placenta could be due to the low content of cytochrome *P*-450 present or to a higher affinity and a high concentration of endogenous steroid substrates, which saturates the enzyme system and prevents access of drugs to the enzyme site.

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The Effect of Diet on Rat Plasma Corticosteroids and Liver Aromatic Hydroxylase Activity

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There is evidence that protein-deficient diets in children may result in adaptive changes of hepatic enzymes concerned with intermediary metabolism and that these are mediated by corticosteroid hormones (Alleyne & Young, 1967; Waterlow, 1968). Further, it has been shown that the microsomal drug-metabolizing enzymes of the liver of growing rats are dependent on the dietary intake of protein and total calories (Dickerson, Basu & Parke, 1971). These drug-metabolizing enzymes of the liver are also concerned with metabolic deactivation of the endogenous steroid hormones, and their activity may be increased by stress or administration of corticosteroids (Driever, Bousquet & Miva, 1966). It was therefore decided to ascertain whether the effect of diet on the activities of the hepatic drug-metabolizing enzymes observed previously were similarly mediated through corticosteroid hormones.

Male weanling rats (24 days old) were divided into three groups: group A, controls, were fed *ad lib.* on stock diet (Spiller's), 21% protein; group B, 'protein-deficient', were fed *ad lib.* on stock diet diluted with starch to contain 7% protein; group C, 'protein- and calorie-deficient', were fed on same amount of protein as group B but without starch. Liver biphenyl 4-hydroxylase activity was determined as a measure of hepatic drug metabolism (Creaven, Parke & Williams, 1965). Liver glycogen (Kemp & Kits van Heijningen, 1954), glucose

6-phosphatase (Cori & Cori, 1952) and plasma corticosteroids (Mattingly, 1962) were also determined.

The protein-deficient animals (group B) after 2 and 4 weeks on the diet showed increases in hepatic biphenyl 4-hydroxylase activity (70–100%) and plasma corticosterone (150–200%). The animals on the diet deficient in both calories and protein (group C) showed only moderate increases in both liver biphenyl 4-hydroxylase activity (25–50%) and plasma corticosterone. Studies of the kinetics of the hepatic biphenyl 4-hydroxylase activity showed that in both groups B and C the K_m value was the same as controls (0.23 nM) but the V_{max} was increased.

Since the hepatic cytochrome *P*-450 in similar protein-deficient rats was either diminished or showed no change (Dickerson *et al.* 1971) and the K_m for the biphenyl 4-hydroxylase was unchanged but the V_{max} increased, the increased hepatic biphenyl 4-hydroxylase activity is unlikely to be due to any change of the active sites or in the total amount or the terminal oxygenase. It is more likely to be due to an increase of some other component of the associated electron-transport chain, e.g. cytochrome *P*-450 reductase, or to some conformational change of the membrane of the endoplasmic reticulum or change of the membrane environment. The simultaneous increase in plasma corticosteroids and the known stimulating effect of these hormones might suggest that the increases observed in the hepatic drug-metabolizing enzyme were mediated through the endogenous steroid hormones.

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Studies on the Hydroxylation of Lysine Occurring in the Non-helical Region at the N-Terminal End of the Collagen Molecule

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In bone collagen from chick tibia (Miller, Lane & Piez, 1969; Lane & Miller, 1969), in contrast with all skin collagens so far examined (Bornstein & Piez, 1966; Kang, Bornstein & Piez, 1967; Kang, Piez &