It will be seen that Case 1 was already ill when the mother took the child to be fed. In Case 2 also there was a suspicion whether the child was really well just before vaccination. The grandfather of the child had died post-operatively in the same house two weeks before the child fell ill, and there was crowding in the house for the funeral. In Cases 3 and 4 careful inquiry did not reveal any history of illness before vaccination. They were the last two cases of the outbreak.

TABLE XI.—Cases Reported After the Use of Sabin Vaccine

Case	Age	Date of Onset	Date of Feeding with Sabin	District
1	3 years	21/8/59	24/8/59	Port Louis
2	3 "	4/9/59	24/8/59	Pl. Wilhems
3	15 months	6/9/59	24/8/59	Savanne
4	21 "	6/9/59	24/8/59	"

How far the Sabin vaccine has influenced the course of the epidemic may be shown by the laboratory studies on blood and stools now in progress in Johannesburg. These studies will also help in establishing the amount of virus circulating in the community and the state of immunity of the population.

Summary

An outbreak of poliomyelitis due to a type 1 strain occurred in Mauritius during June–September, 1959, and lasted 14 weeks. There were 97 paralytic cases reported, and the attack rate was 15.6 per 100,000 population. There were no deaths.

The maximum incidence was in infancy, 75.5% of patients being under 3 years.

The outbreak occurred "out of season"—that is, in winter.

It started in one district and spread to all districts of the island, and the incidence and distribution within the districts were haphazard.

The incidence in those children aged 1–7 years who had received three injections of Salk vaccine was 2.3 per 100,000 and in those not vaccinated 279.1 per 100,000.

11 weeks after the outbreak started Sabin vaccine type 1 was given to about 195,000 children between the ages of 6 months and 10 years. There were no untoward effects after the vaccination.

I am grateful to Mr. P. Teckham, who was in charge of the orthopaedic centre during the outbreak, and his staff, for allowing me to study the patients, and to Mr. C. A. Bathfield, orthopaedic surgeon, for helpful criticism and advice. My thanks are due to Mr. L. Honoré, director of statistics, and to the Statistical Branch of the Medical and Health Department, for help with the statistical data. I am indebted to Dr. E. Losonczy, Director of Medical Services, for his encouragement and guidance and for permission to publish this report. This paper is intended to serve as a background to a subsequent report which will be published on the outbreak and on the large-scale use of Sabin type 1 vaccine.

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SERUM ENZYME ACTIVITY IN MUSCULAR DYSTROPHY*

BY

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1:6-Diphosphofructoaldolase is an intracellular glycolytic enzyme which is particularly abundant in muscle, and its function is specifically the reversible splitting of the molecule of D-fructose-1:6-diphosphate (F.D.P.) into equimolecular amounts of D-glyceraldehyde-3-phosphate (G-3-P.) and dihydroxyacetone phosphate (D.A.P.). It occurs in serum from normal individuals, where its activity may be altered by disease. The *transaminases* are also intracellular enzymes abundant in muscle; they operate the reversible exchange of α -amino groups, and also appear in the serum. The two transaminases examined here are serum glutamic oxalacetic transaminase (S.G.O.T.), which reversibly catalyses the conversion of aspartic and α -ketoglutaric acids to oxalacetic and glutamic acids, and serum glutamic pyruvic transaminase (S.G.P.T.), which similarly converts alanine and α -ketoglutaric acid to pyruvic and glutamic acids.

Warburg and Christian (1943) and Sibley and Lehninger (1949) reported the incidental finding of hyperaldolasaemia in cases of muscular dystrophy. Sibley later extended the scope of his investigations into the clinical significance of serum aldolase activity to include 880 patients suffering from a wide variety of complaints, among whom were five patients with primary myopathy (Sibley and Fleisher, 1954); he observed that while hyperaldolasaemia occurred in primary myopathy it did not do so in neurogenic muscular atrophy.

