Possible Effect of Histamine on Protein Synthesis by the Perfused Rat Liver

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Increases in serum glycoproteins after injury (Keyser, 1949, 1950, 1952; Shetlar, Bryan, Foster, Shetlar & Everett, 1949) are accounted for largely by seromucoid and were tentatively attributed to stimulation of the liver (Keyser, 1960). Increased secretion of adrenocortical hormones is apparently not responsible (Weimer & Redlich-Moshin, 1953; Shetlar & Shetlar, 1955; Keyser, 1959; Keyser, Shuster & Stephens, 1963), though there is evidence for a 'humoral factor' of some sort (Sarcione, Bohne & Krauss, 1965; Bogden, Gray & Fuss, 1966).

Our experiments formed part of a series designed to investigate the effect of physiologically active substances on glycoprotein production. Livers from adult male Wistar rats were perfused with 80 ml of heparinized rat blood plus 90 ml of solution containing NaCl (118.5 mm), KCl (4.75 mm), CaCl₂ (2.54 mm), KH₂PO₄ (1.19 mm), MgSO₄ (1.19 mm) and NaHCO₃ (24.9 mm), 2 g of crystallized bovine plasma albumin (Armour Pharmaceutical Co. Ltd., Eastbourne, Sussex, U.K.), 200 mg of glucose, 10 mg of penicillin and 10 mg of streptomycin, in apparatus essentially as described by Brauer, Pessotti & Pizzolato (1951). [¹⁴C]Glycine infusion was started at 30 min and blood samples were taken after a further 2½ h (specimen A) and 5 h (specimen B). Except in the controls histamine infusion (35 µg-50 mg/h) was started when specimen A was taken. Radioactivity per unit volume and specific radioactivity, and the ratio B/A, were calculated for seromucoid and non-seromucoid.

Histamine did not significantly affect incorporation of [¹⁴C]glycine into seromucoid; however, a slight decrease ($P < 0.05$) occurred in non-seromucoid specific radioactivity. Since the shifts in the means for seromucoid and non-seromucoid were in opposite directions, the ratio of these (i.e. seromucoid/non-seromucoid) should provide a more sensitive index of any change. Statistical analysis showed a highly significant difference ($P < 0.001$) between histamine and control experiments with respect to both radioactivity per unit volume and specific radioactivity. However, since the values derive from a set of ratios and there is little indication of the form of the underlying frequency distribution, any conclusions must be tentative.

These preliminary observations, together with

those described in the following abstract (Keyser & Cawson, 1970), suggest that the possible role of histamine in serum protein changes is worth further investigation.

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Effects of Histamine and of Bradykinin on Incorporation of [¹⁴C]Leucine by Rat Liver Microsomal Fraction

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Rat liver microsomal suspension was incubated with 'pH 5 enzymes', pyruvate kinase, phosphoenolpyruvate, ATP, GDP and L-[¹⁴C]leucine, as described by Keller & Zamecnik (1956). Addition of histamine (down to 0.016 mm or lower) or bradykinin (down to 0.035 mm or lower) significantly decreased the incorporation of labelled leucine into the precipitated proteins. Results with the perchloric acid-soluble ('seromucoid') fraction were erratic, presumably owing to variable contamination with albumin and perhaps other proteins. Fractionation with trichloroacetic acid-ethanol as described by Majumdar, Tsukada & Lieberman (1967) showed that histamine diminished the incorporation of leucine into both albumin and globulin. The effect of histamine was not inhibited by an antihistamine (mepyramine maleate) in molar concentrations up to 80% of that of the histamine.

It is known that the concentration of some serum proteins is increased after trauma whereas that of