MONRO, R. E., CELMA, M. L. & VAZQUEZ, D. (1969). Action of sparsomycin on ribosome-catalysed peptidyl transfer. *Nature, Lond.*, **222**, 356–358.

OWEN, S. P., DIETZ, A. & CAMIENER, G. W. (1963). Sparsomycin, a new antitumour antibiotic. I. Discovery and biological properties. In *Antimicrobial Agents and Chemotherapy*—1962 ed., Sylvester, J. C., pp. 772–779. Ann Arbor, Mich.: Amer. Soc. for Microbiology.

WILEY, P. F. & MACKELLAR, F. A. (1970). The structure of sparsomycin. *J. Amer. Chem. Soc.*, **92**, 417–418.

The influence of glucagon on regional blood flow in the rhesus monkey

R. A. BRANCH*†, A. S. NIES, and D. G. SHAND (introduced by J. F. MITCHELL)

Division of Clinical Pharmacology, Vanderbilt University, Nashville, Tennessee

It has recently been demonstrated that the total liver blood flow is rate limiting for the clearance of drugs which are extensively metabolized by the liver and have a high hepatic extraction ratio. Glucagon, which has been reported to increase splanchnic flow in experimental animals and man might therefore be expected to increase drug clearance. This has been investigated using (+)-propranolol as a marker drug in the rhesus monkey preparation which is known to have similar cardiovascular responses to man (Forsythe, Nies, Wyler, Neutze & Melmon, 1968).

Regional blood flow was measured by the injection of radioactive labelled microspheres into the left ventricle. At the same time systemic haemodynamic parameters, including cardiac output by a dye dilution method were measured. At the conclusion of the experiment, the animal was killed and the radioactivity present in various organs was counted in a Nuclear Chicago gamma 4 scintillation counter. The influence of 30 min infusions of glucagon 1 (μg/kg)/min and 10 (μg/kg)/min) on systemic haemodynamics and regional blood flow was measured, and the high dose infusion was then continued for a further 60 min. Control measurements were made before the first infusion and two hours after the last infusion.

Glucagon induced a dose dependent increase in cardiac output and pulse rate, with an increase in the proportion of the cardiac output going to the splanchnic vascular bed, and a decrease to the skeletal vascular bed. Total liver blood flow increased by $37\% \pm 10\%$ at 1 (μg/kg)/min and $165\% \pm 23\%$ at 10 (μg/kg)/min after 30 min of glucagon infusion and falling to $61\% \pm 11\%$ at 90 min. Smaller increases occurred in the coronary and renal blood flows.

The effect of the same doses of glucagon on the clearance of a steady state infusion of (+)-propranolol was measured in the same monkeys under similar conditions. At the high dose, the clearance increased by $14{\cdot}4\% \pm 3{\cdot}7\%$ while hepatic extraction fell from $32{\cdot}6\% \pm 6{\cdot}2\%$ to $17{\cdot}1\% \pm 1{\cdot}8\%$. The data is quantitatively consistent with a perfusion limited kinetic model which predicts that, for drugs with a high hepatic extraction ratio, increases in liver blood flow of the type induced by glucagon, will significantly increase drug clearance. Drugs with a low hepatic extraction ratio will be relatively unaffected by alterations in liver blood flow.

REFERENCE

FORSYTHE, R. P., NIES, A. S., WYLER, F., NEUTZE, J. & MELMON, K. L, (1968). Normal distribution of cardiac output in the rhesus monkey. *J. Appl Physiol.*, **25**, 736–741.

Biliary excretion of methylmercury in male rats

L. MAGOS and M. OHSAWA*

MRC Toxicology Unit, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

Reabsorption of methylmercury excreted into the gut with the bile is one of the factors responsible for the long biological half life of this compound (Norseth & Clarkson, 1971).

† Present address: Department of Pharmacology, The Medical School, University of Bristol.