin resistance in this patient before thyroxine therapy. A second dose of insulin was required during the initial insulin tolerance test to produce adequate hypoglycaemia—that is, sweating and a blood sugar of less than 40 mg/100 ml. Despite this the growth hormone response was impaired. In contrast, the insulin sensitivity after six months and one year on thyroxine was normal, as was the growth hormone response. The lactogenic activity detected at one year during the insulin tolerance test can be accounted for entirely by the concentrations of growth hormone rather than prolactin.

Bayliss and Van't Hoff (1969) suggested that the postpartum state is a prerequisite for the development of this condition, and thought that the comparative rarity of pregnancy in myxoedema explains why this condition is seldom seen. Of the cases described this is the only one that developed during treatment with an oestrogen-progestogen combination rather than postpartum. Several euthyroid patients have now been reported in whom galactorrhoea has developed in association with oral contraceptive therapy (Shearman and Turtle, 1970). In the above case it seems unlikely that the galactorrhoea was due to the contraceptive therapy alone since it persisted unabated until thyroid replacement was begun. The finding that plasma prolactin levels are raised in some patients with hypothyroidism but without galactorrhoea suggests that some type of oestrogen-progestogen priming of the breast facilitates the development of this syndrome.

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PRELIMINARY COMMUNICATIONS

Creatine Phosphokinase in Facio-scapulohumeral Muscular Dystrophy

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Summary

Study of the serum creatine kinase levels in young patients with facioscapulohumeral muscular dystrophy suggests that enzyme assay may be valuable as a screening procedure for assessing the status of relatives of an affected individual who have no previous clinical history, and that consequently it may be of use in genetic counselling.

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Introduction

It is recognized that serum enzyme estimations are valuable in the early diagnosis of Duchenne muscular dystrophy of the sex-linked recessive type (Chung, Morton, and Peter, 1960; Pearce, Pennington, and Walton, 1964; Hughes, 1965). Enzyme activities, particularly aldolase (Chung *et al.*, 1960; Thomson, Leyburn, and Walton, 1960) and creatine phosphokinase (CPK) (Pearce *et al.*, 1964; Hughes, 1965), are grossly raised at an early stage but decline with age, though in the case of serum CPK seldom reach normal values.

Though Thomson *et al.* (1960) reported that in facioscapulohumeral dystrophy as in Duchenne dystrophy the highest serum aldolase levels were found in young patients, in over half of their series of 15 cases the enzyme activities were below the upper limit of normal, and raised values were found only in patients in whom the "duration" of the disease did not exceed 10-15 years. Consequently a study of serum CPK levels in facioscapulohumeral dystrophy in relation to age seemed worth while in order to assess their value as an aid to early detection of the condition because they are raised to a greater extent than those of aldolase (Heyck and Laudahn, 1967). The usefulness of a biochemical test as an adjunct to clinical examination is apparent when the great variation in clinical expression of this disorder, even within the same family, is considered. As Walton and Gardner-Medwin (1969) pointed out, some individuals may be unaware that they are suffering from the condition and the existence of the characteristic facial weakness may occasionally be difficult to prove.

This communication presents results of serum CPK assays on a number of patients with facioscapulohumeral dystrophy which suggest that this possibility merits further study.

Patients and Methods

The CPK activity was assayed in serum from 19 patients exhibiting the typical clinical pattern of facioscapulohumeral dystrophy with a positive family history—that is, affected first-degree relative—indicative of or consistent with a dominant mode of inheritance, and from a further two subjects with no previous clinical history, though other members of their family were affected. In one subject clinical examination (Dr. R. W. Ross Russell) showed early signs, but in the other examination was refused. Finally, serum was obtained from three patients who had no family history, and in one the initial diagnosis of facioscapulohumeral dystrophy was later thought to be doubtful.

Serum CPK (E.C 2. 7. 3.2) was estimated by the colorimetric procedure of Hughes (1962, 1968).

Results

Comparison of Normal and Dystrophic Values.—The values for serum CPK in patients with facioscapulohumeral dystrophy and in subjects without muscle disease are given in the Table. For the purpose of this comparison only patients with a positive family history are included. In both male and female patients the mean serum enzyme activities were significantly raised ($P > 0.05$) above the means for the corresponding controls. However, of the female patients 2 out of 6 had serum CPK values within normal limits, and these were also normal in 3 out of 16 of the males. In the present series there did not appear to be any significant difference between the means for male and female patients.

Serum Creatine Kinase (IU/litre) in 6 male and 14 Female Patients with Facioscapulohumeral Muscular Dystrophy

	Present Series*		Normal Range
	Mean	Range	
Females	78	27–167	10–44
Males	105	31–192	10–67

*Table includes only patients with a typical clinical picture and a positive family history.

Relation between Serum CPK and Age.—The values for serum CPK in patients with facioscapulohumeral dystrophy plotted against age are shown in the Chart. Age rather than age at clinical presentation has been used because it was felt that in the present group at least the latter gave little idea of the actual time of onset of symptoms. The results indicate that serum CPK is usually raised in subjects up to the age of 45–50 years but may eventually fall to normal. In younger subjects there is no very clearly-defined trend with age as is seen in Duchenne dystrophy but values may lie on a rather ill-defined plateau.

Discussion

Though more data on the relation of serum CPK activity to age and clinical state, etc., are obviously needed certain tentative conclusions are possible. Thus the majority of younger patients have significantly raised serum CPK activities, and this may be true even when clinical signs are slight. When progression to severe disability has been unusually rapid, however, the enzyme level may be normal, so that in the case of two individuals—non-identical twins, brother and sister—the one who was moderately affected had a raised serum CPK; but the severely affected twin sister had a normal CPK (see Chart).

In the present series the older patients with normal CPK were also severely disabled and non-ambulatory. The normal serum CPK in such subjects may indicate that reduced muscle mass and physical activity diminishes efflux of enzyme from the

remaining dystrophic tissue so that the serum level remains within normal limits. This is probably not the sole explanation, however, since one patient aged 50 with a normal CPK was still ambulant though having difficulty in climbing stairs, etc. Possibly serum enzyme levels may return to normal during the periods of clinical arrest to which this condition is subject (Walton and Gardner-Medwin, 1969), but individuals would have to be followed over a period of years and their enzyme levels correlated with changes in muscle strength to establish if this is the case.

One patient aged 26 without family history, first believed to have facioscapulohumeral dystrophy, but for whom a diagnosis of limb girdle dystrophy was later thought to be more probable, had a serum CPK of 406 IU/litre, which is considerably higher than shown by any other individual in the present series (see Chart). Serum CPK levels may thus have value as a discriminant where there are difficulties in making a diagnosis on clinical grounds as, for example, in a case like that described by Fenichel, Emery, and Hunt (1967) of a young woman with neurogenic atrophy simulating facioscapulohumeral dystrophy whose serum CPK was considered to be normal.

Relation between age and serum creatine phosphokinase activity in facioscapulohumeral muscular dystrophy. ■ = Males with positive family history. □ = Males with negative family history. ● = Females with positive family history. ○ = Females with negative family history. * = No previous clinical history.

From the present preliminary study it appears that estimation of serum CPK may provide a useful screening procedure for early detection and for assessing the status of relatives of a patient with facioscapulohumeral dystrophy. If so, it would be of value in genetic counselling or in advising individuals likely to suffer slowly progressive disability.

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