two separate analyses^{2,3} we concluded that from 1956 to 1973 age-specific mortality from ischaemic heart disease increased in both sexes, but the increase was greater in women than in men, except in age groups above 55 years, and in young men this increase was less marked during the 1960s than it was in earlier years. The reasons for the different conclusions arise from the inclusion by Clayton *et al* of deaths due to hypertensive disease in their analyses of ischaemic heart disease trends. It is not, however, clear why they did this. With the introduction of effective treatment for hypertension there are reasonable grounds for believing that the reduction in mortality from hypertensive disease in recent years is real and not simply due to transfer of cases from hypertensive categories into ischaemic heart disease categories.⁴ If such transfer did occur one would expect it to have affected men and women to the same extent, but this did not happen.

If deaths attributable to hypertensive disease are excluded from analyses of ischaemic heart disease trends the conclusions of Clayton *et al* are consistent with ours and together they indicate the need to explain the recent increase in ischaemic heart disease among women.

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- ¹ Clayton, D G, Taylor, D, and Shaper, A G, *Health Trends*, 1977, 9, 1.
² Mann, J I, DM thesis, University of Oxford, 1976.
³ Wald, N J, *Lancet*, 1976, 1, 136.
⁴ Lambert, P M, *World Health Statistics Report*, 1975, 28, 401.

Poisoning with antidepressants

SIR,—We have read with interest recent correspondence (23 July, p 260; 20 August, p 523) concerning overdosage with the new tetracyclic antidepressant mianserin, particularly with regard to the apparent lack of cardiotoxic effects of this compound. Although changes in the electrocardiogram (ECG) can be seen even in healthy subjects taking tricyclic antidepressants,¹ the most serious effects occur after overdosage² or in patients with preexisting heart disease,³ though the latter has been disputed.⁴

We have recently completed a study (to be reported elsewhere) in which we demonstrated a lack of interaction between mianserin and phenprocoumon. Of the 60 hospital in-patients (aged 25-79 years) studied, 54 were suffering from cardiac disease: 38 had recent myocardial infarctions, five had cardiomyopathy, and 11 had cardiac failure. Most of the patients were severely ill and had gravely disturbed ECGs before the start of the study. The patients, all of whom had previously been stabilised on phenprocoumon, were randomly allocated to treatment with mianserin 60 mg daily, mianserin 30 mg daily, or placebo. Thirty-five patients (21 male, 14 female) received mianserin. Medication was given under double-blind conditions over three weeks in three doses each day, the total daily dose increasing to the full level by day six. Heart rate, blood pressure, and ECG were

monitored at variable intervals during the study. There were no sudden deaths during the study and no unexpected deteriorations indicative of adverse drug effects. Statistical comparison of the treatment groups is impeded because of the high level of baseline abnormalities, but comparison of the data from the three treatment groups did not reveal any apparent differences.

We consider that these data, together with recently published evidence from overdose cases⁵ and in-vitro animal studies,⁶ support the conclusion that mianserin lacks cardiotoxic effects even when given, in therapeutic doses, to subjects with pre-existing cardiac disease.

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- ¹ Vohra, J, Burrows, G D, and Sloman, G, *Australian and New Zealand Journal of Medicine*, 1975, 5, 7.
² Petit, J M, *et al*, *Clinical Pharmacology and Therapeutics*, 1977, 21, 47.
³ Moir, D C, *et al*, *Lancet*, 1972, 2, 561.
⁴ Boston Collaborative Drug Surveillance Program, *Lancet*, 1972, 1, 529.
⁵ Crome, P, and Newman, B, *British Medical Journal*, 1977, 2, 260.
⁶ Harper, B, and Hughes, I E, *British Journal of Pharmacology*, 1977, 59, 651.

