fewer suffer from the former. The degree of coronary atheroma discovered in persons killed accidentally has been studied in many parts of the world, and the condition has been found to be equally widely distributed in the United States and United Kingdom. Yet, in contrast, the mortality from ischaemic heart disease is markedly different in comparable populations, the U.S.A.F.:R.A.F. ratio approximating to 10:1.[2] The opinion expressed by Kannel[3] that it is the presence of an effective collateral circulation which determines the clinical picture offers a reasonable explanation of the anomaly.

Carboxyhaemoglobin is easily determined and is therefore a convenient marker of the products of combustion. It is possible that, because of this, carbon monoxide is being artificially promoted as a cause of disease. Workers in Los Angeles[4] have attempted to relate atmospheric CO levels to an increased fatality rate from myocardial infarction; in fact, any relationship must be attributed to atmospheric pollution as a whole. In the same way, postmortem studies designed to show atherogenic properties of cigarette smoke[5] fail to take into account the life style of heavy smokers.

The case for an association between smoking and ischaemic heart disease seems proved beyond doubt. But rather than to attribute an atherogenic property to cigarettes in general and carbon monoxide in particular (Dr. Wald and his colleagues do not claim this to be necessarily so), it might be more valid, and in keeping with the "collateral" theory, to suggest that the carboxyhaemoglobin results reported by them were more significantly reflecting the levels of nicotine, which is known to have a marked pharmacological effect on the cardiovascular system.—I am, etc.,

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1 Morris, J. N., and Dale, R. A., *Proceedings of the Royal Society of Medicine*, 1955, **48**, 667.
2 Mason, J. K., *British Medical Journal*, 1963, **2**, 1234.
3 Kannel, W. B., *New England Journal of Medicine*, 1970, **282**, 1153.
4 Cohen, S. I., Deane, M., and Goldsmith, J. R., *Archives of Environmental Health*, 1969, **19**, 510.
5 Auerbach, O., Hammond, E. C., and Garfinkel, L., *New England Journal of Medicine*, 1965, **273**, 775.

Löffler's Syndrome

SIR,—I am grateful to Dr. Alex Sakula for his letter (7 April, p. 54) referring to the case reported by myself and Dr. C. C. Bailey (24 February, p. 460) of a 4-year-old boy with lymphosarcoma presenting as Löffler's syndrome. As Dr. Sakula reaffirms, Löffler's syndrome refers to a transient condition of eosinophilia with pulmonary radiological opacities; though originally described in association with *Ascaris lumbricoides* infestation, the same syndrome has been observed in a multitude of conditions since then and is thought to be an allergic manifestation.

We described this case as Löffler's syndrome because the lung changes were typical of this condition radiologically; they cleared within a few weeks, as the eosinophilia subsided, in response to steroid therapy. The radiological appearances have not recurred, even when the patient eventually developed his florid lymphosarcoma. We feel that this is adequate evidence that the lung changes were part of an "eosinophilia syndrome" which is known as Löffler's syndrome, and not that they were, as Dr. Sakula suggests, due to lymphosarcomatous infiltration. To the best of our knowledge Löffler's syndrome, which has been described in association with many and varied conditions, has never before been observed with lymphosarcoma.—I am, etc.,

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Advertising of Antibiotics

SIR,—I should like the opportunity to comment on the letter from Drs. J. D. Williams and A. M. Geddes (14 April, p. 116), particularly with reference to the paragraph about cephradine. First they refer to the "advertising booklet produced by one of the companies" and at the end of the letter they "urge [the pharmaceutical companies'] medical departments to curb the enthusiasm of commercial colleagues in the content of their promotional literature." The publication referred to is a technical booklet available usually on request. This is prepared by the medical department for the purpose of providing technical information and, as such, can hardly be described as promotional.

Unfortunately at the time of the launching of cephradine the only in vitro figure we had available in the United Kingdom for the minimum inhibitory concentration against penicillinase-producing staphylococci was the one quoted. This was against one strain available in the Squibb Institute, New Jersey. The claim that cephradine is effective was based on clinical and bacteriological evidence in trials, using the disc sensitivty test. In common with your correspondents we noted the discrepancy between mean inhibitory and peak serum concentrations and initiated further in vitro tests which have been carried out in a number of hospital laboratories in this country. These have shown that the minimum inhibitory, and indeed bactericidal, concentration for the penicillinase-producing organisms to be almost invariably below the mean peak serum concentration following a 500-mg dose of cephradine.

