were reported by Davis *et al.* (1961) in one patient treated with 4 g. of alpha-methyldopa. Similar side-effects were noticed by Collini (1961), who was able to give his patient only 1 g. of alpha-methyldopa for four days. Dubach and Blumberg (1961) had to stop treatment with 2 g. of methyldopa because their patient became disorientated and sluggish. Our third patient could not tolerate more than 1.5 g. of methyldopa because of hypotension and abdominal pain. Side-effects in hypertensive patients treated with methyldopa have been minor (Irvine *et al.*, 1962), so that it does seem that patients with the carcinoid syndrome are more sensitive to the drug. It is possible that in some patients small doses of alpha-methyldopa might actually stimulate serotonin production. Sourkes (1954) observed that alpha-methyldopa at low concentration stimulated dihydroxyphenylalanine decarboxylase. However, 5-H.I.A.A. excretion was not increased in the case with severe side-effects.

Methyldopa has been shown to lower blood-pressure in patients with moderate hypertension (Irvine *et al.*, 1962). Hypotension occurred in two of our patients with the carcinoid syndrome. In the first patient the blood-pressure fell in both standing and lying positions; in the other, hypotension was one of the reasons why she could not tolerate the drug.

The Table lists the reported cases of carcinoid disease treated with alpha-methyldopa or methyldopa, together with the effect of the drugs on symptoms and on urinary excretion of 5-H.I.A.A. and 5-H.T.P. Only 3 out of 12 had decreased excretion of 5-H.I.A.A., while three others showed symptomatic improvement without urinary

Reported Cases of Carcinoid Disease Treated with Alpha-methyldopa or Methyldopa. Effect of the Drugs on Symptoms and Urinary Excretion of 5-H.I.A.A. and 5-H.T.P.

Author		Urinary 5-H.I.A.A. Excretion	Urinary 5-H.T.P. Excretion	Symptoms		
				Flushing	Diarrhoea	Others
Sjoerdsma *et al.* (1960)	1	↓	↑	—	—	—
	2	↓	↑	—	—	—
Nicholson *et al.* (1962)	1	↓	↑	Improved	Improved	Improved
	2	Unchanged	Nil	Unchanged	Unchanged	Unchanged
	3	,,	,,	,,	,,	Abdominal pain
Noble (1961)		,,	,,	Improved	Improved	—
Collini (1961)		,,	,,	Worse	Worse	Worse
Davis *et al.* (1961)	1	,,	,,	,,	,,	,,
	2	,,	,,	Unchanged	Improved	—
	3	,,	,,	,,	Unchanged	—
	4	,,	,,	,,	,,	—
Dubach and Blumberg (1961)		,,	,,	,,	Improved	Worse

changes. Sjoerdsma *et al.* (1960) do not report the symptomatic effect of alpha-methyldopa on their patients. The differing response is not explained. Failure to absorb methyldopa could have occurred in the patients who showed no change. It is unlikely that methyldopa will help many patients with the carcinoid syndrome, but in view of the success with our first case it should be given a trial, especially in patients with severe symptoms.

Summary

Methyldopa, a drug which interferes with the synthesis of serotonin, was given by mouth to three patients with the carcinoid syndrome. In one there was marked clinical improvement, with decreased excretion of 5-hydroxyindoleacetic acid in the urine and increased excretion of 5-hydroxytryptophan; the symptoms of the second patient were unchanged, while the third patient could not tolerate the drug because of hypotension, abdominal pain, and nausea.

Patients with the carcinoid syndrome who are troubled with diarrhoea or flushing attacks should have a trial of methyldopa.

We thank Dr. B. O. Quin for permission to publish the details of Cases 1 and 2; also Dr. K. C. Mezey, of Merck Sharp and Dohme Research Laboratories, for supplies of methyldopa ("aldomet").

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Preliminary Communications

Serum Enzymes in Carriers of Muscular Dystrophy

Recent reports (Chung *et al.*, 1960; Schapira *et al.*, 1960; Aebi *et al.*, 1962) have indicated that some clinically unaffected female carriers of muscular dystrophy of the Duchenne type show raised levels of aldolase and phosphocreatine kinase in their serum. Because it may thus be feasible to detect carriers in a reliable way these reports need to be confirmed as fully as possible. I therefore wish to report some preliminary findings in a survey of families of patients with this form of muscular dystrophy which in general support the findings of other workers.

Classification of Subjects

A similar classification to that of Leyburn *et al.* (1961) was used, and the subjects were divided into two groups:

1. *Known Carriers.*—These were mothers with two or more affected sons, or one affected son and a definitive history—for example, an affected brother or maternal uncle.

2. *Possible Carriers.*—These consisted of the following: mothers with only one affected son and no family history, female sibs and patients, maternal aunts of patients.

Method

Blood was collected in the normal way by venepuncture and allowed to clot for separation of the serum, which was then frozen at −25° C. In most cases estimations were carried out within a few days of collection, but when this was impracticable specimens were stored at −25° C. for not longer than two months.

Aldolase was estimated by the method of Friedman and Lapan (1958) and phosphocreatine kinase by the procedure of Hughes (1962).

Results

Data for known carriers, for possible carriers, and for a group of normal subjects are given in Tables I and II. Unfortunately it was not possible to obtain meaningful values for aldolase on all of the serum specimens because some were haemolysed. Phosphocreatine kinase estimations, on the other hand, are unaffected in these circumstances.

