Metabolism of ketone bodies, oleate and glucose in lymphocytes of the rat

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1. Isolated incubated lymphocytes utilized acetoacetate, 3-hydroxybutyrate or oleate at about 0.5 µmol/min per g dry wt. These rates were not markedly affected by concanavalin A or by starvation of the donor animal. When ketone bodies replaced glucose in the culture medium, they could not support lymphocyte proliferation when cells were cultured for 48 h. 2. Addition of oleate (0.5 mM) to isolated lymphocytes increased the rate of O$_2$ consumption markedly, suggesting that it could contribute about 30% to O$_2$ consumption. The rate of oleate uptake and the stimulated rate of O$_2$ consumption were maximal at 0.5 mM-oleate; this is in contrast with the effect in some other tissues, in which the rate of fatty acid oxidation is linear with concentration up to about 2 mM. Since the normal plasma concentration of fatty acid in the fed state is about 0.5 mM, this suggests that lymphocytes can utilize fatty acids at a maximal rate in the fed state. 3. Ketone bodies or oleate decreased the rate of glucose utilization by incubated lymphocytes; ketone bodies decreased the rate of pyruvate oxidation and increased the intracellular concentration of hexose monophosphate and citrate, suggesting that 6-phosphofructokinase is inhibited by citrate, and hexokinase by glucose 6-phosphate. These effects may be important not so much in conserving glucose in the whole animal but in maintaining the concentrations of glycolytic intermediates necessary for biosynthetic processes during proliferation.

The importance of glucose metabolism in provision of energy for lymphocytes has been known for some time (for review see Hume & Weidemann, 1980) and the importance of glutamine has been established more recently (Ardawi & Newsholme, 1982, 1983a,b, 1984). In contrast, the rates of utilization of long-chain fatty acids or ketone bodies and their quantitative importance for energy production in lymphocytes are unclear. For instance, it is not known how far ketone bodies or long-chain fatty acids can support the proliferative response of lymphocytes in the absence of glucose. The work of Lengle et al. (1978) suggests that 50–90% of the ATP requirement of cultured lymphocytes could be obtained from the oxidation of oleate. In incubated rat spleen slices, in the presence or absence of glucose, the oxidation of endogenous triacylglycerols contributed significantly to energy production (Suter & Weidemann, 1975). In contrast, the rapidly dividing cells of the intestinal mucosa utilize glutamine and ketone bodies, but not long-chain fatty acids, for energy formation (for review, see Windmueller, 1980).

In the present study, the rates of utilization of acetoacetate, 3-hydroxybutyrate or oleate by isolated rat lymphocytes, together with their effects on rates of glucose metabolism, have been investigated. In addition, the effects of concanavalin A, which stimulates mitogenesis, and starvation of the donor animal on the utilization rates have been studied.

Experimental

Animals

Male Wistar albino rats (160–180g) were obtained from Batin and Kingman, Grimston, Hull, N. Humberside, HU11 4QE, U.K.

Chemicals and enzymes

All chemicals and enzymes were obtained from Boehringer Corp. (London), London W5 2TZ, U.K., except for the following: D-glucose, glycine, scintillants and all inorganic reagents were ob-