Muscle Damage in Leprosy[1]

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About 40 per cent of the normal human body is muscle, which is thus the largest single tissue component. This relatively huge bulk provides an extensive depot of chemical units in a state of continual transformation and brisk exchange with the other compartments and tissues of the body. Many of today's biochemical concepts derive from vivid awareness of these dynamic equilibria.

Wasting of muscles is a common occurrence in leprosy. Muscular atrophy has long been recognized as one of the pathologic changes in leprosy ([6]). Muscle involvement may result from interruption of innervation or, in a small proportion of cases, by direct extension and involvement of muscle tissue by the infection.

Changes in the serum levels of certain enzymes reflect damage to the tissues that contain these enzymes. Any change observed in enzymic activity may be the result of release of activators or inhibitors in the experimental media. Examination of blood from patients with progressive muscular dystrophy has disclosed only a few abnormalities. The concentration of creatine in serum is elevated and that of creatinine is normal or perhaps low ([3]), and the concentration of aldolase in serum is elevated ([7, 9]). In leprosy, the only finding reported so far on this subject is that by Ross *et al.* ([6]) who observed the excretion of creatinine to be diminished in leprosy patients with muscle atrophy, lower values for the creatinine coefficient being in the patients having most impairment of muscular function.

The studies reported here are an attempt to determine, if possible, whether there are distinct qualitative biochemical alterations in various types of muscle damage in leprosy.

MATERIALS AND METHODS

The subjects included in the present study were (a) 89 cases of leprosy with clinically definable weakness of muscle, (b) 20 cases of leprosy without any clinically definable involvement of muscle, and (c) 20 normal healthy individuals. Each of the 89 cases in the first group was given a complete clinical testing of muscle conditions in order to determine the extent of the muscle damage in each case. This group was then further subdivided into three grades depending upon the extent of muscle involvement:

(I) Small muscle paralysis in one or two limbs only, and weakness of the muscles;

(II) Small muscle paralysis in three or four limbs, and wasting of the muscles;

(III) Bulk muscle paralysis with or without small muscle paralysis, and wasting of the muscles.

Serum levels of creatinine and creatine, serum aldolase and cholinesterase activity, and blood glucose were determined. The colorimetric method of Sibley and Lehninger ([9]) was employed for the estimation of serum aldolase. This involves conversion of aldehyde and ketone to hydrazones and hydrolysis of phosphates by alkali causing rearrangement to methylglyoxal which forms a colored 2.4-dinitrophenylhydrazone. Serum cholinesterase activity was determined colorimetrically by the method of Huerga and co-workers ([4]), which is based on the principle that hydroxylamine in alkaline solution reacts with esters of fatty acids (acetylcholine ester in the present case) to give hydroxamic acids which produce a red to violet color with ferric chloride. The method of Brod and Sirota ([2]) used for estimation of creatinine and creatine makes use of the Jaffe reaction, which yields a red color with an alkaline picrate solution. The method of Asatoor

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and King (1) was employed for the estimation of glucose in blood, using arsenomolybdic acid.

RESULTS

The data obtained are presented in Table 1. There is no alteration in the levels of blood glucose in the experimental group compared to the control groups. Though the values for cholinesterase, aldolase and creatine do not show any deviation from the normal values in the patients of grade I and grade II of the experimental group, such deviations are observed in patients belonging to grade III, where there is wasting of muscles and paralysis of bulk muscles. The levels of serum aldolase and serum cholinesterase are higher in this group of patients compared to those obtained in the control groups. Estimations of serum creatine and creatinine in the patients if grade III in the experimental group reveal a significant change in the mean values compared to the values obtained in the control groups. Levels of serum creatine are significantly increased in the experimental group (0.70 mgm./100 ml. as against 0.40 mgm./100 ml. in the control patients group) and those of the serum creatinine are decreased in the experimental group (0.86 mgm./100 ml. as against 1.06 mgm./100 ml. in the healthy control group).

DISCUSSION

Because atrophy is accompanied by sweeping structural changes and fundamental deterioration, it would seem likely that assessment of activity of several important enzymic systems susceptible to measurement might provide clues to suggest the nature of the fundamental disturbance. It has been shown that the concentration of aldolase in serum of patients with progressive muscular dystrophy is elevated (7, 9). Skeletal muscle is a rich source of aldolase. When muscle cells, and indeed when other cellular structures disintegrate or lose their relative permeability, their substance is swept into the blood stream. It is likely that similar elevation of the concentration in the serum of other intramuscular substances could be found in muscular dystrophy, and that high serum aldolase activity is a consequence of muscle breakdown. Schapira *et al.* (8) reported that some constituents of muscles, particularly the glycolytic enzyme fructoaldolase, may be elevated in serum derived from patients with some diseases involving muscles. While the action of aldolase in the chain of intracellular glycolysis is highly specific, the enzyme is so ubiquitous that an isolated abnormal value is of little assistance unless appropriately viewed against the patient's clinical background. The cases under investigation in the present study had undergone thorough