Drs. Williams and Geddes also criticize the fact that cephradine's sensitivities are compared only with those of ampicillin, tetracycline, and chloramphenicol. I agree that it might have been more helpful to include other antibiotics, but it is logical surely to compare it with three widely used broad-spectrum antibiotics. While agreeing that chloramphenicol should be prescribed only for limited indications, in a world-wide company it was necessary to carry out this research bearing in mind the most common alternatives. Regrettable though it may be, chloramphenicol is still widely prescribed throughout the world and, to judge by last years' prescription figures, there has either been a higher incidence of typhoid than notified or else it is still being prescribed for less serious conditions in the United Kingdom. Is showng that a cephalosporin compares favourably with a more toxic alternative to be deprecated?—I am, etc.,

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"Hypersensitivity Hepatitis" Associated with Administration of Cyclizine

SIR,—Cyclizine (1-benzhydryl-4-methyl piperazine) hydrochloride, an antihistamine used mainly in the prevention and treatment of nausea and vomiting, has been available since 1954. During this time there has been no reported case of jaundice attributable to the drug. Nevertheless, we have recently seen a patient in whom a diagnosis of "hypersensitivity hepatitis" induced by cyclizine seems very likely.

The patient, an 8-year-old white girl, became ill with malaise, anorexia, nausea, vomiting, and jaundice in the middle of July 1972. The serum bilirubin concentration was 5·5 mg/100 ml, serum alanine aminotransferase (SGPT) 460 units, and alkaline phosphatase 45 K.A. units. Hepatitis B antigen was not found in the serum. A diagnosis of infective hepatitis was made and she was treated with bed rest alone. There were no known cases of infective hepatitis in the patient's family, among her friends, or at her school at that time. Starting eight days before the onset of the illness, she had taken 25 mg of cyclizine hydrochloride by mouth daily for five days to prevent motion sickness. She had not previously received this drug and had taken no others recently. There was a strong family history of penicillin sensitivity and the patient had on a number of occasions developed diarrhoea while receiving that antibiotic; whether or not the latter was due to penicillin sensitivity is not known. By the end of August she was well enough to return to school. On 24 September she was again given 25 mg of cyclizine by mouth to prevent motion sickness. The following day she felt ill and her urine was noted to be dark, and a day later jaundice was obvious. Her urine contained 1+ urobilin and 2+ bilirubin, the serum bilirubin level was 5·2 mg/100 ml, SGPT 400 units, and alkaline phosphatase 37 K.A. units. The serum was again negative for hepatitis B antigen. She was treated with bed rest alone. Eight weeks passed before she was considered well enough to get up and 16 weeks before the serum bilirubin level returned to normal. Liver biopsy was not performed. The patient's serum was examined for antibodies against cyclizine hydrochloride: both a cyclizine-induced Coombs test and a Coombs consumption test for "anti-liver" antibodies were positive. These tests were negative when repeated on the serum of other individuals receiving cyclizine and on jaundiced patients who had not taken the drug. An attempt to induce the patient's lymphocytes to transform with cyclizine failed.

While accepting that acute viral hepatitis cannot entirely be excluded as the cause of our patient's illness, we believe that the recurrence of hepatitis following an inadvertent challenge with cyclizine and the serological findings are more in keeping with a hypersensitivity reaction to the drug. The mechanism or mechanisms involved in "hypersensitivity (or allergic) hepatitis" have not been elucidated, but in some cases the drug is presumed to act as a hapten. This may explain our failure to induce the patient's lymphocytes to transform when exposed to cyclizine.—We are, etc.,

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Arterial Haemorrhage in a Drug Addict

SIR,—The recent paper by Mr. R. Pollard (31 March, p. 784) discussing some surgical complications of intravascular injections in

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drug addicts prompts us to report a case we have recently managed.

A 25-year-old methadone addict who had been injecting his femoral veins for the past year was admitted after inadvertently puncturing his left femoral artery (day 1). At the time of injection he noted severe shooting pain from groin to foot. During the course of the next three days he developed fever and a tender swelling in the left groin. On examination there was swelling and oedema of the left groin and thigh, with prominent psoas spasm. The distal pulses were normal and there was no oedema of the leg or foot. For four days the case was managed with ampicillin and flucloxacillin, but this failed to suppress the remittent pyrexia. Drainage of the infected haematoma was performed on day 7 and *Staphylococcus aureus* was cultured from wound swabs. The following afternoon there was a brisk haemorrhage from the wound and five units of blood had to be transfused. On day 10, while the wound pack was being removed in theatre, a profuse haemorrhage occurred. Exploration of the groin and thigh showed that a 3-cm length of femoral artery distal to the profunda femoris had sloughed; the venous system was intact. The superficial femoral artery had to be ligated 3 cm below the inguinal ligament and the patient was transfused with nine units of blood.

Subsequently his fever resolved by lysis. Circulation of the left leg and foot remained satisfactory, though the distal pulses did not reappear.

This case is reported in detail to draw attention to a further potentially fatal complication of "main-lining."

We wish to thank Professors M. D. Milne and H. Ellis for permission to report this case.
—We are, etc.,

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Longevity of Women G.P.s

SIR,—It is quite true that I did refer, in a slightly light-hearted way, to the relative longevity of male and female doctors, but my remarks were indeed based on actuarial evidence.

