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LETTERS TO THE EDITOR

NODULAR LIVER FROM PONCEAU MX—HYPERPLASTIC OR NEOPLASTIC?

Sir,—We refer to the article by Grasso *et al.* (*Fd Cosmet. Toxicol.* 1969, 7, 425) entitled "Nodular hyperplasia in the rat liver following prolonged feeding of Ponceau MX". Between the submission of this paper for publication and its appearance in print, sections of the liver lesions were submitted to us for opinion. Later we met Dr. P. Grasso to discuss the nature of the liver changes. Dr. Grasso took the view (expressed in the article) that the liver nodules were indicative of hyperplasia, while we classified them as hepatomas of uncertain malignancy. Methods were discussed by which their malignant potentiality, if such existed, might be demonstrated.

Our purpose is to make clear to your readers that, in our opinion, both the naked-eye and microscopical appearances of the liver nodules were fully consistent with the view that they were neoplasms, indistinguishable from lesions induced by other chemical agents whose carcinogenicity is widely accepted. From the limited histopathological material submitted to us, we could see no evidence of malignancy, but by the same token we could not exclude the possibility that some of the lesions were malignant.

We believe, therefore, that the limited interpretation of the lesions given in the paper is misleading and that Ponceau MX should be regarded as hepatocarcinogenic in the rat unless and until further studies of the behaviour of the lesions indicate to the contrary.

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Sir,—I appreciate the views of your contributors, Dr. G. M. Bonser and Dr. F. J. C. Roe (see above) regarding the interpretation of the nodules found in the livers of rats fed Ponceau MX for a long period.

The classification of liver nodules is not a new issue in experimental pathology. Chloroform and carbon tetrachloride have been regarded in the past as carcinogenic to rat and mouse liver because of the production of such lesions (Eschenbrenner & Miller, *J. natn. Cancer Inst.* 1946, 6, 325; *idem, ibid* 1945, 5, 251), but recent investigations of the problem have revealed that the biological behaviour of these nodules differs from that which would be expected from a neoplastic growth (Confer & Stenger, *Cancer Res.* 1966, 26, 834).

Turning to the Ponceau MX lesions (Grasso *et al. Fd Cosmet. Toxicol.* 1969, 7, 425), I should like to stress that careful examination revealed the nodules to be totally different from the malignant growths reported from administration of hepatocarcinogens such as aflatoxin (Newberne, in *Mycotoxins in Foodstuffs*. Edited by G. N. Wogan. The MIT Press, Massachusetts, 1965), dimethylnitrosamine (Rubin *et al. Proc. Soc. exp. Biol. Med.* 1964, 115, 381) or butter yellow (Edwards & White, *J. natn. Cancer Inst.* 1941, 2, 157). On the other hand the nodules produced by Ponceau MX did not appear to differ in their macroscopic or microscopic features from those that have been reported to follow administration of carbon tetrachloride. Such hepatic nodules have been reported after the administration of compounds whose carcinogenicity is widely accepted, but the connexion between these lesions and the production of malignant growths is doubtful (Epstein *et al. Cancer Res.* 1967, 27, 1702). On this basis it was felt that there was insufficient evidence to conclude that neoplastic growths developed in the livers of rats treated with Ponceau MX.

In reply to the point concerning the limited histopathological material submitted, I should point out that the lesions seen by Dr. Bonser and Dr. Roe included the most advanced seen in our experiment. I think it is relevant that in none of these was there any evidence of malignancy.

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