Meanwhile Schapira and his co-workers had begun a systematic study of several serum enzymes in progressive muscular dystrophy and related conditions, including aldolase (Schapira, Dreyfus, and Schapira, 1953) and S.G.O.T. and S.G.P.T. (Dreyfus and Schapira, 1955). All three enzymes were found to be elevated in the serum of patients with progressive muscular dystrophy but not in those with muscular atrophy due to disorders of the central or peripheral nervous system. Several workers have since confirmed these original findings (Jacob and Neuhaus, 1954; Beckmann, 1956; Aronson and Volk, 1956, 1957; Pearson, 1957; Evans and Baker, 1957; White and Hess, 1957; Rowland and Ross, 1958; White, 1959; Thompson and Vignos, 1959).

The assay of these serum enzymes has thus become an established procedure in the diagnosis of muscular dystrophy and in the clinical investigation of muscular weakness and atrophy of obscure origin. However,

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although the reports of many workers in this field include a number of undoubted cases of Duchenne type ("pseudohypertrophic") muscular dystrophy, many of the series refer to groups of clinically ill-defined cases of muscular dystrophy from which it is difficult to draw conclusions. The object of the present investigation is to compare the activities of these three enzymes present in the serum of dystrophic patients of different ages, each exhibiting one of four clearly defined clinical forms of the disease, in an attempt to relate these biochemical findings systematically both to the clinical characteristics of the condition and to its duration in the patient. The cases have been classified on clinical and genetic grounds according to the criteria suggested by Walton and Natrass (1954).

Methods

Serum aldolase may be estimated colorimetrically by the method of Sibley and Lehninger (1949) as carried out by Evans and Baker (1957), or enzymatically by using a coupled system dependent on reduced diphosphopyridine nucleotide (D.P.N.-H) according to the method of Bruns (1954). The unit of activity of serum aldolase determined by either method is reported as μ l. of F.D.P. substrate split per hour by 1 ml. of serum under the conditions stated.

In the colorimetric method, serum is incubated with buffered F.D.P. substrate in the presence of hydrazine to trap the G.-3-P. and D.A.P. formed, which are then read against a substrate-free blank similarly treated, after removal of the protein by trichloroacetic acid and of phosphate moieties by cold dilute alkali, as the alkaline mixed triose osazones at 540 $m\mu$; initially, determinations of alkali-labile phosphate are made to relate the readings to the amounts of G.-3-P. and D.A.P. formed, so that from them may be derived the aldolase units defined above.

In the enzymatic method* the products of a similar incubation are converted by the addition of triose phosphate isomerase almost entirely to D.A.P., which in turn is then converted to glycerophosphate by D.P.N.-H in the presence of added glycerophosphate dehydrogenase. The rate of formation of D.A.P., and hence the activity of the serum aldolase, is measured by the rate of change of optical density of the system at 340 $m\mu$ due to the oxidation of the D.P.N.-H by D.A.P.

S.G.O.T. and *S.G.P.T.* may each be estimated colorimetrically by the method of Reitman and Frankel (1957), or by the enzymatic method devised by LaDue, Wróblewski, and Karmen (1954) and by Karmen (1955).

In the colorimetric method,† serum is incubated with aspartate/ α -ketoglutarate or alanine/ α -ketoglutarate substrate respectively, the 2:4-dinitrophenylhydrazine of the reaction product is prepared directly from the treated incubation mixture, and the optical density in excess alkali determined at 505 $m\mu$ against water; this is then converted from a standard graph to Frankel units, which are arranged to correspond with those originally defined by Karmen. The results are again expressed as units per ml. of serum.

*In this study, both colorimetric and enzymatic methods have been used, and by suitable adjustment of incubation temperatures the same units (Bruns) have been derived from each. Reagents for the enzymatic method were supplied by C. F. Boehringer, of Mannheim (British agents: Courtin and Warner, Ltd., Lewes, Sussex).

†For the colorimetric method of assay, which has been used throughout, standardized reagents were supplied by the Sigma Chemical Co., St. Louis, U.S.A. (British agents: G. T. Gurr, London).

In the enzymatic method, coupled D.P.N.-H-dependent systems are used as in the estimation of aldolase activity. Oxalacetate and pyruvate produced by the transaminases from their particular substrates are reduced by D.P.N.-H to malate and lactate respectively in the presence of added malic and lactic dehydrogenase, and enzyme activity is determined by the rate of change of optical density of the system at 340 $m\mu$ due to the oxidation of the D.P.N.-H.

