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Cheng, J. Ye-O., Ming-Ho, Y., Miller, G. W. & Wilkie, G. N. (1968). *Environ. Sci. Tech.* **2**, 367.

Peters, R. A. & Shorthouse, M. (1967). *Nature, Lond.* **216**, 80.

Stimulation of Incorporation of Precursors into Protein and Ribonucleic Acid of Rat Liver Slices by Bovine Growth Hormone *in vitro*

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Stimulatory effects of growth hormone on RNA and protein synthesis can be observed when it is added to the medium perfusing rat liver (Jefferson & Korner, 1967), but Jackson & Sells (1967) reported that growth hormone *in vitro* had no effect on RNA labelling in liver slices. The concentration of amino acids present during perfusion affects the response to growth hormone, so it seemed possible that the absence of an effect of growth hormone on liver slices was due to the absence of amino acids. This point was investigated and the effects of growth hormone on amino acid incorporation into protein in liver slices were also studied.

Liver slices from male Sprague-Dawley rats, weighing 100–120g., were incubated for 1 hr. in Krebs-Ringer bicarbonate medium containing 3% bovine serum albumin, 8mm-glucose and a mixture of twenty amino acids in the proportions in which they occur in rat serum (Schimassek & Gerok, 1965), with a constant specific radioactivity of [^{14}C]leucine and 1 μC of [^3H]orotic acid/ml. The slices were homogenized in 0.9% NaCl at the end of the incubation period and after precipitation with 0.5M-HClO₄, the protein was freed of amino acids, RNA and lipids, and radioactivity was measured by the procedure of Munro, Jackson & Korner (1964). When labelling of RNA was studied, the homogenate was treated with 20% (w/v) trichloroacetic acid and RNA was extracted and counted as described by Jefferson & Korner (1967).

It was found that optimum amino acid incorporation into protein occurred when the concentration of amino acids in the medium was six times that in rat plasma, but that the labelling of RNA was virtually unaffected by changes in amino acid concentration. At six times plasma concentration of amino acids, addition of growth hormone at a concentration as low as 10ng./ml. stimulated incorporation of amino acids into protein by 30% and of labelled precursor

into RNA by 27%. No effect of the hormone on labelling of protein *in vitro* was observed when the amino acid concentration was at the normal plasma value. Preliminary observations suggest that RNA labelling is stimulated by the hormone under the latter conditions but not when amino acids are absent entirely.

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Jackson, C. D. & Sells, B. H. (1967). *Biochim. biophys. Acta*, **142**, 419.

Jefferson, L. S. & Korner, A. (1967). *Biochem. J.* **104**, 826.

Munro, A. J., Jackson, R. J. & Korner, A. (1964). *Biochem. J.* **92**, 289.

Schimassek, H. & Gerok, W. (1965). *Biochem. Z.* **343**, 407.

Studies on Drug-Metabolizing Activity in Rats Pretreated with Phenobarbitone and Compounds Related to Emetine

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Protein synthesis at the liver microsomal level *in vitro* can be stimulated maximally in incubations of preparations from female albino rats pretreated with sodium phenobarbitone at 315 $\mu\text{moles/kg.}$ daily for 3 days (Kato, Jondorf, Loeb, Ben & Gelboin, 1966), or with (–)-emetine dihydrochloride (Jondorf & Szapary, 1968) or ($\pm$)-2,3-dehydroemetine dihydrochloride (Jondorf, Drassner, Johnson & Miller, 1969) at 18 $\mu\text{moles/kg.}$ for 1 day.

Although the microsome-specific stimulation of protein synthesis in phenobarbitone-pretreated animals is also associated with stimulation of microsomal drug-metabolizing activity (Conney, 1967), this is not the case in experiments with microsomal material from rats treated with emetine or 2,3-dehydroemetine. These compounds inhibit drug metabolism *in vitro* (Jondorf, Johnson & Drassner, 1969) measured by liver microsomal *N*-demethylation of aminopyrine (Jondorf, Simon & Avnimelech, 1966) and azo-reduction of neoprontosil (Hernandez, Gillette & Mazel, 1967).

It therefore seemed worth while to test whether the co-administration of phenobarbitone and emetine or 2,3-dehydroemetine would lead to diminished drug metabolizing effects. Two injection schedules were devised, to differentiate between effects of emetine and 2,3-dehydroemetine on already existing, phenobarbitone-induced stimulation and effects on incipient induction. In the