treated with propionate, but increased threefold in the deficient group. These changes were accompanied by a dramatic fall in the hepatic acetyl-CoA content from 0.109 ± 0.17 (11) $\mu\text{mol/g}$ to 0.016 ± 0.006 (12) $\mu\text{mol/g}$ after propionate loading. The corresponding values for normal livers were 0.086 ± 0.012 (7) $\mu\text{mol/g}$ and 0.053 ± 0.029 (7) $\mu\text{mol/g}$ respectively.

The decrease in acetyl-CoA, an activator of pyruvate carboxylase, together with a probable increase in methylmalonyl-CoA, a potent inhibitor of this enzyme (Utter, Keech & Scrutton, 1964) provide an explanation for the accumulation of lactate and pyruvate in these experiments and for the hyperlactataemia and lactate intolerance that can accompany methylmalonic acidemia in humans (Lindblad, Lindblad, Olin, Svanberg & Zetterström, 1968).

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- Lindblad, B., Lindblad, B. S., Olin, P., Svanberg, B. & Zetterström, R. (1968). *Acta paediat. scand.* **57**, 417.
 Oberholzer, V. G., Levin, B., Burgess, E. A. & Young, W. F. (1967). *Archs Dis. Childh.* **42**, 492.
 Utter, M. F., Keech, D. B. & Scrutton, M. C. (1964). In *Advances in Enzyme Regulation*, vol. 2, p. 49. Ed. by Weber, G. Oxford: Pergamon Press Ltd.
 Weidemann, M. J., Hems, R., Williams, D. L., Spray, G. H. & Krebs, H. A. (1970). *Biochem. J.* **117**, 177.

Uptake of Ketone Bodies by Rat Brain *in vivo**

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Measurements of metabolite concentrations in blood sampled from the internal jugular bulb and the aorta of human subjects undergoing prolonged starvation indicate that ketone bodies are utilized as a fuel of respiration (Owen *et al.* 1967). However, it is not clear whether this is due to an enhanced ability of the brain to utilize ketone bodies or to raised ketone-body concentrations. The enzymes necessary for ketone-body utilization are present in rat brain but their capacities are unaltered by starvation (D. H. Williamson, M. A. Page, M. Bates & H. A. Krebs, unpublished work).

Ketone-body utilization by rat brain was investigated by simultaneous sampling of femoral-artery and cerebral-sinus blood. During starvation arteriovenous differences of ketone bodies rose in proportion to circulating ketone-body concentrations from negligible values to $0.16 \mu\text{mol/ml}$ at 48 h.

* Dedicated to Professor Sir Hans Krebs on his seventieth birthday.

When acetoacetate was infused into fed rats the same arteriovenous differences as for starved rats were observed at corresponding concentrations. Thus ketone bodies may be used by rat brain whenever they are present in blood. Control of cerebral ketone-body utilization operates through change in blood concentrations, at least in the rat.

The mean arteriovenous difference of glucose across brain was $0.51 \mu\text{mol/ml}$ in fed rats and decreased to $0.43 \mu\text{mol/ml}$ after 96 h starvation. Lactate production rose on starvation from 0.04 to $0.2 \mu\text{mol/ml}$ after 48 h and decreased thereafter. The oxygen calculated to be necessary to oxidize glucose and ketone bodies was $3.08 \mu\text{mol/ml}$ in fed rats, and remained constant throughout starvation. Ketone bodies accounted for 3% of the oxygen consumption in fed rats and 20% after 48 h starvation.

In 16–22-day-old suckling rats, which are normally hyperketonaemic, the capacity of the enzymic pathway of ketone body utilization is threefold greater than that of adults (Page & Williamson, 1971). Brains of suckling rats also extracted ketone bodies in proportion to circulating concentrations but arteriovenous differences were three times those of adult rats at a given concentration. Arteriovenous differences for glucose were similar to, or lower than, adult values and a greater proportion was converted into lactate. Ketone bodies could account for 25–70% of the oxygen consumption.

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- Owen, O. E., Morgan, A. P., Kemp, H. G., Sullivan, J. M., Herrera, M. G. & Cahill, G. F., jun. (1967). *J. clin. Invest.* **46**, 1589.
 Page, M. A. & Williamson, D. H. (1971). *Biochem. J.* **121**, 16P.

The Metabolism of Homoanistic Acid in Man and Guinea Pigs

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Although the metabolism of phenylacetic acid and its substituted derivatives have been extensively studied in man and other animal species (Williams, 1959), there is no information on the fate of *p*-methoxyphenylacetic acid (homoanistic acid). In man, phenylacetic acid is almost exclusively conjugated with glutamine, the halogeno derivatives with glycine, and the hydroxy acids are excreted free (Ambrose & Sherwin, 1933), whereas benzoic acid is excreted as hippuric acid, the