Results

Estimations of serum aldolase, S.G.O.T. and S.G.P.T. activities have been carried out in a total of 55 patients, of whom 14 were suffering from the Duchenne ("pseudohypertrophic") variety of muscular dystrophy, 15 were cases of the facioscapulohumeral type, 14 were of the limb-girdle type and 12 patients were suffering from dystrophia myotonica. Clinical classification of the cases was carried out independently by two of us (P.L. and J.N.W.), and one of us (W.H.S.T.) was responsible for all biochemical estimations. Of the 14 Duchenne-type cases, 12 were male and all showed typical

TABLE I.—*Serum Enzyme Activities in Patients with Muscular Dystrophy*

Case No.	Age and Sex	Duration of Disease in Years	Degree of Disability	Serum Aldolase (Units)	S.G.O.T. (Units)	S.G.P.T. (Units)
<i>Duchenne Type</i>						
1	7 M	4	A	55.9	120	134
2	8 M	4	A	119.6	159	135
3	9 M	4	A	105.3	154	185
4	10 M	5	A	111.8	192	154
5	12 M	7	A	43.5	98	110
6	12 M	8	B	38.9	67	66
7	14 M	10	B	39.9	42	23
8	15 M	10	B	22.7	36	27
9	17 M	12	B	18.4	—	—
10	20 M	15	B	15.8	47	32
11	26 M	21	B	13.2	50	35
12	27 M	22	B	13.4	—	—
13	13 F	12	B	10.6	21	19
14	10 F	7	A	30.0	—	—
<i>Limb-girdle Type</i>						
15	63 M	10	A	5.4	20	15
16	35 M	12	A	5.4	19	11
17	26 M	13	A	14.7	34	18
18	45 M	20	B	5.0	19	11
19	49 M	20	A	4.9	16	13
20	35 M	21	B	5.6	21	16
21	41 F	25	B	1.3	—	—
22	43 F	25	B	6.0	—	—
23	35 F	25	A	4.9	16	13
24	47 M	26	A	5.8	19	13
25	37 M	29	A	8.3	19	12
26	45 M	37	B	8.3	23	15
27	48 M	38	B	7.6	31	38
28	61 F	48	A	3.7	13	8
<i>Facioscapulohumeral Type</i>						
29	18 M	2	A	22.2	38	23
30	43 M	3	A	11.2	24	16
31	21 M	4	A	11.7	—	—
32	18 M	5	A	7.7	19	13
33	34 F	10	A	7.9	32	26
34	21 F	11	A	10.8	32	17
35	31 F	13	B	9.2	32	17
36	27 F	14	B	7.8	18	14
37	35 F	17	A	4.3	18	17
38	33 F	20	B	7.1	—	—
39	37 F	23	A	3.6	16	9
40	48 M	28	A	8.8	26	22
41	44 F	30	A	4.7	—	—
42	59 F	41	A	4.3	—	—
43	71 F	55	B	3.3	13	4
<i>Dystrophia Myotonica</i>						
44	18 F	3	A	19.8	36	15
45	22 M	3	A	8.3	20	14
46	25 M	8	B	4.9	22	22
47	30 M	10	A	7.5	37	26
48	34 M	10	B	7.0	16	11
49	35 F	10	B	9.9	26	17
50	38 M	10	A	5.4	21	22
51	37 M	15	B	7.9	19	22
52	60 M	15	A	8.0	26	10
53	48 F	20	A	4.4	27	22
54	35 F	30	A	5.3	19	16
55	58 F	30	A	6.3	28	20

manifestations of this severe form of the disease; two were female and were probably suffering from the more benign autosomal recessive form of Duchenne-type dystrophy (Blyth and Pugh, 1959). All cases of the facioscapulohumeral variety and those of dystrophia myotonica showed the typical pattern of muscular involvement. In the 14 cases of the limb-girdle type, the shoulder-girdle muscles were predominantly or exclusively affected in five, the pelvic girdle in nine. In each category the patients have been arbitrarily divided into two broad groups—namely, A and B—according to the severity of their disability at the time when the estimations were made.

