*ENZYMES IN A GLYCOGEN STORAGE MYOPATHY**

By Joseph Larner and Carlos Villar-Palasi

DEPARTMENT OF PHARMACOLOGY, SCHOOL OF MEDICINE, WESTERN RESERVE UNIVERSITY

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McArdle has reported a "myopathy due to a defect in muscle glycogen breakdown"[1] which appears to be a type of glycogen storage disease distinct from the previously reported classes.[2] Schmid and Mahler[3] using muscle homogenates from a patient similar to the one described by McArdle have found that lactate is formed from added glucose 1-phosphate at a rate comparable to that of controls, but addition of muscle glycogen did not increase production of lactate. The content of glycogen in the muscles of this patient ranged from 2.4 to 3.0 per cent. Estimation of phosphorylase indicated a markedly reduced activity of this enzyme.

Recently it has become apparent[4-8] that there is a uridine linked pathway of glycogen synthesis present in animal tissues which involves two enzymes UDPG† pyrophosphorylase, and UDPG glycogen transglucosylase. It was therefore of interest to determine the enzymes of the uridine linked pathway in the muscle of a patient with McArdle's disease. Schmid, Robbins, Traut, and Lipmann[9] have already estimated levels of phosphorylase, phosphoglucomutase, and UDPG glycogen transglucosylase. We report here further results with a sample of the same muscle biopsy, including confirmation of the extremely low phosphorylase activity, and in addition normal activities of UDPG pyrophosphorylase, amylo-1,6-glucosidase, and phosphoglucomutase.

Materials and Methods.—The biopsy of the patient with the disease was obtained from the back. Two control biopsies of rectus and pectoral muscles were obtained during surgical procedures.‡ Homogenates of the rapidly frozen tissue (1:10 w/v) were made in 0.05 *M* Tris 0.005 *M* EDTA pH 8.

Amylo-1,6-glucosidase was determined by the method of Hers (10), using phosphorylase limit dextrin instead of glycogen. UDPG pyrophosphorylase, phosphoglucomutase, and phosphorylase were determined spectrophotometrically (see Table I), using extracts prepared from homogenates by centrifugation at 3000 × *g* for 10 minutes. Activities have been expressed in the units used by Hers.[10]

Results and Comments.—A phosphorylase activity corresponding to 0.23 per cent of the control value was found in the diseased muscle (Table 1). No significant differences in the activities of amylo-1,6-glucosidase, phosphoglucomutase, or UDPG pyrophosphorylase were noted when compared to controls.

It appears that the increased muscle glycogen content in this disease is associated with a markedly diminished phosphorylase activity. From the present and previous data[9] it is apparent that the two enzymes of the uridine pathway are present in the diseased muscle. There appears to be no deficiency in phosphoglucomutase or amylo-1,6-glucosidase activities.

Previous experiments have shown that activation of phosphorylase by epinephrine or glucagon is associated with glycogen breakdown.[11] Glycogen synthesis stimulated by insulin in rat diaphragm in short time experiments takes place with a ratio of inorganic phosphate to glucose 1-phosphate of 305.[7] Activation of phosphorylase in muscle homogenates by addition of phosphorylase kinase results in

TABLE 1

ENZYME ACTIVITIES IN MUSCLE

Patient*	Amylo-1,6-glucosidase Activity, per 1000/mg/hr	Phosphorylase† Activity, μm/g/min	UDPG‡ Pyrophosphorylase Activity, μm/g/min	Mutase§ Activity, μm/g/min
1. McArdle's disease	.006	0.025	28.6	63.4
2. Control	.004	9.20	32.0	67.5
3. Control	.010	10.65	26.3	56.4

* Patient 1, age 52, back muscle; patient 2, age 54, rectus muscle; patient 3, age 55, pectoral muscle.

† Reaction mixture contained (final concentration): inorganic phosphate buffer pH 7.2 1.7×10^{-2} *M*; Mg^{++} 1.7×10^{-3} *M*; TPN, 1×10^{-3} *M*; glucose-1,6-diphosphate 1.7×10^{-6} *M*; phosphoglucomutase (freshly dialyzed) 0.05 ml; AMP 8×10^{-4} *M*; glucose 6-phosphate dehydrogenase (5 mg./ml) 0.01 ml; reaction started by addition of rabbit muscle glycogen, 1 mg.

‡ Reaction mixture contained (final concentration): glycylglycine buffer pH 7.45 2.5×10^{-2} *M*; Mg^{++} 2×10^{-2} *M*; TPN 1×10^{-3} *M*; glucose-1,6-diphosphate 2×10^{-6} *M*; glucose 6-phosphate dehydrogenase (5 mg/ml) 0.01 ml; phosphoglucomutase (freshly dialyzed) 0.05 ml; UDPG 4×10^{-4} *M*; reaction started by addition of pyrophosphate 2×10^{-2} *M*.

§ Reaction mixture as for UDPG pyrophosphorylase except that glucose 1-phosphate 2×10^{-2} *M* was used in place of UDPG and pyrophosphate, and phosphoglucomutase omitted.

glycogen breakdown.[6] These previous findings together with the results reported here may best be explained on the basis of a cyclic mechanism of glycogen synthesis and degradation in which the uridine linked pathway catalyzes the synthesis and phosphorylase the degradation of glycogen.

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† The following abbreviations have been used: UDPG, uridine diphosphate glucose; Tris, tris (hydroximethyl) aminomethane; EDTA, ethylene diamine tetra-acetic acid; AMP, adenylic acid; TPN, triphosphopyridine nucleotide.

‡ The muscle biopsy from the patient was kindly supplied by Drs. R. Schmid and P. W. Robbins. The control biopsies were obtained locally through the cooperation of Dr. W. R. Drucker.

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