which became manifest only 1-3 days after parental treatment with safrole, was found to be completely inhibited by actinomycin D and is therefore attributed largely to synthesis of enzyme protein *de novo*. The increase in activity of biphenyl 2-hydroxylase, which started to become manifest 3h after treatment with safrole, was only partially inhibited by treatment with actinomycin D and is therefore attributed partly to increased protein synthesis and partly to changes in conformation and environment of the membrane-bound enzyme.

Treatment of rats with safrole decreased the amount of glycogen in the liver, from which it may be inferred that adenylate cyclase and 3:5-cyclic-AMP may be involved, but treatment with nor-adrenaline did not however result in any increase in the activities of biphenyl 2- or 4-hydroxylases. Isosafrole (4-propenyl-1,2-methylenedioxybenzene) administered to rats produced changes similar to those resulting from safrole administration, but treatment with piperonyl alcohol, piperonal, piperonylic acid, piperonylacrylic acid and allylbenzene did not result in either liver hypertrophy or enzyme induction.

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The Effect of Development on the Activity of Drug-Metabolizing Enzymes in the Liver of the Rat

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The chemical development of rat liver has been studied extensively, but little information appears to be available on the changes in the activity of drug-metabolizing enzymes. The liver microsomes of newborn mice and rabbits are deficient in certain drug-metabolizing enzymes (Jondorf, Maickel & Brodie, 1958). The activity of these enzymes rises during the first 14 days after birth and by 28 days the activity is almost equal to that found in adult animals (Fouts & Adamson, 1959). Similarly, newborn rats show little capacity to metabolize a number of drugs, and the capacity expressed per unit of microsomal protein progressively increases until 30 days of age; the metabolic capacity then decreases gradually with age (Kato, Vassanelli, Frontino & Chiesara, 1964).

In the present study the activity of microsomal drug-metabolizing enzymes has been determined at various ages between 6 and 100 days after birth.

The enzymes studied were biphenyl 2-hydroxylase and biphenyl 4-hydroxylase (Creaven, Parke & Williams, 1965), *p*-nitrobenzoate reductase (Bratton & Marshall, 1939) and cytochrome *P*-450 (Omura & Sato, 1962). Microsomal protein (Lowry, Rosebrough, Farr & Randall, 1951) and liver DNA (Zamenhof & Chargaff, 1951) were also determined.

Liver weight relative to body weight gradually rose from 12 days of age to reach a peak value of 4.7% at 38 days, after which it slowly declined to 3.7% at 100 days. The absolute amount of total protein in the liver rose to a maximum value at 70 days and remained constant thereafter. Microsomal protein followed a similar pattern. The absolute amount of DNA reached a maximum at 85 days.

The activity of biphenyl 2-hydroxylase, expressed per g liver weight, per 100g body weight and per unit of DNA attained a maximum value at 21 days and subsequently fell to an almost negligible value by 52 days. The maximum activity of the biphenyl 4-hydroxylase was reached at 24 days and subsequently declined to 40% of this value at 85 days. The peak activity of *p*-nitrobenzoate reductase was reached at 38 days, which was followed by a slow decline to 60% of this value at 100 days. The peak activity of cytochrome *P*-450 was reached at 31 days, which was followed by a sharp fall to almost the value for mature animals at 38 days.

Possible explanations of the above changes in enzyme activity will be discussed.

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Cytochrome *c* and the Oxidation of *C*₁ Compounds in *Pseudomonas* AM1

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Pseudomonas AM1 is a pink bacterium capable of growth on *C*₁ compounds. Energy for growth is obtained by oxidation of methanol or methylamine