The group A cases were those in whom disability was mild or moderate, and group B those in whom it was severe. Thus most of the patients in group A were still ambulant, while most of those in group B were confined to wheel-chairs or were bedridden. The results of the estimations are given in Table I. These results may be compared with those obtained by Rowell and Smith (1959), who used similar methods of assay, in a series of 50 healthy adults. The normal upper limit (mean + 2S.D.) of serum aldolase activity is taken as 9.2 units (range 2.3–8.8 units, mean 5.7 units), that of S.G.O.T. as 28 units (range 12–36 units, mean 19 units), and that of S.G.P.T. as 21 units (range 4–24 units, mean 12 units). It should be noted that, as Schapira, Dreyfus, Schapira, and Kruh (1955) have pointed out, the mean normal activity of serum aldolase in children aged 5–10 years is approximately twice that of adults. It will readily be seen, however, that age alone could not account for some of the values we obtained in children with muscular dystrophy (Table I). The mean values for serum enzyme activity in the cases of limb-girdle and facioscapulohumeral muscular dystrophy and in dystrophia myotonica are given in Table II. The findings in the Duchenne-type cases are not included in this table, as the values obtained in individual cases

TABLE II.—Mean Values (in Units) of Serum Enzyme Activity in Certain Types of Muscular Dystrophy

	Limb-girdle	Facioscapulo-humeral	Dystrophia Myotonica	Normal Adults (Rowell and Smith, 1959)
Aldolase	6.21 (14 cases)	8.31 (15 cases)	7.89 (12 cases)	5.7 (50 cases)
S.G.O.T.	20.8 (12 ")	24.0 (11 ")	24.8 (12 ")	19 (50 ")
S.G.P.T.	15.3 (12 ")	16.2 (11 ")	18.1 (12 ")	12 (50 ")

varied so widely that the mean of results in this group would possess little significance. However, serum aldolase activity in the male cases of this type is correlated with the age of the patient in Fig. 1, while in Fig. 2 it is correlated with the duration of the disease in cases of all four groups.

FIG. 1.—Activity of the serum aldolase in cases of the Duchenne-type muscular dystrophy, charted against the age of the patient.

Discussion

The activities of the serum enzymes are remarkably constant for any given healthy individual, a fact which probably indicates a dynamic balance between production and removal. It is often inferred, therefore, that rapid destruction of tissue will temporarily overwhelm the serum clearance mechanisms for those enzymes which are present, and perhaps peculiarly abundant, in that tissue, thus raising their activities in the serum; as, for instance, in the well-known rapid rise of S.G.O.T. activity shortly after myocardial infarction. This simple and attractive hypothesis, however, fails to explain many relevant clinical and experimental findings.

The enzymes isocitric dehydrogenase (I.C.D.) and lactic dehydrogenase (L.D.H.) occur in mammalian heart muscle and liver, the former in considerable abundance; but in myocardial infarction the serum activity of L.D.H. is considerably raised while that of I.C.D. remains normal, and in infective hepatitis the serum activity of I.C.D. is grossly elevated while that of L.D.H. barely exceeds the upper limit of normal (White, 1958). Further, intravenous injection of L.D.H. in dogs raises the serum activity of the enzyme immediately to ten times the normal value, but after one hour the greater part of the L.D.H. has already been cleared from the serum (Wróblewski and LaDue, 1958); and after the intravenous injection of crystalline aldolase in rats the activity of the serum aldolase rises sevenfold within the first 15 minutes, falling almost to normal twelve hours later (Sibley and Lehninger, 1949).

In myocardial infarction it is known that the serum activities of lactic dehydrogenase (Wróblewski, Rueggesser, and LaDue, 1956) and aldolase (Volk, Losner, Aronson, and Lew, 1956) are raised considerably for several days; yet in view of these high enzyme-clearance rates and the known enzyme content of the myocardium it is difficult to see how the average myocardial infarct could possibly liberate sufficient of these enzymes to maintain a high serum activity for such a period. Similarly, intravenous injection in dogs of purified G.O.T. and G.P.T. concentrates causes a rapid and considerable rise in the serum activities of both enzymes; 24 hours later 97% of the administered G.O.T. has disappeared from the serum and all of it within 72 hours, while in 24 hours only 58% of the administered G.P.T. has been eliminated and after three days 18% of it still remains in the serum (Fleisher and Wakim, 1956). This disparity in serum clearance may perhaps be explained by the molecular weight of G.O.T. being only a third of that of G.P.T. (Green, Leloir, and Nocito, 1945), and in turn may help to explain the later elevation and later return to normal of S.G.P.T. compared with S.G.O.T. activity in cases of myocardial infarction (Rowell and Smith, 1959).

