

(Schöpf, Gänshirt, Hutzler, Klug & Reinshagen, 1969). Although the (–)-isomers of these racemic compounds have the essential structure thought to be associated with biological potency, they are inactive in the rat liver protein synthesizing system *in vivo* and *in vitro*. This leads us to support the idea first put forward by Lietman (1971) that structural subtleties among emetine derivatives not originally envisaged by Grollman (1966) may emerge as different protein synthesizing systems are methodically studied.

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Vascular changes in tumours after treatment with ICRF 159

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Mice implanted subcutaneously with the Lewis lung (3LL) carcinoma regularly develop pulmonary metastases, which can be prevented by treatment with [(±)-1,2-bis (3,5-dioxopiperazin-1-yl) propane] (ICRF 159) (Hellman & Burrage, 1969). The poorly defined sinusoids which act as vascular channels in the periphery of control primary tumours are replaced by well formed discrete blood vessels in tumours treated with ICRF 159 (Burrage, Hellmann & Salsbury, 1970). These changes in the structure of the blood vessels are probably responsible for preventing the escape of malignant cells from the primary tumour into the circulation.

The distribution and character of these 3LL blood vessels has now been further investigated by means of X-ray angiography and by a colloidal carbon technique which specifically outlines damaged and inflamed blood vessels (Majno, Palade & Schoeff, 1961). A comparison has also been made of the effects of ICRF 159 treatment of rats inoculated with the Walker carcinosarcoma.

A polythene catheter was inserted into the inferior vena cava through the exposed right heart of animals anaesthetized with Avertin. Micropaque was introduced slowly by retrograde injection and care was taken that introduction of contrast medium was performed in exactly the same way each time.

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 μ m 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 excised, 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