

# BRITISH MEDICAL JOURNAL

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Correspondents are urged to write briefly so that readers may be offered as wide a selection of letters as possible. So many are being received that the omission of some is inevitable. Letters should be signed personally by all their authors.

## Liver tumours and the pill

SIR,—In their article on carcinoma in a hepatic tumour associated with oral contraceptives Dr M Davis and his colleagues (29 November, p 496) say that "these focal proliferations of hepatocytes associated with blood-filled cysts . . . have been described only in patients taking oral contraceptives." This is not so. Similar dilated, thin-walled blood vessels in focal nodular hyperplasia are mentioned in three patients in one report,<sup>1</sup> in which one of the patients was a 6-year-old girl. Two other cases of hepatic carcinoma occurring in patients on oral contraceptives have been reported,<sup>2,3</sup> but it is worth recalling also an account of hepatic carcinoma in pregnant women.<sup>4</sup>

If indeed the pill is to be incriminated in any of these cases, then it is a remarkably efficient carcinogen with a much shorter latent period than the 15 years generally accepted for human carcinogens. I think that the authors perform a disservice in talking of "pill" tumours while the association is still unproved. However, I strongly support them in their view that a central panel should be set up so that all such cases can be assessed histologically. If every case in the United Kingdom, in both sexes and at all ages, were examined, then it would quickly become apparent if there was a true association with oral contraceptives.

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<sup>1</sup> Whelan, T J, Baugh, J, and Chandor, S, *Annals of Surgery*, 1973, 177, 150.

<sup>2</sup> Hermann, R E, and David, T E, *Surgery*, 1973, 74, 715.

<sup>3</sup> Christopherson, W M, Mays, E T, and Barrows, G H, *Obstetrics and Gynecology*, 1975, 46, 221.

<sup>4</sup> Partilo, D T, Clark, J V, and Williams, R, *American Journal of Obstetrics and Gynecology*, 1975, 121, 41.

SIR,—Your leading article (29 November, p 484) raises the point of a registry for liver tumours occurring in young women on oral contraceptives. Since our publication on their possible pathogenesis,<sup>1</sup> we have maintained a registry of both benign and malignant primary liver tumours occurring in young women. To date we have had the opportunity to examine over 50 examples. With the exception of one or two women in the last trimester of pregnancy or early postpartum period, all had ingested oral contraceptives. We have seen two additional cases of interest in women who had been taking Premarin. The vast majority of the tumours have been examples of focal nodular hyperplasia; others have been liver cell adenomas. In addition to these there were several examples of primary liver cell carcinoma, some of which had ruptured, all occurring in non-cirrhotic livers. One of the latter is illustrated in a more recent publication.<sup>2</sup> The heretofore infrequent encounter of benign liver tumours supports the postulated causal relationship with oral contraceptives. The greater frequency with which liver cell carcinoma is known to occur, even in the young, makes the role of oral contraceptives much less clear.

In addition to clinical résumés and pertinent medication usage, we are interested in receiving histological material on any or all cases that come to the attention of your readers. We are especially interested, when possible, in receiving either paraffin blocks or wet tissue in order to study the vascular

lesions, histochemical reactions, and, when possible, the ultrastructure of these tumours. We would be very grateful to receive material on both previously published and unpublished cases.

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<sup>1</sup> Mays, E T, Christopherson, W M, and Barrows, G H, *American Journal of Clinical Pathology*, 1974, 61, 735.

<sup>2</sup> Christopherson, W M, Mays, E T, and Barrows, G H, *Obstetrics and Gynecology*, 1975, 46, 221.

## Effect of replacement therapy with natural oestrogens on blood clotting

SIR,—I was interested to read the article by Dr Jean Coope and others (18 October, p 139) regarding the use of natural oestrogens in postmenopausal women and their effect on blood clotting since their results differ considerably from those of a recently published investigation.<sup>1</sup> In the latter study 45 postmenopausal women were selected at random and were treated with conjugated oestrogen (Premarin) for one year. Blood samples were tested before treatment, at the end of three and nine months' therapy, and one month after treatment had been suspended (after a year's therapy). Estimations included fibrinogen, platelet count and aggregation, single-stage prothrombin time, kaolin partial thromboplastin time, factors V and X, and euglobulin lysis time. The only statistically significant alteration noted was a depressant effect on the platelet count (mean  $\pm$  SEM  $257.45 \pm 13.33 \times 10^6/l$  before,  $204.95 \pm 9.54 \times 10^6/l$  after nine months' treatment). The raised level of factor X and the accelerated prothrombin time reported by Dr Coope and her colleagues was not recorded.

It is difficult to compare results since the absolute values (and the standard error) on