"Zip injury" to the penis

SIR,—The complaint of zip fly injury to the penis is sometimes made by sexually promiscuous men attending hospital accident and emergency departments in order to avoid attending sexually transmitted disease clinics or to obtain prompt treatment. If the house officer is fully conversant with the appearance of a primary syphilitic sore or a spontaneously healing painless genital chancre the case is referred to a specialist. However, when he trusts the statement of such patients the correct diagnosis may be missed. If the patient is given an injection of penicillin or another treponemocidal drug the incubating syphilis will be masked and the disease will pass to the secondary stage.

Two such cases have recently been detected in the accident and emergency department at this hospital. The first patient was the French Algerian boy-friend of a local girl. He did not speak English and the girl was acting as interpreter. Under the circumstances he had little choice but to deny any other sexual contact. On persuasion he agreed to give blood, urine, and a urethral smear. His serum tests for syphilis proved positive, as did those of his girl-friend. The girl was treated and information was sent to her boy-friend in Paris.

The second case was that of a patient who had enlargement of the inguinal lymph nodes and a healed primary lesion on the penis. There was initial denial of sexual exposure. On examination a very scanty mucoid discharge was found. He was strongly seropositive and *Neisseria gonorrhoeae* was cultured from his urethral smear.

In such cases it is wise to follow the dictum that "any lesion on the external genitalia should be investigated on the lines of syphilitic chancre until proved otherwise."

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Levamisole-induced arthritis

SIR,—It is suggested by Dr A W Segal and his colleagues (27 August, p 555) that arthritis due to levamisole administration is a complication specifically related to Crohn's disease. The following case history suggests that this is not so.

A 67-year-old woman was noted to have severe mouth ulcers in 1966. In 1970 she developed a spontaneous deep venous thrombosis of the leg and has had recurrent bilateral superficial thrombophlebitis of the legs since then. In 1971 she had an episode of episcleritis and has required systemic steroids to prevent relapse. A clinical diagnosis of Behçet's syndrome was made in 1974 when oral ulceration again became a problem. No genital ulcers have been noted and apart from radiological evidence of right-sided sacroiliitis she has had no joint involvement.

Systemic steroids have not influenced her mouth ulcers and she has been unable to take chlorambucil, cyclophosphamide, and azathioprine because of bone marrow suppression. There was no improvement with local carbenoxolone, cromoglycate, and idoxuridine and systemic penicillamine, colchicine, and indomethacin. Her mouth ulcers were so bad that she tried local application of paw-paw fruit!

Levamisole has been shown to be effective in the treatment of recurrent aphthous stomatitis^{1,2} and this was given in a dose of 150 mg per day for three consecutive days every two weeks. After the first course she complained of diffuse arthralgia affecting mainly the knees and elbows, which settled spontaneously within 48 h of stopping the drug. Ten days later, following the second course, the patient was rendered immobile by severe and generalised arthralgia which again resolved spontaneously during the following week. Investigation showed no other cause for her symptoms.

Arthralgia may be a manifestation of Behçet's syndrome and it seems to have been drug-induced in this case. It has been suggested that levamisole may have a deleterious effect on the joints in rheumatoid arthritis.³ This reinforces the hope that elucidation of the mechanism of action of levamisole may help to determine the pathogenesis of arthritis.

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- ¹ De Meyer, J, *et al*, *British Medical Journal*, 1977, 1, 671.
² Lehner, T, *et al*, *Lancet*, 1976, 2, 926.
³ Dinai, Y, and Pras, M, *Lancet*, 1975, 2, 556.

Interaction between azapropazone and warfarin

SIR,—Dr P R Powell-Jackson, reporting interaction between azapropazone and warfarin (7 May, p 1193), suggests that the mechanism may be similar to that of the warfarin-phenylbutazone interaction, since the drugs are chemically similar. The mechanism of the latter drug interaction may be twofold: (1) due to displacement of warfarin from plasma albumin binding sites or (2) due to an effect on the renal clearance of the R and S isomers of warfarin. Azapropazone is approximately 96% bound to plasma proteins¹ and hence may interfere with the binding of warfarin.