These and other difficulties have led Hauss and Leppelmann (1958) to postulate that the enzyme changes in serum are not due to specific localized tissue damage alone but are part of an "acute syndrome," and represent a complex and non-specific reaction by the entire organism to various afflictions; and they offer certain experimental evidence to support this hypothesis (Hauss, Leppelmann, and Plänitz, 1957). In muscular dystrophy, however, these observations need not apply, since this condition is chronic and in no way an acute syndrome; moreover, it has become evident, particularly in the Duchenne type of muscular

dystrophy, that the enzymes whose serum activities are characteristically elevated in the condition are derived specifically from skeletal muscle.

Normally there is a slight diffusion of aldolase from intact skeletal muscle, which may account for the normal serum activity (Zierler, 1956, 1957); dystrophic muscle, however, shows increased membrane permeability and a much greater efflux of aldolase, and compared with normal muscle it has a greatly reduced total aldolase content (Dreyfus, Schapira, and Schapira, 1954; Zierler, 1958). Furthermore, it has been suggested that the high activity of serum aldolase and S.G.O.T. in malignant cachexia may be due not simply to tumour necrosis but to the nutritional deprivation of skeletal muscle by the protein demands of the tumour, with consequent metabolic distress, wasting, and the liberation of aldolase and G.O.T. into the serum; and it has been found that in the absence of liver metastases the activities in the serum of these enzymes may rapidly be reduced towards normal by massive administration of oral protein and intravenous protein hydrolysate. This treatment, however, entirely fails to influence the raised activities of serum enzymes in muscular dystrophy, thus emphasizing the primary nature of the muscular abnormality (White, 1958).

The primary nature of the lesion is still further emphasized by the fact that in neurogenic muscular atrophy, such as occurs in poliomyelitis, motor-neurone disease, nerve injury, and polyneuritis, normal serum activities of aldolase (Schapira, Dreyfus, and Schapira, 1953; Aronson and Volk, 1957; Thompson and Vignos, 1959) and G.O.T. (Siekert and Fleisher, 1956; Pearson, 1957) occur even when the rate of muscular wasting, as in convalescent poliomyelitis, is proceeding at a rate much greater than is seen in muscular dystrophy. In the acute phase of neurogenic muscular atrophy of sudden onset there may be an initial trivial rise in the serum activities of these enzymes, but this is always transient and very quickly reverts to normal; experimental confirmation of these observations has been forthcoming for both aldolase and G.O.T. by carrying out surgical nerve section in dogs (Aronson and Volk, 1957).

The validity of any observation on the serum enzyme activity in muscular dystrophy depends first on accurate clinical diagnosis of the type of dystrophy from which the patient suffers. In several recent publications the accuracy of clinical diagnosis and classification was open to doubt. In this study diagnosis and classification were carried out according to rigid

FIG. 2.—Activity of the serum aldolase charted against the duration of the disease. (A) Duchenne-type muscular dystrophy. (B) Limb-girdle muscular dystrophy. (C) Facioscapulohumeral muscular dystrophy. (D) Dystrophia myotonica.

clinical and genetic criteria, and in most cases the diagnosis was confirmed by electromyography and often by muscle biopsy. We have determined in serum the activities of the three enzymes—aldolase, G.O.T., and G.P.T.—in four clearly defined clinical forms of the disease—namely, in 14 cases of Duchenne-type dystrophy, 14 cases of limb-girdle dystrophy, 15 cases of facioscapulohumeral dystrophy, and in 12 cases of dystrophia myotonica.

