I feel strongly that those in medical charge of boys' schools should be cognizant of this total situation, and should, in the rare intractable case, even suggest to the boy and his parents that future plans for a service career should be revised. Obversely, it should go without saying that, whether or not the removal of many a distinguished general's vest would reveal many an acne scar, one is entitled now to expect uniformity of action on this problem from all the relevant Service medical boards.—I am, etc.,

IAN W. CALDWELL.

Royal South Hants Hospital, Southampton.

Subcutaneous Ossification of Legs

SIR,—I have followed with interest the discussion on subcutaneous ossification of legs (2 July, p. 27; 30 July, p. 300; 1 October, p. 830). It seems to me that, although there are a number of explanations for the phenomenon, the place of trauma appears to be one of importance, and I would accordingly make the following speculations. Thus, by the action of the intermittently distensible veins on the fatty subcutaneous tissues, areas of fat necrosis are produced, and in a similar manner interfascial haematomata may develop. As a result of both these processes small localized areas of chronic inflammation are initiated, the end effects of which are patchy regions of calcification and ultimately ossification.

It has also been postulated[1] that large perforating veins lying close to bone may cause shearing off of osteoblasts. By their action local small extravasations of blood may ossify in much the same way that myositis ossificacans is produced. Finally, an "ossifying diathesis" has been described.[2] Trauma may lead to the release of "inductors" from damaged cells.[3] These activate the conversion of fibroblasts to osteoblasts and thus stimulate the development of osseous tissue from the granulation tissue following chronic inflammation.

Whatever the explanation for the heterotopic bone, when it comes to treatment of leg ulcers in the floor of which are spicules or plaques of bone, it may be as well to remember that healing may be delayed until the ectopic bone is removed.—I am, etc.,

SYDNEY COHEN.

Capetown, South Africa.

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Cervical Cytology: Its Value and Limitations

SIR,—Professor T. N. A. Jeffcoate's interesting paper (5 November, p. 1091) contains some statements on which there will be difference of opinion.

When I reviewed 500 cases of invasive carcinoma of the cervix[1] I found that all had been diagnosed at the first visit to the outpatient department by the three methods of inspection, biopsy, and cytology. There were quite a number of cases in which any one or two of these methods failed: these included both inspection and biopsy by skilled gynaecologists. Provided the smears are well taken there will not be many false negatives from invasive cases, though there will be some.

Professor Jeffcoate is wrong in comparing the exceptional diagnostic methods available for cancer of the cervix with what we can offer for other organs, with the possible exception of the skin and rectum. More cases of cancer of the breast may be found in the clinics because it is a commoner disease and occurs more frequently in women of the upper social classes, who are the ones making use of the clinics. When working in a "cancer prevention clinic" in the U.S.A. it was not uncommon to hear a discussion on a case, passed as normal a month or so earlier, which had developed a cancer of some organ such as the breast. An annual inspection of the breasts is more likely to be mischievous than valuable. For this the right "preventive" measure is instruction of the woman in the technique of self-examination.

It is to be hoped that attention will be paid to Professor Jeffcoate's statement that cone biopsy is not a simple procedure. Any gynaecologist who does not achieve complete removal of the lesion in at least 75% of cases should visit a master of the operation. Some well-known gynaecologists do not agree that cone biopsy leaves permanent injury to the cervix and prejudices future childbearing.

I agree that the cytologist and the histologist should be the same person. There is no doubt that different pathologists report the same lesion in different ways on occasion; this is a reflection on the pathologists and not the lesion. I am now convinced that cancer of the cervix has a long and complicated story. The stages of typical in-situ carcinoma and invasive carcinoma are easy enough, but this is not true of their preceding stages. Erosions and squamous metaplasia are not in the cancer family. But what of "dyskaryosis"? What I understand by this is a precursor of carcinoma-in-situ; it is therefore in the same family. It is possible to clarify ideas by seeing the company a lesion keeps. Invasive cancer is usually associated with in-situ cancer. It is generally said that carcinoma-in-situ has an abrupt transition to the normal, but in many cases this is not true; in its turn it keeps company with "basal hyperplasia" or "dyskaryosis." When we know enough we will no doubt relegate these terms to Professor R. A. Willis's category of "nicknames." When this happens there will be far fewer "doubtful" reports to annoy the gynaecologist.

Professor Jeffcoate is quite wrong in stating that the domiciliary service to "housebound" women is uneconomic. Dr. Leyshon[2] has proved it to be the most economic as well as the most rewarding. These women can only be reached by the home nurses on the staff of the M.O.H., and he alone can put their affairs in order so that they can have the same treatment as their more fortunate sisters.