We have recently carried out some preliminary in-vitro studies on warfarin binding to albumin in both the presence and absence of azapropazone. An ultrafiltration technique was used for these binding studies; this is a modification of the method described by Blatt *et al*.² The binding medium used was 0.2% lyophilised human serum albumin in aqueous buffer (37°C, pH 7.4). This system

has already been used successfully in assessing the warfarin-phenylbutazone interaction.

Preliminary results do in fact show that the binding of warfarin to human serum albumin is decreased in the presence of azapropazone. These preliminary observations suggest that the protein binding interaction mechanism will occur in the case of azapropazone. This may or may not be the main interaction mechanism. Elucidation of the overall mechanism will be complete only when the effect of azapropazone on warfarin clearance is known. However, as we have shown warfarin displacement by azapropazone, we strongly support Dr Powell-Jackson's view that a different analgesic anti-inflammatory agent should be used in patients taking anti-coagulants.

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¹ Jones, C J, *Current Medical Research*, 1976, 4, 3.

² Blatt, W F, Robinson, S M, and Bixler, H J, *Analytical Biochemistry*, 1968, 26, 151.

Femoral vein thrombosis after total hip replacement

SIR,—In a study by myself and Hoffman in 1975¹ of the incidence of postoperative ilio-femoral thrombosis in 138 patients using the Doppler ultrasound probe no case of ilio-femoral thrombosis was detected during the first six postoperative days. The patients had undergone a variety of general surgical procedures but none had had surgery to the lower limbs. Calf vein thrombosis, detected by the ¹²⁵I-fibrinogen uptake test, developed in 28.

This finding supports the view of Mr J D Stamatakis and his colleagues (23 July, p 223) that femoral vein thrombosis occurring after total hip replacement is due to a local factor which is not present in other surgical situations.

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¹ Bolton, J P, and Hoffman, V J, *British Medical Journal*, 1975, 1, 247.

Place of chlormethiazole in treatment of alcoholics

SIR,—The warning inherent in Dr Joan M Horder's observations on fatal chlormethiazole poisoning in chronic alcoholics is timely (3 September, p 614). I have been surprised to hear from some alcoholic patients that they regard chlormethiazole as a treatment for alcoholism and it is even prescribed for them without explanation that its only use in this condition is to suppress the symptoms of withdrawal. In my opinion chlormethiazole has no place in the outpatient or general practice management of alcoholism. Its anticonvulsant and sedative effects make it the most effective treatment for planned alcohol withdrawal (including acute delirium tremens) in a hospital setting (exceptionally it may be used in the patient's own home if a reliable spouse is able to act as a nurse). Given in gradually decreasing dosage it should not be necessary to give it for more than two weeks. There is no indication for a discharge prescription, as it can itself be addictive.

Dr Horder's reports suggest that chlor-

methiazole had been used as an antidepressant. I have no knowledge of it having anti-depressant activity and it is not recommended for treatment of depression by the manufacturers. Depressive symptoms are common both as a secondary effect of alcoholism and as an underlying condition. However, the pharmacological treatment of depression is impossible unless the patient has been thoroughly "dried out" (for which chlormethiazole is invaluable). That operation alone may well achieve an increased sense of well-being. It is pointless to prescribe any psychotropic drug to the alcoholic who is continuing to drink in or out of hospital, as it becomes an invitation to fatal interaction or suicidal over-dosage.

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Acute gastric dilatation in anorexia nervosa

SIR,—Dr G K Brook (20 August, p 499) fails to discuss the possibility of malrotation or mesenteric artery compression, or both, as the cause of symptoms in his patient. These conditions are closely related and can be effectively treated by Ladd's operation—that is, freeing the entire duodenum and placing it in the right paravertebral gutter.¹ Chronic duodenal ileus from either cause is characterised by prolonged illness and emaciation and may start in adolescence.¹⁻³ It is often misdiagnosed because dilatation develops slowly^{2,3} and because x-ray examinations are discontinued before the filling of the third part of the duodenum. This again may be due to the fact that the patient vomits the barium ingested.