Duchenne Type of Muscular Dystrophy

In our series of cases of the Duchenne type of muscular dystrophy the patients ranged from active 7- and 8-year-old boys to immobile and helpless terminal cases in 26- and 27-year-old men. In the early stages of the disease very high serum activities of aldolase were found, falling steadily as the disease progressed, until in terminal cases the activity was not greatly raised above the upper limits of normal. Plotting age against these serum aldolase activities gave characteristic graphs (Fig. 1), starting with very high and rather scattered readings in the young active cases, falling steeply with increase in age, and latterly falling much less steeply among the advanced cases, where there was no significant scatter. There are indications (Thompson and Vignos, 1959) that wide individual variation tends to occur in the serum aldolase activities of young patients, and that this may sometimes be related to muscular activity.

Graphical representation against duration of disease instead of age gave a similar graph which was rather less convincing (Fig. 2, A) probably because, given a disease process which usually begins early in life and a rate of evolution which tends to remain constant with time, the age of the patient provides a more accurate indication of status than does duration of symptoms. The two female patients in this series, aged 10 and 13 years, showed (see Fig. 1) serum aldolase activities which were much less elevated than might have been expected for their age, a finding which is in accord with the sex difference reported by other workers (Schapira, Demos, Schapira, and Dreyfus, 1957; Thompson and Vignos, 1959). Very probably these two girls were suffering from the benign autosomal variety of the Duchenne-type muscular dystrophy. Their serum aldolase activities were comparable to those seen in cases of limb-girdle or facioscapulohumeral muscular dystrophy (Fig. 2, B and C).

Our findings are in full agreement with those of Thompson and Vignos (1959), who have derived similar graphs in a larger series of patients. They adduce a linear relationship between serum aldolase activity and functional muscle mass by means of an involved and exhaustive physical examination of muscle bulk and power in each patient, showing that the serum aldolase activity diminishes with the mass of muscle still functional and therefore, given constant evolution, with increasing age and decreasing functional ability. The graph of serum aldolase activity against age of patient may possibly be explained, therefore, as follows. It has been shown experimentally that, after the intravenous injection of known amounts of crystalline aldolase in animals the rate of clearance of the aldolase is proportional to its initial activity in the serum (Sibley, 1958). In the early stages of the disease, therefore, when a large bulk of muscle is steadily liberating large amounts of aldolase, the serum-clearance mechanisms are probably saturated and high serum activities of

aldolase result; later, when the muscle bulk has diminished and with it the amount of aldolase entering the serum, the accelerated clearance mechanisms may be better able to meet the demands now made and the activity of serum aldolase falls rapidly. Finally, when there is little muscle left and a minimal liberation of aldolase, the stimulus of serum activity towards clearance of aldolase falls steadily away as does the remaining muscle bulk, and thereafter the passage of time has little effect on the serum aldolase activity, which remains now only slightly raised above the upper limit of normal.

Recent investigations indicate that in dystrophic patients the increased transaminase (G.O.T.) activity of the serum is derived, like that of aldolase, from the diseased skeletal musculature, but that the ratio of its activity to that of aldolase in healthy skeletal muscle is only a sixth of that in the myocardium (White and Hess, 1957); further, homogenates of healthy cardiac and skeletal muscle both display G.O.T. activity about 20 times greater than that of G.P.T., the activity of each of these enzymes being about one and a half times greater in cardiac muscle than the corresponding activities in skeletal muscle (Wróblewski and LaDue, 1956). In our series of 10 male cases of representative ages with Duchenne-type muscular dystrophy, however, we have found that both S.G.O.T. and S.G.P.T. activities were very high in the youngest cases, and that these activities decreased progressively with the increasing age and disability of the patient and thus with the corresponding diminution of functioning muscle mass. Even in terminal cases they still exceeded the upper limits of the normal range. Our results agree fully with those of other workers (Pearson, 1957; Murphy and Cherniak, 1958), who confined their investigations to S.G.O.T. only, but in larger though not more representative series of cases.

The findings, however, were not so readily amenable as the serum aldolase activity to graphical representation against age or duration of symptoms, and thus provided rather less sensitive, though reliable, indications of the clinical status of the patient. In our series the mean of S.G.O.T. was 96.5 units (5.08 times normal mean) and of S.G.P.T. was 90.1 units (7.51 times normal mean), which accords with the much slower clearance of S.G.P.T. (Fleisher and Wakim, 1956) outweighing its probably lesser, though steady, production from the degenerating skeletal muscle. The ratio of the dystrophic multiple of the normal mean of S.G.P.T. to that of the normal mean of S.G.O.T. was 1.48 in our series of 10 cases, compared with a corresponding ratio of 1.59 in the series of 30 cases reported by Dreyfus, Schapira, and Schapira (1958).

