Exercise by means of bilateral stimulation of the sciatic nerves at rates of 1/s and 5/s did not significantly increase the removal of acetoacetate nor did it increase the release of 3-hydroxybutyrate.

Exercise increased the uptake of glucose (5mm) in the absence of insulin, confirming the findings of Szabo, Mahler & Szabo (1969). In contrast with the findings with perfused rat heart (Williamson & Krebs, 1961) addition of acetoacetate to the perfusion medium containing 5mm-glucose did not inhibit the increased uptake of glucose in the presence of insulin, nor did it inhibit the increased uptake of glucose during exercise in the absence of insulin.

Although the rate of removal of acetoacetate by this preparation was less than 10% of that reported for the perfused rat heart, sufficient acetoacetate was removed to account for 70–80% of the fuel of respiration at rest.

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Activity of Ketone-Body Utilization Pathway in Brain of Suckling and Adult Rats*

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The capacity of brain to utilize ketone bodies has been measured in suckling and adult rats by determining the activities of 3-hydroxybutyrate dehydrogenase (EC 1.1.1.30), 3-oxo acid CoA-transferase (EC 2.8.3.5) and acetoacetyl-CoA thiolase (EC 2.3.1.9). The activity of 3-hydroxybutyrate dehydrogenase in brain at birth was about two-thirds that of adult brain. The activity rose throughout the suckling period and at the time of weaning (20–22 days) reached values about three times higher than those for the adult. Similar findings have been reported by Klee & Sokoloff (1967). The changes in 3-oxo acid CoA-transferase paralleled those of 3-hydroxybutyrate dehydrogenase. The transferase activity at birth was about 1 U/g fresh wt. of brain, rose to 6 U at 21 days and then gradu-

ally declined to the adult value of 2.5 U. In contrast, brain acetoacetyl-CoA thiolase remained virtually constant at 4.0 U for 30 days after birth, which is higher than the adult activity of 2.5 U. The activities of these enzymes in kidney and heart gradually increased but did not reach the adult values until 3–4 weeks after birth. Thus during the suckling period rat brain, because of its size in relation to kidney and heart, is potentially the most important site of ketone-body utilization.

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Metabolic Effects of Propionate Administration to Normal and Vitamin B₁₂-Deficient Rats*

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Oberholzer, Levin, Burgess & Young (1967) reported that an oral load of propionate caused hypoglycaemia in a patient with congenital deficiency of methylmalonyl-CoA mutase (EC 5.4.99.2), which interconverts methylmalonyl-CoA and succinyl-CoA. To investigate possible reasons for this effect, propionate was administered to normal and vitamin B₁₂-deficient rats. The latter are unable to utilize propionate effectively (Weidemann, Hems, Williams, Spray & Krebs, 1970) because vitamin B₁₂ is an essential cofactor for the mutase. The rats were starved for 48 h and were killed 30 min after intraperitoneal injection of either propionate (1mmol) or 0.9% NaCl. The liver was freeze-clamped and blood collected from the aorta.

Propionate caused a slight increase (about 1 μ mol/ml) in blood glucose in both normal and vitamin B₁₂-deficient rats. The concentration of lactate in blood was not significantly altered in control animals given propionate, but rose from $1.26 \pm 0.44 \mu$ mol/ml (s.d.; $n = 9$) to 3.05 ± 1.77 (10) μ mol/ml in the deficient group. The changes in blood pyruvate followed a similar pattern.

The lactate concentrations in livers from normal and vitamin B₁₂-deficient rats were the same at 0.39 μ mol/g. After propionate the lactate concentration did not change significantly in the control livers, whereas in the deficient livers it increased to 1.20 ± 0.71 (12) μ mol/g. Similarly, hepatic pyruvate concentrations did not alter in normal animals

* Dedicated to Professor H. A. Krebs, F.R.S., on his seventieth birthday.

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