PROCEEDINGS OF THE BIOCHEMICAL SOCIETY

The 511th Meeting of the Society was held jointly with the Association of Clinical Biochemists at the Royal Postgraduate Medical School, Hammersmith Hospital, London W.12, on Thursday and Friday, 17 and 18 December 1970, when the following papers were presented:

COLLOQUIUM ON 'REGULATION OF PLASMA LIPID METABOLISM'

Insulin, Amino Acid Metabolism and Lipolysis in Isolated Fat-Cells

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The isolated fat-cells of the mouse have been used as a model for investigating the effect of insulin on amino acid transport and leucine metabolism. The amino acid analogue α -aminoisobutyrate has been shown to be taken up and accumulated by an energy-dependent process. Although insulin failed to increase significantly the uptake of α -aminoisobutyrate when large concentrations of unlabelled pyruvate or glucose were present in the incubation medium, it did stimulate this process in fat-cells incubated without any substrate. [U- ^{14}C]Leucine metabolism by isolated fat-cells, i.e. oxidation to CO_2 or incorporation into total lipids or proteins, was stimulated by insulin. This effect of insulin was observed in the presence of unlabelled glucose as well as in that of unlabelled pyruvate in the incubation medium. In the absence of added substrate from the incubation medium, the stimulatory effect of insulin on leucine incorporation into proteins almost completely disappeared, whereas the effect on incorporation of label from leucine into CO_2 or total lipids persisted, suggesting that the stimulatory effect of the hormone on leucine incorporation into proteins occurred only when sufficient energy was available. The energy requirement of insulin-stimulated leucine incorporation into proteins was also illustrated by the finding that the observed decrease in the cellular ATP content brought about by the removal of Na^+ from the incubation medium was accompanied by a disappearance of the insulin effect. Further, this effect reappeared when the concentration of ATP within the adipocytes was restored towards normal by adding Na^+ (144mM) to the incubation medium. Since lipolysis and antilipolysis have been shown to be also accompanied by changes in energy availability (Bihler & Jeanrenaud, 1970; S. W. Cushman, J.-J. Heindel & B. Jeanrenaud, unpublished work), it was decided to see whether leucine incorporation into

proteins would be altered by lipolytic agents and by insulin. Adrenaline, adrenocorticotrophin, caffeine and DB-cyclic AMP were all found to inhibit leucine incorporation into protein at a time when they increased lipolytic activity, increased intracellular free fatty acids and decreased the concentration of cellular ATP. When insulin was added together with lipolytic hormones or with xanthine derivatives, the inhibitory effect of these agents was relieved. In addition, insulin partly prevented the decrease in ATP and the rise in intracellular free fatty acids induced by the lipolytic agents. The rise in intracellular free fatty acids induced by lipolytic hormones appeared to precede the decrease in ATP, thus suggesting that the former could be the cause of the latter. In summary, these and other experiments to be reported indicate that optimum α -aminoisobutyrate uptake or leucine incorporation into proteins appears to be favoured by conditions ensuring optimum energy availability, the latter being often associated with low concentrations of cyclic AMP and low free fatty acid concentrations within the adipocytes. Conversely, these processes are inhibited and the energy availability decreased by conditions associated with high concentrations of cyclic AMP and free fatty acids. Although it is not possible to decide at the present time which of cyclic AMP or of intracellular free fatty acids is responsible for such a modulation of amino acid metabolism, the data gathered from this and other laboratories suggest that free fatty acids are likely to be of crucial importance. Since very little is known about blood flow through adipose tissue and since changes in blood flow may well be critical in the building-up of intracellular free fatty acids, it is not clear whether the fluctuations in intracellular free fatty acids and ATP observed *in vitro* also occur under physiological conditions or whether they may exist only under extreme conditions such as stress, starvation or diabetes.

Bihler, I. & Jeanrenaud, B. (1970). *Biochim. biophys. Acta*, **202**, 496.