Duodenal obstruction by the superior mesenteric artery in emaciated combat casualties⁴ has been ascribed to loss of the periaarterial fat pad.^{2,4} This suggests a vicious circle which may have been operating in the case reported by Dr Brook. It is unknown, however, how often chronic duodenal ileus is misdiagnosed as anorexia nervosa.^{2,3} Anorexia, nausea, vomiting, and wasting are conjoint characteristics, and young persons experiencing these disheartening symptoms over prolonged periods will, as might be expected, also develop psychiatric symptoms.^{2,3}

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¹ Wang, C A, and Welch, C E, *Surgery*, 1963, 54, 839.

² Burrington, J D, and Wayne, E R, *Journal of Pediatric Surgery*, 1974, 9, 733.

³ Akin, J T, *Surgery*, 1976, 79, 515.

⁴ Wayne, E R, *Annals of Surgery*, 1971, 174, 339.

Names of drugs

SIR,—The biggest single factor in helping me to keep abreast of medical advances since I qualified some 40 years ago has been the more or less regular perusal of the *British Medical Journal*; and with the advent of the double-blind trial there came a powerful instrument to sharpen the necessary scepticism in one's attitude to new drugs and the claims made for them by their vendors.

In the last year or two, however, at a time when, for me, the evanescence of memory obtrudes with ever-increasing insistence, you, sir, have condoned the trend of most of your contributors in referring to drugs by their

official names only. This may be acceptable to academics; I am well aware of the arguments in its favour; but I suggest that general practitioners, surely the majority of your readers, would prefer the inclusion in brackets of the trade name. Most of us can identify promazine and chlorpromazine, but how many of us would write prochlorperazine for that old friend Stemetil, and, a fortiori, metoclopramide for Maxolon?

It is obviously correct that students should learn their drugs by the official names, but there is a sanctimonious smell about the rigid exclusion of trade names in postgraduate writing. I for one am glad to mark the successful outcome of a drug firm's research by not entirely forgetting their name for their product.

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* * * The use of non-proprietary names for drugs in the *BMJ* is determined not by our contributors but by long-standing editorial policy. The main objection to Dr Hay's suggestion that trade names should also be included is their multiplicity. For example, prochlorperazine is marketed under at least two different trade names at home and three abroad, while for metoclopramide the figures are two and six respectively. As patents run out these will no doubt multiply. The *BMJ* circulates widely abroad, and among their other virtues approved non-proprietary names have the advantage, with very few exceptions, of international acceptance. Identification with the corresponding trade names is made easy for British general practitioners by the inclusion of cross-checking lists in the *British National Formulary*.—Ed, *BMJ*.

Seniority payments and service in HM Forces

SIR,—I would like to draw your attention to one aspect of the terms that our negotiators have agreed with the Department of Health and Social Security regarding seniority payments. It relates to the amount of time that the applicant has been a principal providing unrestricted general medical services under the NHS or medical service in HM Forces since 5 July 1948 recognised for this purpose by the Secretary of State. On application I am informed that two years' National Service as a medical officer in the RAMC does not count towards seniority, only the service of senior medical officers.

The general duty medical officer in the RAMC looked after the health not only of regiments but also of their wives and children as well, in some cases abroad and in trouble zones. I cannot recall senior medical officers doing sick parades, family medical officer duties, or house calls. In fact, the family doctoring was done by the national servicemen and short service commission men.

The postponement of the awards for two years affects only a small proportion of doctors, but it affects them quite severely financially now, later in further awards, and ultimately in superannuation. I think that this injustice should be corrected not only for the sake of the doctors concerned but because, in my view, the non-recognition of this service is an insult to the regiments and families of Her Majesty's Forces that we were privileged to look after.