I would say, therefore, in reply to Dr. J. G. Denholm (14 April, p. 119) that no valid conclusions can be drawn from a study of obituaries in the *B.M.J.*; statistically, the figures are meaningless. The position has been succinctly summarized by Mr. Alistair Low, consultant actuarial adviser to the B.M.A. He has written (personal communication) with reference to the N.H.S. superannuation scheme: The argument has been put forward that female members' contributions to the scheme should be lower than those of male members. In fact, the extra cost in respect of male members arising from the automatic provision of widow's pensions is, broadly speaking, offset by the greater life expectancy of female members, whose own pensions are therefore substantially more expensive to provide than those of male members. No real case can be made, therefore, on financial grounds, for a reduction in female members' contribution rate below that of males."

It was in the light of this knowledge that my remarks in the General Medical Services Committee debate were made.—I am, etc.,

ROBERT A. KEABLE-ELLIOT

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Secondary Posctpartum Haemorrhage after Caesarean Section

SIR,—Secondary postpartum haemorrhage from dehiscent lower-segment caesarean section incisions is certainly not a common condition, but it is perhaps not so rare as the absence of references to previous reports in the article by Messrs. John Macvicar and R. M. Graham (7 April, p. 29) would imply. There have in fact been at least two earlier publications[1 2] describing a total of six cases of this type. Two[1] of these six cases were successfully treated by packing the uterus alone. Of the other cases,[2] two were treated by supravaginal hysterectomy after severe haemorrhage had recurred after removal of uterine packs (in one instance 75 days after the original caesarean section), one by internal iliac artery ligation after packing the uterus had failed to control bleeding, and one by supravaginal hysterectomy as the initial procedure. Although packing the uterus usually controls haemorrhage in the first instance, there is evidently a high risk of recurrent bleeding after removal of the pack, and immediate hysterectomy as practised by your contributors is probably the safest procedure in these cases.

It is remarkable that a Shirodkar suture was in situ in one of my patients as well as in one of those described by Messrs. Macvicar and Graham. The odds against this being coincidental must be very high and in my view the association is more likely to be with uterine distension due to defective drainage than with infection. In this regard your contributors' assertion that drainage in their case was not impaired appears to be contradicted by their earlier statement that "the Shirodkar suture was removed . . . and obviously much blood and clot had been dammed back in the uterine cavity." Indeed, I would suggest that defective drainage could well have led to the infection they observed.—I am, etc.,

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1 Hanford, D. P., and Weed, J. C., *Obstetrics and Gynecology*, 1953, 1, 317.
2 Heys, R. F., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1963, 70, 647.

Fatal Paralytic Ileus Due to Strongyloidiasis

SIR,—We read with interest the report by Dr. J. B. Cookson and others on a fatal case of paralytic ileus due to strongyloidiasis (30 December, p. 771) and would like to report a similar case seen recently.

The patient, who was a 2-year-old boy, came from French West Africa six days before admission. For four weeks he had had diarrhoea, ankle swelling, and anorexia. His parents and two brothers were well. He was dehydrated and emaciated, with pitting oedema of both feet and a swollen, non-tender abdomen. There was no clinical evidence of ascites and no significant lymphadenopathy. Microscopical examination of the stools showed an exceptionally heavy infestation with strongyloides larvae and trichuris ova. No pathogenic organisms were isolated on culture.

After admission he started vomiting, his temperature fell to 35°C, and his blood sugar at that time was 33 mg/100 ml. His infestation was treated with intragastric thiabendazole and he was fed parenterally. His bowel sounds six days after admission were hyperactive, but the following day were absent. At the same time large amounts of fluid were aspirated from his nasogastric tube and his abdomen became grossly distended. A diagnosis of paralytic ileus was made. Soon after, his respiratory rate increased and there were signs of pneumonia at his right base. He was then started on cephalothin. A blood culture at that time grew klebsiella. His condition continued to deteriorate and the following day he had a cardiac arrest and attempts at resuscitation were unsuccessful.

Permission to make a postmortem examination was refused. The sudden onset of the patient's paralytic ileus, gross abdominal distension, and klebsiella septicaemia suggest the severe invasive form of strongyloidiasis.—We are, etc.,

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Short-term Service Abroad

SIR,—I write in response to the intermittent correspondence appearing in your columns concerning medical practice in the Republic of South Africa.

I fear that British doctors contemplating short-term service in developing countries may be put off South Africa because of the apartheid question. In many ways the emerging homelands of the Transkei and Kwazulu (Zululand) are eminently suited for such service by English-speaking doctors. This is especially so for those with families, for in this land, unlike many in the "third world," law and order prevail. The medical needs of the Bantu population are great and present a fascinating challenge to those tackling the problems involved. In many places facilities have been established, but shortage of doctors threatens their closure. This is an acute problem in the Transkei at the moment.

Most hospitals in the homelands are mission-sponsored and government-financed. A medical officer is paid a salary of about £4.000 per annum. Housing is provided. The climate is sunny but not too hot for comfort. Beautiful countryside, interesting flora and fauna, and proximity to a totally different culture all add to the quality of life. The people are very friendly, with a good sense of humour. Language is not a serious problem as all trained nurses speak English well and can act as interpreters.

I appeal to those thinking of undertaking service aboard to consider South Africa. Surely sanctions of money or manpower can only retard the Africans in their development.—I am, etc.,

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