It is very doubtful if a positive smear found during pregnancy calls for no further investigation in the absence of obvious tumour. I agree with those who take multiple punch biopsies or superficial cervical curettings.—I am, etc.,

G. R. OSBORN.

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Cervical Smear Campaign in a Group Practice

SIR,—Darbishire House Health Centre has about 12,000 patients, and we have at our disposal secretarial help and nursing assistance, and with the help of these latter we have carried out a campaign to take cervical smears.

A letter was sent to 1,775 women in the age group 25 to 55 years—carefully worded in order not to alarm them—inviting them to attend our centre during surgery hours to have an Ayres smear done. The number of women who attended was 665—a response of 37%. In America and Denmark, where a similar mailing campaign was undertaken,[1] but where the vaginal pipette or do-it-yourself-techniques were used, the response was 84%, but in a similar campaign in Aberdeen the response was only 39%. Out of the 665 smears taken 660 were classes 1 and 2, 4 were class 3, and 1 was class 4—an abnormal rate of 0.75%.

Owing to the poor response it was decided to send out a second letter, but at the suggestion of Mr. Baric, a sociologist of the Department of Social Medicine at Manchester University, the letter was sent to the husbands in half the cases where patients were married. Letters sent out numbered 1,097, but only 61 women attended; 41 came in response to the letter to the husband. Out of these smears 1 was class 3.

In spite of this being the most publicized medical need of the moment it is striking that only a third of the women at risk, in a well-knit group practice, could be persuaded to come. Possibly some women might prefer the examination done by a woman doctor, rather than by their own doctor. Further, the much better response reported to the do-it-yourself vaginal pipette technique calls for a definite answer as to whether this is a satisfactory method. Finally recent work from America seems to show that as a result of all the campaigns the morbidity rate but not the mortality rate has been reduced, and the writer of this American article finishes with the thoroughly dampening statement that[1] "the case for provision of universal screening facilities is still very far from being established."—We are, etc.,

H. W. ASHWORTH.
H. M. DAVIE.
H. GOLDIE.
J. LENTEN.

Darbishire House Health Centre, Manchester 13.

REFERENCE

1 *World Medicine*, 1966, **1**, No. 13, 25.

Cervical Cytology

SIR,—I hope that it is not presumptuous for a layman to enter the discussion in your columns, but if it is possible for me to speak on behalf of many of the women actively pressing for a comprehensive cervical cancer cytology service it may help to clear misunderstandings between the women "at risk" and the medical profession.

This campaign was launched in 1965 to co-ordinate the efforts of the many groups of women throughout the country striving to extend and improve the facilities for the smear test. Its terms of reference include a

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study of the difficulties in the way of setting up such a service. We have a Medical Advisory Committee whose members include the representatives of the B.M.A., the Royal College of Obstetricians and Gynaecologists, the Society of Medical Officers of Health, and the British Society for Clinical Cytology. Under their guidance we have been made aware of the problems in the way of population screening and the relative needs of different groups of women. As a national coordinating body we hope to control and direct what Mr. J. G. Lawson calls the "irresponsible enthusiasm and uncritical optimism [which] threaten to discredit this potentially valuable procedure" (19 November, p. 1260). Because we are aware of the difficulties we seek to work with the medical profession, fully realizing the debt we owe them. They in turn can help us by encouraging local cervical cancer campaigns to affiliate themselves to the national campaign. In this way a concerted medical–lay attack can be made on the problem, taking into account the need to extend investigations beyond the taking of a cervical smear to include clinical investigations and any other relevant means of detection.

In our initial effort towards the elimination of this particular scourge we shall not lose sight of the changes resulting from medical research, the differing forms of cancer, the varying techniques of detection, and the demands of other forms of preventive medicine. It would not be right to ignore the voices of women seeking protection against cancer. But with the help of the profession it should be possible to educate and lead them until, as preventive medicine advances on a broad front, everyone can take advantage of it.—I am, etc.,

ELIZABETH KAYE,
Hon. Secretary,
National Cervical Cancer Prevention Campaign.
London W.C.1.

Renal Failure and Low-molecular-weight Dextran

SIR,—The letter of Mr. N. A. Matheson (12 November, p. 1198) would imply that only nine cases of renal failure associated with dextran 40 have been reported in the medical literature; six cases in America[1] and at least one case in Sweden[2] have been published and a further five cases were presented at the Third International Congress of Nephrology held recently in Washington, D.C.[3 4] Three patients with acute renal failure associated with dextran 40 infusions have been seen in this hospital over the past two years, two cases following vascular surgery and the other, previously reported,[5] associated with a left atrial myxoma and multiple tumour emboli. This series has not been reported previously as the aetiology of the acute renal failure was often obscure and the patients were prone to develop renal failure in the absence of dextran 40 infusions.

