sive cervical-smear specialists should realize that carcinoma may be present in other parts of the urogenital system and, of course, elsewhere. The only symptom that this patient had had was two rather excessive periods.—I am, etc.,

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Oral Contraceptives and Breast Cancer

SIR,—Mr. J. J. Shipman has aired an important question by his letter on this subject (5 September, p. 629). He reports two patients who presented with evidence of breast cancer and who were, at the time, taking oral contraceptives. In view of the very widespread use of oral contraceptives among young women, and the fact that breast cancer is the commonest malignancy in females, it would indeed be surprising if none of these young women developed breast cancer. The similar question of whether oestrogens (which are used very widely also) are liable to induce breast cancer is one which has been discussed for the last 25 years,¹ but is still undecided. An answer to both questions could only be provided by a careful sampling of the population.

Mr. Shipman, however, suggests that an existing hormone-sensitive breast cancer may be influenced adversely by these progestogen-oestrogen tablets. It is, of course, equally possible that the tumour may be influenced favourably by these hormones, and in fact the experimental evidence appears to favour the latter possibility. Professor Huggins, of Chicago, demonstrated in 1959 that dimethylbenzanthracene-induced mammary adenocarcinoma in rats was hormone-sensitive. It responds to oophorectomy, adrenalectomy, hypophysectomy, and androgen administration, as does the hormone-sensitive human breast cancer. Huggins² further demonstrated that combined high-dose progesterone and low-dose oestrogen administration was capable of *extinguishing* the tumour in over 50% of the rats. This observation may possibly have an application in the treatment of human breast cancer, although a suitable progestogen and dosage level still remain to be worked out. Nevertheless, the experimental evidence to date is in favour of depression, and not stimulation, of tumour growth by the hormone combination.

Finally, Mr. Shipman suggests that as oral contraceptives may cause an increased blood flow to the breast, their use should be discontinued in patients with suspected or proved breast cancer. While I agree with such a decision until further experience is accumulated, I do not agree with the reasoning. Westberg³ reported 224 cases of breast cancer in pregnant and lactating women. He concluded that pregnancy does not appear to exert any great effect upon the prognosis of breast cancer, except for the tendency to delay in diagnosis and treatment. Surely one would expect the grossly increased blood flow to the breasts in pregnancy to be even more dangerous than the premenstrual congestion seen with the use of the "pill"?—I am, etc.,

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BASIL A. STOLL.

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Haemodialysis Disequilibrium

SIR,—Dr. S. M. Rosen and others (12 September, p. 672) reported further investigations into the haemodialysis-disequilibrium syndrome. We note that they were able to confirm our findings that this appears to be due to delay in clearance of urea from the cerebrospinal fluid, with consequent creation of an osmotic gradient between plasma and cerebrospinal fluid.¹ The authors conclude that this upset can best be prevented by frequent haemodialysis at low levels of biochemical disturbance. This is not the only answer to the problem, however, and we should like to point out that we have published further work on the pathogenesis of this syndrome and have demonstrated that clinical and electroencephalographic evidence of disequilibrium can be prevented by a four-fold increase in the glucose concentration in the rinsing fluid.^{2,3} This modification in dialysis technique is an extremely simple one and permits efficient dialysis, which is of particular value when dealing with patients with a high level of catabolism.—We are, etc.,

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Percutaneous Transhepatic Cholangiography

SIR,—I am glad to see that Drs. S. G. Elkington and D. C. Bernstein have recorded a small series of cases investigated by percutaneous transhepatic cholangiography (19 September, p. 733), but the technique they describe carries a greater risk of complication than that which I have described in two papers^{1,2} and at the Association of Surgeons of Great Britain and Ireland meeting in 1957. The risk of haemorrhage and biliary peritonitis is much reduced by inserting a needle 25 cm. in length and 1 mm. bore just below the ninth costal cartilage at a point at the junction of the outer and middle third of a line drawn from the midline to the lateral margin of the abdominal wall. The needle is inserted at an angle of 45 degrees to the horizontal and 15 degrees internal to the vertical plane. Aspirations should be made with a 5 ml. syringe at frequent intervals during the introduction and withdrawal of the needle. The point selected is external to the gall-bladder but reaches the right hepatic duct system at a depth of some 15 centimetres from the surface of the liver. The long track prevents oozing of bile or blood from the puncture wound on the surface of the liver and avoids risk of direct penetration of the common hepatic duct or vessels. In over 60 cases in which this technique has been used the mortality rate has been nil and no case of biliary peritonitis or intra-abdominal haemorrhage has occurred. If the gall-bladder is entered (as shown by the injection of contrast media) then the abdomen should be opened, and this has had to be done on three occasions.

There was a discussion on this subject at the Royal Society of Medicine in 1962, and

it is to be hoped that this valuable method of investigation of cases of jaundice will be more widely used. The technique is, however, most important if accidents are to be avoided.—I am, etc.,

London, W.1.

H. A. KIDD.

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Leukaemia and Phenylbutazone

SIR,—I read with interest the communications relating to the association of leukaemia and phenylbutazone appearing in recent issues of your journal,¹⁻³ and I followed the relevant communications which appeared in earlier issues of your journal.^{4,5} I have also come across one instance of acute myeloid leukaemia in a 46-year-old male who had taken phenylbutazone intermittently for a significant period before the onset of leukaemia. It appears that, in general, myelotoxic agents have a leukaemogenic propensity.⁶ In this context, and against the background of informations listed above, the suggested association between phenylbutazone and leukaemia must be more critically evaluated. I write this letter to draw the attention of all concerned to one particular aspect of this problem. Examination of relevant clinical data would show that most of the subjects so far reported and discussed with reference to the leukaemogenic propensity of phenylbutazone were elderly or old persons who had been suffering from some sort of painful condition affecting the bones. Is it possible that inflammatory, degenerative, and collagenous affections of osseous tissue tend to make the enclosed haemopoietic tissue more vulnerable to the damaging effect of a myelodepressive agent like phenylbutazone? The higher incidence of leukaemia that has been reported in patients with spondylitis deformans receiving deep x-ray therapy may in this perspective be considered as illustrative of the greater vulnerability of such patients to the damaging effects of x-rays.—I am, etc.,

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Prolonged Arteriospasm after Ergotamine

SIR,—Dr. E. Byrne-Quinn's report of a case of overdose with ergotamine tartrate (29 August, p. 552) gives further warning of the great caution which must be exercised in the use of this drug, and the importance of such warnings cannot be over-emphasized.

It is not true, however, that there are "no reported cases of arteriospastic disease from the oral administration of ergotamine tartrate or its related alkaloids in migraine" (our italics). Fuchs and Blumenthal¹ recorded two cases of ergotism in 1950. Both had severe symptoms but in neither was amputa-