Other Varieties of Muscular Dystrophy

The activities of serum aldolase, S.G.O.T., and S.G.P.T. obtained in our cases of three other clinical varieties of muscular dystrophy were much less striking than those shown by the cases of Duchenne-type dystrophy, though the mean values exceeded normal in each of the three varieties. In the patients with facioscapulohumeral muscular dystrophy and dystrophia myotonica there was a moderate rise in mean values, while in limb-girdle dystrophy the rise was only slight. It is at first sight surprising that the mean level should have been higher in the very benign facioscapulohumeral variety than in the less benign limb-girdle type. This can be explained by the fact that the series of

facioscapulohumeral cases was "weighted" by the inclusion of four early cases, while in no patient in the limb-girdle group had the disease been in progress for less than 10 years. In none of the three forms, however, was there such gross elevation of the serum enzyme activities as in the Duchenne type of dystrophy with its very rapid and extensive evolution and grave prognosis. In only 5 out of 15 cases of the facioscapulohumeral type, 2 out of 12 cases of dystrophia myotonica, and 1 out of 14 cases of the limb-girdle type was there a significant, though moderate, increase of serum enzyme activity, particularly of aldolase. This always tended to occur in younger cases of shorter duration with a greater functioning muscle mass. Similar sporadic and modest elevations of serum enzyme activity in these clinical forms of muscular dystrophy have been reported in the smaller series studied by other investigators (Pearson, 1957; Rowland and Ross, 1958; Kuhn and Wörner, 1959; Salvi, Ambanelli, Rosati, Carreras, and Mironi, 1959; Thompson and Vignos, 1959).

Conclusions

It is concluded that assay of these serum enzyme activities, particularly of aldolase, is of considerable value in the diagnosis of muscular weakness of insidious onset and obscure origin in young children, particularly in boys. Normal findings do not exclude a neurogenic origin but do exclude a diagnosis of Duchenne-type dystrophy, while greatly increased levels in the absence of other florid disease confirm its presence and carry a correspondingly grave prognosis. In older children and in young adults the same observations apply; though the diagnosis of the Duchenne-type dystrophy will usually be evident clinically at this stage, it will be supported by the finding of greatly raised serum enzyme activities. In the other and milder clinical forms of muscular dystrophy discussed here the serum enzyme activities afford little help since normal findings do not exclude the diagnosis. It must also be admitted, in agreement with the views of other workers, that the findings of increased activities of these enzymes in the serum appears to be a secondary result of leakage from diseased muscle cells. There is no evidence that any disorder of function of any of the enzymes referred to is of fundamental importance in the pathogenesis of the disease.

Summary

The serum activities of the enzymes aldolase, glutamic oxalacetic transaminase, and glutamic pyruvic transaminase, have been estimated in 55 cases of muscular dystrophy (14 Duchenne type, 14 limb-girdle, 15 facioscapulohumeral, 12 dystrophia myotonica).

In the Duchenne-type dystrophy the serum activity of all three enzymes was elevated at every stage of evolution of the disease, being particularly high in the early stages and lower terminally. A quantitative relationship, which appears to depend upon the amount of functioning muscle mass, was demonstrated to exist between the serum aldolase activity and the age of the patient. In the other varieties of muscular dystrophy only moderate and sporadic increases in the serum activities of these enzymes were discovered, but again the highest activities were always obtained in the early stages of the disease. Even in these comparatively benign varieties of muscular dystrophy, however, the mean serum activity of the three enzymes was raised above normal.

It is concluded that estimation of the serum aldolase activity is of considerable value in the diagnosis of the Duchenne-type muscular dystrophy, but it is of little help in the diagnosis of the other varieties. These abnormalities in serum enzyme activities probably indicate pathological diffusion of enzymes from diseased muscle cells, but evidence is still lacking that disorder of their function is fundamental in the pathogenesis of progressive muscular dystrophy.

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Rumania has undertaken a nation-wide five-year plan of cancer control and is spending \$23m. to develop hospital services, dispensaries, and training facilities.