

hydrogen bond chain, with an essentially higher molecular weight through the residue *R*, with which it is closely connected.

In the case of  $\text{NH}_3$ , the conditions are quite different. One hydrogen atom joins the  $\text{>CO}$  group again. The  $\text{NH}_3$  does not form a further hydrogen bond with the  $\text{COOH}$  group, but a salt bond. The heat of formation of a salt bond is higher than that of a hydrogen bond, but the hydrogen bond is much more rigid. Water molecules can change from anion to cation and vice versa and in the case of the hydrogen bond being separated by a molecular impact a new bond is difficult to establish because the salt bond is no longer in its original position.

$\text{HCN}$ , however, links up with the  $\text{>NH}$  group and its hydrogen forms a salt bond with the  $\text{H}_2\text{N}-\text{CHR}$  residue.

The same applies to  $\text{HCl}$ ,  $\text{HBr}$  and  $\text{HI}$ .  $\text{Cl}_2$ ,  $\text{Br}_2$  and  $\text{I}_2$ , however, form a second hydrogen bond and therefore their odour is much stronger than that of the corresponding acids.

Diacetyl, which has a distinctly strong and long-lasting odour, is an example of the simultaneous attachment to two  $\text{>NH}$  groups. The small molecule is securely held by the two bonds and it may be embedded so safely in the adjacent amino-acid residues that it can scarcely be removed by molecular impacts.

This model clearly explains the many olfactory impressions in that they are produced simultaneously through the common action of the receptor organ and the odoriferous substance. The theory requires only one kind of receptor, and all electron micrographs of the olfactory epithelium reveal only one kind of receptor, namely, the cilia, which are all identical.

The steric conditions of the  $\alpha$ -helix are clearly defined and it is therefore possible to check the applicability of this working hypothesis. It is possible to synthesize chemical compounds with the same spatial arrangement as parts of the  $\alpha$ -helix. These would have to form addition compounds with the corresponding odoriferous substances by means of the existing secondary valencies the presence of which should be provable by examination of their various spectra.

The calotte model of the  $\alpha$ -helix makes it possible to study the theoretically possible reaction of the odoriferous substances. If this working hypothesis is correct, it should be possible to find various classes of odoriferous substances which correspond to their spatial arrangement and the location of the secondary valencies in these substances.

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## Defect of Coenzyme-A Activity in Progressive Muscular Dystrophy

STUDIES of the final stages of glycolysis and the initial stages of the citric acid cycle in progressive muscular dystrophy have used indirect methods, such as the de-

termination of serum levels of corresponding metabolites. In this context two facts are interesting: the increase of pyruvicaemia<sup>1-4</sup> simultaneous with the decrease of citric acid<sup>3,4</sup>, and the normality of lactate,  $\alpha$ -cetoglutarate and oxalacetate serum values<sup>3,4</sup>. Only the decrease in the concentration of citric acid would be exclusively specific to progressive muscular dystrophy<sup>3,4</sup>.

The conversion of pyruvate to citrate is probably inhibited in dystrophic muscle, and the role of coenzyme-A in this process justifies its direct investigation in muscular tissue.

Muscle samples obtained by biopsy from proximal muscles (deltoid and quadriceps) of ten subjects with Duchenne's type progressive muscular dystrophy (stage 1-4 in Thomson and Vignos's scale) and nine normal subjects (5-8 yr old boys) were homogenized at 0°C in 0.25 M sucrose buffered with *tris*-HCl at pH 8.0. The supernatant was obtained by centrifugation of homogenate at 8,000g, for 10 min at 0°C, and the activity of coenzyme-A was determined by Novelli's method<sup>5</sup>.

Table 1. ACTIVITY OF COENZYME-A (MEAN VALUES)

Group	Coenzyme-A activity	
	Serum ( $\mu\text{M}/\text{ml}/\text{h}$ at 37°C)	Muscle ( $\mu\text{M}/\text{mg}$ Biuret-protein/h at 37°C)
Normal	1.13 $\pm$ 0.05	6.03 $\pm$ 0.21
Duchenne	1.54 $\pm$ 0.07*	3.96 $\pm$ 0.22*

Biuret-protein includes non-collagen protein only. It was obtained by extraction in 0.25 M sucrose, pH 7.6, for 18 h at 4°C.

\*  $P < 0.01$ .

The mean activity of coenzyme-A in the muscle of dystrophic patients was significantly lower than in normal muscle ( $P < 0.01$ ). Taking 5  $\mu\text{M}$  as a critical value, it is clear that seven normal muscle samples show higher patterns compared with only three dystrophic muscle samples.

The damage to coenzyme-A activity in dystrophic muscle may be a consequence of its passage into the extracellular space, because there is a significant difference between serum levels of coenzyme-A activity in normal and dystrophic subjects ( $P < 0.01$ ); the significant correlation between increased serum activity and decreased muscular activity of the enzyme in dystrophic patients ( $r = +0.62$ ;  $P < 0.05$ , calculated according to Kendall's rank method) support this idea. The presence of sarcoplasmic enzymes in the serum is a distinctive feature of muscular dystrophy.

The dystrophic muscle might also be characterized by a genetically determined defect with respect to coenzyme-A.

A metabolic block at the stage of acetate activation is the most likely explanation for the accumulation of pyruvate and the decrease in citrate in the serum of myopathic patients. The blocks in the initial stages of the citric cycle contribute to the disruption in the processes of energy production in dystrophic muscle fibres<sup>6</sup>. The normal concentrations of  $\alpha$ -ketoglutarate and oxalacetate show that the citric acid cycle is partially compensated by the utilization of glutamate and aspartate respectively.

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