TABLE I.—*Known Carriers*

Subject	P.C.K. (μM/ml./hr.)	Aldolase D.H.A. Units
R.W.	*22·0*	*56·4*
L.S.	*13·1*	16·8
D.G.	*9·5*	4·7
S.V.	*7·4*	9·4
A.D.	*6·3*	*66·8*
J.P.	*3·3*	11·0
E.N.	1·9	—

Units and normal values:
Aldolase: Dihydroxy acetone (D.H.A.) units. Normal adult range ($\bar{x} \pm 2$ S.D.) for 73 subjects = 12·8 ± 8·8 (Hughes, 1962).
Phosphocreatine kinase (P.C.K.): μ moles creatine per ml. serum per hour at 37° C. Normal adult range ($\bar{x} \pm 2$ S.D.) = 1·6 ± 1·0 (40 female subjects).
Values in this table (and also in Table II) which are in italic lie above the normal range as defined above.

TABLE II.—*Possible Carriers*

Mothers with One Affected Son			Females with Affected Sibs			Maternal Aunts of Patients		
Subject	P.C.K. μM/ml./hr.	Aldolase D.H.A. Units	Subject	P.C.K. μM/ml./hr.	Aldolase D.H.A. Units	Subject	P.C.K. μM/ml./hr	Aldolase D.H.A. Units
F.D.	*22·2*	11·6	E.C.	*66·5*	—	N.M.	*3·9*	11·0
B.B.	*13·5*	*26·1*	B.P.	*5·1*	15·0	R.K.	2·6	11·0
V.S.	*3·8*	*26·6*	Z.N.	*4·4*	—	E.H.	2·0	9·7
C.B.	2·1	—	M.P.	*3·2*	11·6	P.C.	1·5	16·7
T.C.	1·8	1·2	G.N.	2·4	—	J.G.	1·1	10·6
P.R.	1·4	5·3	Y.W.	2·3	87·5*			
M.S.	1·0	12·4	B.C.	2·1	—			
			T.S.	1·8	16·0			

* This value is probably normal because the subject was an infant aged 2 years, and serum aldolase levels in infants are sometimes considerably higher than in adults (Friedman and Lapan, 1958). All other subjects were aged 10 years or older.

Discussion

These results confirm recent reports that a high proportion of carriers of the Duchenne type of muscular dystrophy show serum enzyme abnormalities. In our subjects the proportion of known carriers with raised phosphocreatine activity (7 out of 8) is similar to that reported by Aebi *et al.* (1962)—that is, 8 out of 9. Compared with this enzyme, the proportion with raised aldolase levels (2 out of 7) was smaller.

A considerable number of cases arise by fresh mutation in the mothers (Walton, 1960), who would not themselves exhibit systemic changes. Consequently deviations from normal would be expected less frequently in mothers with only one affected son and no relevant family history. The results shown in Table II are consistent with this expectation. The proportion of female sibs of patients who had serum phosphocreatine kinase activity above the normal range, and were therefore probably carriers, was 50%. In view of the small numbers this result is partly fortuitous even though it is the proportion to be expected from the mode of inheritance, assuming that all the mothers were in fact carriers. In the remaining subgroup of maternal aunts all were normal with one exception (N. M.).

These data lend further support to the hope that serum enzyme studies can be used successfully for the detection of carriers of this form of muscular dystrophy. However, studies on a larger group are still necessary to assess accurately the reliability of the method.

Summary

Serum phosphocreatine kinase and aldolase have been estimated in a number of female relatives of patients with the Duchenne form of muscular dystrophy. Seven out of eight known carriers had serum phosphocreatine kinase levels above the normal range; three also had elevated serum aldolase. A smaller proportion of possible carriers also showed serum enzyme abnormalities.

I thank Dr. J. N. Walton and Dr. J. van den Bosch for making available the family histories of the subjects in the investigation, and Professor J. N. Cumings for helpful advice and criticism. Dr. van den Bosch was also kind enough to provide a number of serum specimens.

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Medical Memoranda

Seminoma in Identical Twins

Testicular neoplasms are uncommon, comprising about 1.5 to 2% of all malignant tumours in the male (Dean, 1935; Gilbert and Hamilton, 1940). About two-fifths (Dixon and Moore, 1952) to two-thirds (Gordon-Taylor and Wyndham, 1947) of all testicular new growths are seminomas. A familial incidence of rare tumours is of interest, but only a few accounts of a familial occurrence of testicular neoplasms are on record. Raven (1934) reported the cases of two brothers, the younger of whom died at the age of 19 from a metastasizing testicular growth. The elder brother underwent a left orchidectomy for seminoma testis at the age of 38. Lownes and Leberman (1939) also described the cases of two brothers, the younger of whom died, aged 32, of a seminoma with pulmonary metastases. The older brother had a right orchidectomy at the age of 53 for a malignant growth regarded by the authors as a teratoma. Willis (1960) mentions a similar occurrence in brothers aged 15 and 31 years respectively, whose grandfather had died at the age of 30 from "bilateral ulcerated cancer" of the testes.

So far as we have been able to ascertain there have been only two previous reports of testicular neoplasms in identical twins. In the first of these, by Champlin (1930), one of the twins died at the age of 24 from cerebral and abdominal metastases of a testicular