TABLE 1. *Muscle damage in leprosy.*

Type	No. of cases	Cholinesterase units/ml.	Aldolase units/-100 ml.	Glucose mg./-100 ml.	Creatinine mg./100 ml.	Creatine mg./100 ml.
Grade I	36	210 (155–303)	4.00 (2.2–6.6)	87 (65–114)	1.08 (0.75–1.37)	0.35 (0.20–0.53)
Grade II	22	221 (158–290)	4.22 (1.9–6.6)	91 (68–109)	1.00 (0.71–1.32)	0.50 (0.22–0.70)
Grade III	31	175 (133–285)	4.40 (2.2–6.1)	76 (62–101)	0.86 (0.54–1.23)	0.70 (0.39–0.99)
Control patients	20	206 (134–281)	3.23 (2.2–6.1)	83 (66–112)	1.04 (0.85–1.33)	0.40 (0.21–0.56)
Normal healthy controls	20	216 (131–212)	3.46 (1.7–6.6)	85 (62–114)	1.06 (0.85–1.28)	0.41 (0.29–0.53)

clinical testings to detect the extent of muscle damage. In this light the elevated value of serum aldolase in the group of patients where the damage is maximum, may be considered as a significant finding. The prognostic value of serum aldolase in muscular dystrophy has been a matter of dispute. Pearson ([5]) observed a positive correlation between the rate of the dystrophic process and the enzyme levels. In the present study, we also have obtained a similar finding, i.e., the enzyme levels are maximally elevated where there is bulk muscle deterioration.

In the present study, elevated values of creatine and diminished values of creatinine were found in the serum of patients of grade III. Cumins ([3]) observed that in patients with progressive muscular dystrophy the concentration of creatine is elevated and that of creatinine is normal or perhaps low, a finding similar to that reported here. It has been well known that the concentration of a number of substances within muscle is large compared to the concentration of the same materials outside muscle. When muscle cells are disrupted by disease, these substances may be expected to pour from muscle into the surrounding interstitial fluid and pass thence into circulating plasma. In case of some substances (e.g., potassium) the rate of loss in urine in the presence of normal kidney function tends to keep pace with the loss from muscle, so that its concentration in plasma is apt not to rise appreciably. In the case of other substances, such as creatine, normal renal function is not geared to quantitative exertion, and the concentration of the substance increases in plasma.

It is well established that creatine is synthesized in liver, diffuses into the blood stream and is supplied to many types of cells, particularly those of muscle. In muscle, creatine is phosphorylated to yield a labile reservoir of so-called high-energy phosphocreatine. From either creatine or phosphocreatine, it is uncertain which, creatinine is formed at a steady rate. Whenever the total quantity of extracellular creatine, or phosphocreatine, is diminished, as by loss of muscle mass, the quantity of creatinine formed each day is reduced and so is its concentration in the serum.

In addition to the loss of material from muscle which accompanies continuing disorganization of muscle cells, the reduced mass of muscle is responsible for further changes in the composition of plasma. A further problem is posed for substances which are synthesized in other tissues and are normally carried by blood to be concentrated in muscle. When muscle bulk is reduced these substances accumulate in plasma as in creatinuria.

On the basis of these considerations it is reasonable to assume that the changes here reported are related more to the mass of muscle involved than to the quality of such muscle involvement.

SUMMARY

Biochemical investigations were carried out in leprosy patients with varying degrees of muscle damage. These included determinations of serum levels of creatinine, creatine, aldolase, cholinesterase and blood sugar.

The results indicate that blood glucose levels in any of the patient groups did not show any deviation from those for the control groups. Serum levels of the enzymes and creatine in patients with lower degrees of muscle damage are comparable to those of normal controls. However, in the group of patients with severe muscle damage, slight increases in the levels of the enzymes and of creatine are observed.

The findings appear to suggest that the changes observed are related to the mass of the muscle involved.

RESUMEN

Se hicieron investigaciones bioquímicas en pacientes con lepra con diversos grados de daño muscular. Estas investigaciones incluyeron determinaciones de los niveles séricos de creatinina, creatina, aldolasa, colinesterasa y glicemia.

Los resultados indican que los niveles de glicemia en los grupos de pacientes no mostraron ninguna diferencia con los de los grupos controles. Los niveles séricos de las enzimas y de creatinina en pacientes con grados inferiores de daño muscular son comparables con los de los controles normales. Sin embargo, en el grupo de pacientes con daño muscular severo, se ob-

servaron ligeros aumentos en los niveles de las enzimas y de la creatinina.

Estos hallazgos parecen sugerir que los cambios observados están relacionados con la masa de músculo comprometida.

RÉSUMÉ

Des investigations biochimiques ont été poursuivies chez des malades atteints de lèpre et présentant divers degrés de lésion musculaire. Ces investigations ont compris les déterminations des taux sériques de la créatinine, de la créatine, de l'aldolase, de la cholinestérase et du sucre sanguin.

Les résultats indiquent que les taux de glucose du sang dans n'importe quel groupe, n'ont montré aucune déviation par rapport au taux observé dans les groupes témoins. Les taux sériques des enzymes et de la créatine chez les malades souffrant d'un moindre dommage musculaire sont comparables à ceux relevé chez les témoins normaux. Toutefois, dans le groupe de malades atteints de lésions musculaires graves, on a noté une légère augmentation dans les taux des enzymes et des créatines.

Ces observations semblent suggérer que les modifications observées sont en relation avec la masse du muscle atteint.

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