involved in endogenous steroid metabolism. For many substrates, the activity of these enzymes is greater in male rats than in females. (Conney, 1967, Pharmacological Review, 19, 317). It has been suggested that their activity is related to the level of circulating steroid hormones and, further, that enzyme induction by substances such as phenobarbitone is mediated through interaction with an endogenous, steroid hormone-dependent, control mechanism. However, since induction is hardly impaired in male rats which are depleted in steroid hormones as a result of castration and adrenalectomy, it appears that this cannot be the case (Marshall & McLean, 1969, Biochemical Journal, 115, 279).

Dietary steroids also influence microsomal enzyme activity. If rats are fed a purified diet containing 20% protein, the level of their microsomal enzymes is reduced in comparison with animals fed a commercial Chow diet; phenobarbitone still brings about induction, but to a reduced extent. A 'normal' response (i.e., characteristic of animals fed a Chow diet) is re-attained if small amounts of oxidized sterols are added to the purified diet. Such substances may well be involved in the control of microsomal enzyme activity and induction.

6. DRUG-METABOLIZING CAPACITY AND DRUG DEPENDENCE
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(Introduced by A. Goldberg)

Stevenson & Turnbull (Biochemical Pharmacology, 1968, 17, 2297) have previously reported that liver drug-metabolizing enzyme activity is elevated in barbitone-dependent animals but that, at some time after withdrawal of the barbiturate, in vitro metabolism is lower than normal. In agreement with this, withdrawn animals were found to have a hypersensitivity to hexobarbitone. Further results, from in vivo studies on the tissue levels of hexobarbitone and its metabolites in control and withdrawn animals awakening from a hypnotic dose of hexobarbitone confirmed the earlier indication that drug-metabolizing capacity is reduced after barbiturate withdrawal.

This phenomenon, if it occurred in man, would be of considerable clinical relevance. A test procedure, utilizing the antipyrine half-life procedure, as described by Vessel & Page (Journal of Clinical Investigation, 1969, 44, 2202), has been established to assess drug-metabolizing capacity in barbiturate-dependent patients. The results obtained with the first few patients in this survey would indicate that, as expected, the antipyrine half-life is shorter than normal during the period of barbiturate administration. After gradual withdrawal of the barbiturate, the antipyrine half-life increased and at several weeks after withdrawal, was within the range of normal values. There was no indication of a diminished drug-metabolizing capacity in the withdrawn patients.

7. INDUCTION OF DRUG METABOLIZING ENZYMES IN MAN
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We have studied the ability of several drugs to stimulate the microsomal oxidation of warfarin. Administration of Dichloral phenazone (Welldorm) 1300 mg nightly for 4 weeks, caused a fall in mean steady state plasma warfarin level from 3±18±0.17 to 1±30±0.06 µg/ml with a corresponding rise in thrombotest (Owren) in five patients. 1000 mg of Chloral nightly caused a small but significant fall in plasma warfarin level but no change in thrombotest while Phenazone (Antipyrine) 600 mg/day caused a fall in plasma warfarin level from 2±93±0.13 to 1±41±0.09 µg/ml with a rise in thrombotest. Antipyrine half-lives in these five patients varied between 7 and 26 h. The percentage fall in steady state plasma warfarin level from the control pretreatment value was correlated with the antipyrine half-life (r = -0.83). Those patients with a larger antipyrine half-life showed a greater percentage fall of plasma warfarin level after induction. In two patients [14C] warfarin (0.5 mg/kg) was administered before and after the administration of Phenazone 600 mg/day for 28 days. There was no change in the faecal excretion in either patient but the percentage of the dose excreted in the urine increased in both patients and the half-life of [14C] warfarin was reduced in both patients.

8. LEUCINE NAPHTHYLAMIDASE ACTIVITY IN RAT PANCREAS
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A previous histochemical study showed that rat pancreatic leucine naphthylamidase (LNA) activity rises following various forms of pancreatic damage (Pirola et al., 1970, American Journal of Digestive Diseases, 15, 21). To gain further information regarding the mechanism of this increased activity the properties of rat pancreatic LNA in pooled homogenates of control pancreases have been studied and have been compared with those with ethionine-induced necrosis.

The optimum pH was 7-0. Ion activation studies on dialysed homogenates at this pH showed complete dependence on the presence of a divalent