for female carriers of the disease is also significantly raised compared with those in normal muscle ($P < 0.001$), neurogenic disease ($0.01 < P < 0.02$), foetal muscle ($0.02 < P < 0.05$) and adult muscular dystrophy ($0.001 < P < 0.01$).

D-Glucitol was identified as a probable intermediate in the conversion of glucose into fructose by the appearance of [^{14}C]glucose and [^{14}C]fructose as the major labelled components in extracts of muscle fibre-bundles incubated with [^{14}C]glucitol. Further evidence for this route of formation came from measurement of the activities of polyol-NADP oxidoreductase (EC 1.1.1.21) and L-iditol-NAD oxidoreductase (EC 1.1.1.14). In muscle extracts polyol oxidoreductase activity (μmol of substrate transformed/min per g fresh wt. at 25°C) was 2.17 ± 2.13 (14) for Duchenne-type dystrophy, compared with 0.17 ± 0.53 (13) for normal subjects ($0.001 < P < 0.01$) and 0.71 ± 1.45 (14) for a group of subjects with either polymyositis or neurogenic muscle disease ($0.02 < P < 0.05$). L-Iditol oxidoreductase activity (same units) for the same three groups was 1.64 ± 2.14 (15), 0.45 ± 0.91 (14) and 0.54 ± 0.81 (14) respectively. The differences between the 'dystrophy' group and the other two are significant at the level $0.05 < P < 0.1$.

These results indicate the presence in human muscle of a subsidiary pathway of glucose metabolism, whose importance is increased in Duchenne-type muscular dystrophy and carriers of the disease.

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Activation of Liver Glycogen Synthetase *in vitro*

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Glycogen synthetase (EC 2.4.1.11) exists in a non-phosphorylated (*a*) form and a phosphorylated (*b*) form. In a fresh liver extract glycogen synthetase is predominantly in the *b* form, and it is activated to the *a* form on incubation at 20°C (Gold & Segal, 1967; Merseman & Segal, 1967). Activation is preceded by a lag period, which Hers and co-workers (Stalmans *et al.*, 1971) suggest represents the time taken for phosphorylase *a* activity to diminish and thus remove the inhibition it normally exerts on synthetase *b* phosphatase (the enzyme involved in the conversion synthetase *b* $\rightarrow$ synthetase *a*). The coupling of activation of synthetase (synthetase *b* $\rightarrow$ synthetase *a*) with deactivation of phosphorylase (phosphorylase *a* $\rightarrow$

phosphorylase *b*) is believed to be a regulatory mechanism of glycogen metabolism (Stalmans *et al.*, 1971; DeWulf *et al.*, 1970).

Synthetase activation is stimulated by several inorganic salts (Hers *et al.*, 1969) that do not influence phosphorylase *a* phosphatase (Stalmans *et al.*, 1970) (catalysing the conversion phosphorylase *a* $\rightarrow$ phosphorylase *b*). We have confirmed that the activation synthetase *b* $\rightarrow$ synthetase *a* in a liver preparation under the conditions reported by DeWulf *et al.* (1970) occurs after a well-marked lag period in the presence of 5 mM-sulphate. In the presence of chlorides (5 mM), however, this lag is not evident. Added phosphorylase *a* increases the lag period in the presence of sulphate (Stalmans *et al.*, 1971), but when MgCl_2 (5 mM) is used to replace sulphate little inhibition is observed, and in the presence of both salts the lag period is further prolonged. The glucose and AMP effect on synthetase activation (DeWulf *et al.*, 1970) is not observed in the presence of 5 mM- MgCl_2 . Further evidence suggests that the lag period is not exclusively regulated by phosphorylase *a* concentration but is partly a sulphate-dependent effect.

The immediate activation of synthetase by 5 mM- MgCl_2 is modified by addition of ATP (3 mM) and the lag period is reinstated. The duration of the lag period is dependent on the $\text{Mg}^{2+}/\text{ATP}$ ratio but independent of phosphorylase *a* concentration, which could be manipulated by the presence of 5 mM-caffeine. Activation of synthetase beings as soon as ATP is hydrolysed, and EDTA inhibits at this point. The observed effects of ATP and Mg^{2+} on the activation are not explicable in terms of their effects on synthetase *a*.

These results suggest that ATP concentrations may contribute to the regulation of synthetase phosphatase activity and hence synthetase activation by controlling the availability of Mg^{2+} . The possibility that changes in the conformational state of the substrate (i.e. synthetase *b*) may be involved in these studies *in vitro* rather than direct effects on the enzyme (i.e. synthetase phosphatase) is worth considering.

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