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Maximum activities of some enzymes of glycolysis, the tricarboxylic acid cycle and ketone-body and glutamine utilization pathways in lymphocytes of the rat

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1. The maximum activity of hexokinase in lymphocytes is similar to that of 6-phosphofructokinase, but considerably greater than that of phosphorylase, suggesting that glucose rather than glycogen is the major carbohydrate fuel for these cells. Starvation increased slightly the activities of some of the glycolytic enzymes. A local immunological challenge *in vivo* (a graft-versus-host reaction) increased the activities of hexokinase, 6-phosphofructokinase, pyruvate kinase and lactate dehydrogenase, confirming the importance of the glycolytic pathway in cell division. 2. The activities of the ketone-body-utilizing enzymes were lower than those of hexokinase or 6-phosphofructokinase, unlike in muscle and brain, and were not affected by starvation. It is suggested that the ketone bodies will not provide a quantitatively important alternative fuel to glucose in lymphocytes. 3. Of the enzymes of the tricarboxylic acid cycle whose activities were measured, that of oxoglutarate dehydrogenase was the lowest, yet its activity (about 4.0 μmol/min per g dry wt. at 37°C) was considerably greater than the flux through the cycle (0.5 μmol/min per g calculated from oxygen consumption by incubated lymphocytes). The activity was decreased by starvation, but that of citrate synthase was increased by the local immunological challenge *in vivo*. It is suggested that the rate of the cycle would increase towards the capacity indicated by oxoglutarate dehydrogenase in proliferating lymphocytes. 4. Enzymes possibly involved in the pathway of glutamine oxidation were measured in lymphocytes, which suggests that an aminotransferase reaction(s) (probably aspartate aminotransferase) is important in the conversion of glutamate into oxoglutarate rather than glutamate dehydrogenase, and that the maximum activity of glutaminase is markedly in excess of the rate of glutamine utilization by incubated lymphocytes. The activity of glutaminase is increased by both starvation and the local immunological challenge *in vivo*. This last finding suggests that metabolism of glutamine via glutaminase is important in proliferating lymphocytes.

It has been known for many years that rapidly dividing cells utilize glucose at a high rate (Warburg, 1956; Roos & Loos, 1973); more recently evidence has been obtained that glutamine oxidation may also be important for such tissues (for review see Krebs, 1981). Glucose metabolism in lymphocytes, which can undergo rapid cell division, has been investigated in some detail (Cooper *et al.*, 1963; Hume *et al.*, 1978), but the pathway of metabolism of glutamine and other fuels (such as ketone bodies) and their quantitative relationship to that of glucose have not been investigated.

It has been established that, for muscle, a quantitative indication of the maximum capacity of some metabolic pathways can be obtained from the maximum catalytic activity *in vitro* of key enzymes in those pathways (Newsholme *et al.*, 1980; Cooney *et al.*, 1981). The maximum activities of the following enzymes have been measured in lymphocytes to provide information about the capacities of some metabolic pathways: hexokinase (EC 2.7.1.1) for the pathway of glycolysis from glucose; glycogen phosphorylase (EC 2.4.1.1) for the pathway of glycolysis from glycogen; oxoglutarate dehydrogenase (EC 1.2.4.2) for the tricarboxylic acid cycle. In addition, the activities of 3-oxo acid CoA-transferase (EC 2.8.3.5) and 3-hydroxybutyrate dehydrogenase (EC 1.1.1.30), provide qualitative information on the ability to oxidize ketone bodies (Beis *et al.*, 1980). The activity of phosphate-de-

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