For venograms, the animals were placed in a supine position on a transparent tray with the X-ray tube 45 cm above them. The X-ray film was placed on another shelf 45 cm below. Thus each radiograph was twice life size. Focal spot of the tube was 0·3 mm. Venograms of control tumours showed avascular areas, pooling of Micropaque and an irregular vascular network with many tortuous vessels. In treated tumours the venous pattern was discrete and well organized.

The colloidal suspension used was carbon black in the form of dilute Pelikan biological ink CII/143Ia. Animals were left for 1 h after intravenous injections of the dilute ink (0·12 mg/20 g mouse and 0·75 ml/150 g rat) after which the tumours were quickly removed and placed in 10% formol saline for 14 days. Frozen sections cut at 25–35 μm were lightly stained with Mayer's Carmalum. Virtually no carbon labelling was found in the treated Lewis lung tumours, whereas controls showed vessels outlined with carbon in zones of growing tumour. The Walker tumours of control rats showed areas of carbon labelling both peripherally and centrally near necrotic and haemorrhagic zones. Treatment with ICRF 159 reduced but did not abolish the labelling of vessels.

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Influence of phenobarbitone on liver regeneration and microsomal N-demethylating activity in partially hepatectomized rats

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Normal rat liver is capable of remarkable adaptations to meet the functional demands upon it. For example, the low resting mitotic rate increases dramatically when part of the liver is exised, the magnitude of the response being inversely related to the amount of liver remaining. In addition, oxidative enzymic activity in the intact liver can be greatly increased by drugs. For example, phenobarbitone increases the synthesis of the microsomal enzymes responsible for its metabolism. Each of these processes involves the hepatocyte in considerable reorganization and in synthesizing new protein for such specialized structures as the mitotic spindle or the endoplasmic reticulum. These two processes represent quite different types of adaptation, since regeneration involves a less differentiated activity (mitosis) than the synthesis of drug metabolizing enzymes. It is therefore of interest to know if both processes can occur simultaneously or whether one has priority.

This study investigated these possibilities in partially hepatectomized and sham operated male Wistar rats (250–350 g), pretreated 12 h before surgery with phenobarbitone (80 mg/kg i.p.) and 1 h before death with metaphase inhibitor colchicine

(1 mg/kg i.p.). At different time intervals after the operation, rats were weighed and killed by exsanguination. Having weighed the liver, microsomes were prepared (Ernster, Sickevitz & Palade, 1962) and assayed (Orrenius, Ericsson & Ernster, 1965) for cocaine N-demethylating activity. In addition, liver sections were stained using a modified Heidenhain's iron haematoxylin stain (Gurr, 1965) and examined microscopically.

Phenobarbitone increased liver weight and microsomal N-demethylating activity in normal and sham operated rats. Partial hepatectomy increased the mitotic index and was followed by rapid liver regeneration. When the responses to partial hepatectomy and phenobarbitone were examined in the same rat, the normal responses to both treatments were modified. In this case, the magnitude of the enzyme induction produced by phenobarbitone was reduced but its duration was prolonged. In addition, the normal rate of liver weight gain after partial hepatectomy was considerably increased by phenobarbitone. This effect was due to cell growth rather than increased cell division, the rate of which was reduced in these rats. The former result confirms that of Chiesara, Conti & Meldolesi (1970). The results suggest that there is some mutual interference between liver regeneration and microsomal enzyme induction.

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Absorption, distribution and excretion of methsuximide in male rats

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Methsuximide (N, 2-dimethyl-2-phenyl succinimide) is used clinically in the management of petit mal epilepsy (Chen, Weston & Bratton, 1963). However, there is no information available regarding the fate of this drug in animals and man.

Methsuximide was labelled with ^{14}C in the N-methyl position and the distribution of this compound (0·1 μCi/mg in a dose of 100 mg/kg) was determined in male rats (90–100 g, CFHB strain, Carworth Europe, Huntingdon). Soon after oral administration significant levels of radioactivity appeared in the brain, liver, kidney, heart, adrenal, spleen, testis, lung, salivary gland, eye, fat and skeletal muscle. This rapid distribution into the tissues is probably related to the nonpolar, lipophilic character of the drug. The levels of radioactivity in body fat tended to be higher than in most other tissues. Using a gas–liquid chromatographic assay procedure, the maximum concentration of ^{14}C-methsuximide in the plasma (27 μg/ml) was reached 1 h after administration. The level of radioactivity in most tissues declined with time.

Radioactivity was excreted into the urine (25·6% in 24 h), bile (13·7% in 6 h), faeces (8·6% in 24 h) and expired air (28·6% as $^{14}CO_2$ in 24 h). The total excretion of radioactivity after 72 h was 69·5% of the administered dose. The expiration of $^{14}CO_2$ suggests that ^{14}C-methsuximide is demethylated to 2-methyl-2-phenyl succinimide.