Correspondence

Letters to the Editor should not exceed 500 words.

Work After a "Coronary"

SIR,—Many readers who have to advise patients after a myocardial infarct will be grateful for the sound general principles outlined in your excellent leading article on "Work after a 'Coronary'" (19 September, p. 703).

We share their gratitude but are sure that the sentence, "Avoidance of foods with a high content of fat or cholesterol is also sound advice . . ." should not be allowed to stand without critical comment. In fact we know of no conclusive evidence to support this advice to patients who have already developed the overt clinical features of ischaemic heart disease. Few formal long-term studies of the effects of such a diet have been made and none has shown that the prognosis is improved. Moreover, so far as drugs are concerned, you yourselves point out that "none of the cholesterol-lowering agents has been shown to have a favourable clinical effect." This is also true for diet; recently Ball and his colleagues¹ have reported a four-year study of the effect of a low-fat diet. They showed clearly that, despite reduction of cholesterol levels, the diet had no demonstrable effect in lowering the relapse rate after myocardial infarction.

We presume that the line of thought in your leader is that the correlations which have been shown to exist between a high-fat diet and ischaemic heart disease in population studies can be interpreted as indicating that the high fat diet is a cause of the ischaemic heart disease. This assumption has not been substantiated and there are certainly many other possible and important aetiological factors in coronary atherosclerosis. It should also be pointed out that, even if the assumption were true, it still does not follow that the institution of a diet low in fat or cholesterol would be of any value to patients whose atherosclerosis has advanced to the stage of angina or myocardial infarction.

Clinicians concerned with the management of patients have to be wary of the dual approach revealed in population studies. It is all too easy to assume false correlations; pre-supposition that low-fat diets are of value in the management of ischaemic heart disease is one unfortunate result.

We recognize that many proved advances in medicine have been based initially on unproved hypotheses. It is, however, wise to realize just how unproved dietetic restrictions are in the management of ischaemic heart disease. It is perhaps appropriate to remember Dr. Armand Vincent's patient² who said: "We are prevented from dying; we are not helped to live." Your leading article recognizes this criticism of medicine. It emphasizes the need to encourage patients to resume a normal way of life after myocardial infarction. It is a pity to spoil it by advocating "hope-it-may-do-good" dietetic measures when these are unsubstantiated and may make

our patients miserable and prevent them living in the fullest sense.—We are, etc.,

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SIR,—It is interesting that, at this time, you can still include in your leading article of 19 September (p. 703) the recommendation that persons with ischaemic heart disease should reduce their intake of fat, and exclude any suggestion that they should take less sugar.

There has never been any direct evidence for the hypothesis that fat consumption has anything to do with causing the disease; indeed, recent evidence points increasingly against it. For example, studies in East Africa have shown that cardiac ischaemia is rare both in the Samburu¹ and in the Masai,² who consume very large amounts of fat, almost all of it from meat and milk. Results have recently been published of a prospective study in American men, in which no difference in fat intake was found between those who developed ischaemic heart disease and those who did not.³

On the other hand, there is now quite impressive evidence that a high intake of sugar (sucrose) may be an important factor in producing coronary disease. Firstly, epidemiological studies in which populations are compared show a rather better relationship of the incidence of the disease with sugar consumption than with fat consumption.^{4,5}

Secondly, the increasing incidence of the disease that is found in many countries has followed an increasing consumption of sugar rather than of fat. This was demonstrated in Israel amongst Yemeni immigrants,⁶ and more recently in the United States.⁷ The latter study has shown that in the last 70 years there has been only a 12% rise in fat consumption, and a simultaneous increase in the ratio of polyunsaturated to saturated fats. During the same period, in which the number of people dying of coronary thrombosis has increased very considerably, the consumption of sugar has more than doubled.

Thirdly, although studies with individual subjects have shown no difference in fat intake between those with and those without cardiac ischaemia, they have shown considerable differences in sugar intake.⁸ On average, people that have recently had a first known myocardial infarction have been taking twice as much sugar as control subjects, mostly in their tea and coffee. This is the first time that any difference in diet has

been found between individuals with and without the disease.

It will no doubt be several years before we know whether the reduction of dietary sugar will improve the prognosis of those who have suffered their first coronary attack. In the meantime, however, we might reasonably suggest that people at risk should be advised to cut their intake of sugar. One knows of no evidence whatever that this could be harmful, whereas there is increasing suspicion that continued high intake of sugar could be harmful.⁹—I am, etc.,

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Misleading Exfoliative Cytology

SIR,—I was glad to see Dr. J. Elizabeth Macgregor being a little more realistic about negative smears in the presence of clinical carcinoma of the cervix (19 September, p. 754). There can be little doubt, as she says, that biopsy is required for any cervix which has the appearance of malignancy, and I wish she had gone a little further and said that smears in such cases are chiefly of academic interest and not necessary to the acceleration of the patient's diagnosis and treatment.

I would like her to reconsider her last sentence where she says that cervical and vaginal smears should be examined before curettage, when body carcinoma is suspected. I have turned her sentence round to make the position a little clearer, for I believe it imperative that where body carcinoma is suspected diagnostic curettage should be arranged—once more, as for clinical cancer of the cervix, *whatever* the smear report.—I am, etc.,

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A. F. ANDERSON.

SIR,—I was very pleased to see the letter from Dr. J. Elizabeth Macgregor of the Department of Midwifery and Gynaecology at Aberdeen (19 September, p. 754). I recently had a "neurotic" patient who was seen by a first-class consultant gynaecologist and reassured on three occasions, especially after the last time when a cervical smear was taken, that there was no cancer present. However, I regret to say that some two months later she had a total hysterectomy for a carcinoma of the body of the uterus.

While I would obviously agree with cervical smears I do feel that some of the obses-

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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D. V. MORGAN-JONES.

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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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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- 1 Kennedy, A. C., Linton, A. L., and Eaton, J. C., *Lancet*, 1962, **1**, 410.
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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.

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- 2 ———, *Transactions International Congress of Surgery, Copenhagen, 1955*.

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-