Correspondence

Propranolol disposition in cirrhosis

SIR.—The study by Arthur *et al* (*Gut* 1985; **26**: 14–19) calls attention to the potential dangers of the use of propranolol in patients with cirrhosis, because of the alteration of the drug's pharmacokinetics. After oral administration, the pharmacokinetics of propranolol conform to the venous equilibrium model of hepatic clearance;¹ its elimination is thus sensitive to changes in dose size and hepatic metabolising enzyme capacity (intrinsic clearance) only. Propranolol intrinsic clearance depends on an intact, functioning microsomal enzyme system and may be inhibited by co-administration of cimetidine,^{2,3} for example. Thus the first pass removal of oral propranolol would be expected to be substantially decreased by cirrhosis. In addition, the first pass elimination would be expected to be further decreased by intra- and extrahepatic shunting of portal venous blood.

The poor correlation between protein binding of propranolol and serum albumin concentrations in this study is not surprising, as propranolol binds principally to alpha-1-acid glycoprotein (AAG).^{4,5} The binding of a basic drug such as propranolol to AAG has important implications. Alpha-1-acid glycoprotein is an acute phase protein which is raised in a number of diseases.⁶ If propranolol is given to an acutely ill cirrhotic with alcoholic hepatitis, or superadded infection, the free or unbound – that is, pharmacologically active – concentration of propranolol may be temporarily decreased because of raised serum AAG concentrations; with improvement in the patient's acute decompensation, the free concentration of propranolol may increase substantially as AAG levels fall, with resultant excessive beta blockade. This reinforces the authors' conclusion that therapy with propranolol should be started in hospital, with regular monitoring of the heart rate.

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Books

The biology of epithelial cell populations. Vols 1 & 2. N Wright, M Alison. (Pp 536 [Vol 1] and pp701 [Vol 2]; illustrated; £39.40 [Vol 1]; £44.50 [Vol 2].) Oxford: Oxford University Press, 1984.

Many books pass through the office of this journal every year, but among these are few that even a generous person would describe as works of scholarship. Most literate gastroenterologists can manage one good chapter; it will appear time and again in different packages, each time slightly altered to conform to a different package (*Current Trends, Clinics, Frontiers*, etc, etc) and perhaps a different audience. Remembering the outstanding Research Medallists lecture given by Nicholas Wright to the British Society of Gastroenterology, I guessed that this book might be out of the ordinary, and I have not been disappointed.

The authors have attempted a comprehensive description of the biology of epithelial 'population' kinetics. This introduces a new problem; to quote the authors, 'in this field, there has been a major information explosion, but . . . much effort has, in our opinion, been negated or obscured by the choice of inappropriate methodology. The book has much to say on this point . . .' and indeed it does. This is not merely an attempt to cover the literature; it is an attempt to explain the general theory of renewing cell populations and the methodology involved in their study by a critical appraisal of relevant data. In volume 1, the reader is guided through simple and