Previous workers[6 7] have reported the highly viscous urine following dextran 40 infusions in dehydrated patients but a prompt diuresis usually ensues following appropriate treatment without any evidence of renal impairment. The observations of Langsjoen[1] in patients with myocardial infarctions and the experimental work of Mailloux *et al.*[3] have confirmed that renal ischaemia, often in the absence of systemic hypotension, is associated with an inappropriate tubular reabsorption of water, and infusions of dextran 40 under these circumstances can be associated with severe oliguria or anuria.

The addition of mannitol[7] by the manufacturers of dextran 40 and the measurement of urinary specific gravity[1] in addition to urine volume may be of assistance in reducing the incidence of this type of renal failure.—We are, etc.,

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L. J. LAWSON.
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Spectacle Frames and Driving

SIR,—The points regarding the above subject made by Mr. J. V. Brooke (10 September, p. 643) and Mr. G. V. Catford (3 September, p. 585) amplify and corroborate our original observations (20 August, p. 445). Mr. Brooke is correct in assuming that our spectacle frames were aphakic. The subject photographed wore contact lenses and we wished to draw attention to the fact that the hazards associated with ill-designed spectacle frames are not confined to people wearing corrections. Anyone can wear sun-glasses, and, if at the wheel, constitute a hazard on that score. The October issue of *Popular Motoring* advertises on p. 79 safety sunglasses made of Triplex glass. The width of the shaft is approximately half that of the lenses. The comment includes the remark: "This is another step towards safer motoring." No comment.—We are, etc.,

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H. P. RUFFELL SMITH.
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Neomycin and Anaphylaxis

SIR,—I agree with Dr. K. H. Burdick (12 November, p. 1198) that Dr. Rhoda Pippin's diagnosis of anaphylactoid reaction to neomycin is unjustified by the facts as reported in her letter (7 May, p. 1172), but I would like to dispel any complacency he may harbour as to such an event being inherently unlikely.

Dr. Burdick rightly distinguishes between delayed and immediate (anaphylactoid) type hypersensitivity, but these may coexist in the same patient, as is well shown even in such a classical delayed type hypersensitivity as that due to tuberculin. Experimentally it is often difficult to produce delayed hypersensitivity without at the same time producing circulating antibody. It is therefore slightly misleading to say categorically that "delayed hypersensitivity of the contact allergic type in a patient is in no way related to anaphylaxis" for they are certainly not mutually exclusive states. The patients described by Stoddart,[1] who had both types of hypersensitivity to nickel, illustrate that the association may on occasion be clinically significant. That immediate type hypersensitivity may result from administration of drugs usually associated with delayed type allergy is also shown by the following patient, a detailed description of whom is to be published elsewhere.[2]

A housewife, aged 49 years, suffered a systemic reaction of anaphylactoid type on three occasions (once with severe hypotension) following topical application of medicaments containing neomycin and bacitracin (but no enzymes) to her varicose ulcer. It was later established on the basis of skin testing and serological evidence that she was in fact extremely hypersensitive to bacitracin.

The possibility of such reactions is a real one, and since the population at risk is large similar events may be commoner than hitherto realized. General practitioners should be aware of the possibility of absorption of significant quantities of potentially sensitizing substances from large areas of skin, particularly if raw or ulcerated, and complaints of dizziness or faintness, generalized pruritus, or rash after such applications should be taken very seriously.—I am, etc.,

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Royal Victoria Infirmary, Newcastle upon Tyne.

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Poisoning with Mandrax

SIR,—Mandrax is a hypnotic preparation presented as tablets containing methaqualone (250 mg.) and diphenhydramine HCl (25 mg.).

There appears to be no information available regarding acute poisoning with Mandrax, but the toxic effects of methaqualone itself have been described.[1-5]

During the seven months following the introduction of Mandrax, 5% of poisoned patients admitted to this centre had taken an acute overdosage of the drug. The severity of poisoning was assessed by the level of consciousness and duration of unconsciousness, by evidence of neurological abnormality, and by the presence of other medical complications, such as shock, hypothermia, and respiratory or renal failure. Methaqualone in plasma and urine was estimated spectrophotometrically.[6] All the patients were treated by intensive supportive therapy to maintain vital functions; active measures which might have hastened the elimination of the drug were not used.

Of the 28 patients 19 (6 males and 13 females) were mildly poisoned. None of these cases presented any clinical features distinctive from overdosage due to other hypnotic drugs, and all made an uneventful recovery. The remaining nine patients (3 males and 6 females) were more severely poisoned, being either deeply unconscious or less severely affected but with characteristic clinical features. None of these cases proved fatal.

The most striking clinical features were pyramidal signs such as marked hypertonia, increased tendon reflexes, and myoclonia. One patient, in addition, had bilateral extensor plantar

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