evidence of the sort carefully collected by Dr Page suggests strongly that mianserin should join the list of drugs known to cause blood dyscrasias. Only if journals which are widely read continue to publish such data will the medical community recognise rare drug side effects of this type, which mimic naturally occurring disease.

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¹ Adams PC, et al. *Postgraduate Med J* (in press).

² McHarg AM, McHarg JF, 1979. *Br Med J* 1979;i:623-4.

³ Adverse Drug Reactions Advisory Committee. *Med J Aust* 1980;ii:673-4.

⁴ Curson DA, Hale AS. *Br Med J* 1979;i:378-9.

Sterile microenvironment in prevention of wound infection

SIR,—Mr John M Scott and his colleagues (29 May, p 1594) report a wound infection rate of 21% for patients undergoing nail plate fixation of femoral neck fractures and imply that the main problem is due mainly to the physical circumstances under which the patients are nursed. Our unit is housed in Victorian buildings with open wards and none of the modern facilities, the lack of which Mr Scott laments. In a recent study of 137 patients undergoing nail plate fixation for intertrochanteric fractures we had two significant wound infections as defined by Mr Scott, a rate of 1.5%. However undesirable ancient hospitals may be for other reasons, they are not necessarily responsible for the reported very high wound infection rates.

The question of whether the device described is effective remains, to our minds, unproved. It is not clear from the paper why patients were paired in the first place; neither are the criteria for pairing stated. Given that pairing was necessary, why were only some pairs withdrawn from the trial? The patients who died, those allergic to the wound isolator, and the patient who was hepatitis B positive were withdrawn, but the patients with whom they were paired were not. The conclusion that the wound rate is reduced from 21% to 1.8% makes remarkable reading. However, of the original 21% of infections, nearly one-half were clinically insignificant and the reduction in significant wound infections was from 11% to 1.8%. Of the seven infected controls, three were shown to have autogenous infection. Exogenous infection was implicated in four controls and one study patient—numbers which are insignificant in the small number of patients studied.

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SIR,—Mr J M Scott and his colleagues (29 May, p 1594) do a great service by drawing attention to the importance of secondary (ward-acquired) wound infection after clean operations. Skin wounds are resistant to bacterial invasion within a few hours, provided they remain dry.¹ The fact that one wound in five among the patients in the control group became infected suggests that their wounds did not remain dry.

I would like to know the following: (1) What was the incidence of wound infection in the

174 patients rejected from analysis? (2) What sort of skin sutures were used? (3) What sort of drains were used, and did they emerge from the wound itself?

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¹ du Mortier JJ. *Surg Gynecol Obstet* 1933;56:762-6.

* * * We sent this letter to the authors, who reply below.—Ed, *BMJ*.

SIR,—In his letter Mr A V Pollock rightly recognises the importance of those post-operative wound infections attributable to the environment of the wards dealing with such cases. In large multibedded wards epidemic strains of wound pathogens have frequently been shown to reach high environmental contamination levels, and the infections they cause arise in both wet and dry wounds with or without drainage, although the frequency of infection is always greater in wet wounds. This is hardly surprising when one considers the lesions caused by *Staph aureus* even in intact unbroken and apparently healthy skin.

In answer to the questions raised by your correspondent, the incidence of infection in the 174 patients rejected from the trial was the same as in the control group. A variety of sutures from silk to man-made fibre were used, and the wounds had suction drains, the tube emerging well away from the wound. Perhaps the most significant observation made during this trial was the rapidity with which a statistical proof of the benefit of the wound isolator was reached despite the relatively small number of patients studied.

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Side effects of benoxaprofen

SIR,—Many clinicians with experience of the use of benoxaprofen would agree with Drs J P Halsey and N Cardoe (8 May, p 1365) and Dr Colin Hindson and others (p 1368) that cutaneous side effects are relatively common. These may not all be harmful, however, and the chance observation of improvement in the skin lesions of a psoriatic patient who was being treated with the drug for an associated arthritis prompted us to carry out a pilot study of 14 patients with psoriasis.

All were suffering from severe extensive disease which had failed to respond to standard measures including, in most cases, cytotoxic drugs and psoralen-UVA. In seven patients there appeared to be no improvement at all and one of them developed erythema multiforme. In the remaining seven the response was dramatic. There was symptomatic improvement within 24 hours, which was associated with a lessening of erythema. Thereafter, improvement continued over a further three to four weeks with steady clearing of the lesions. One of these patients had to stop the drug because of gastrointestinal side effects and one relapsed despite continued treatment. Thus five out of our original 14 patients have been cleared of otherwise intractable psoriasis. These cases are to be reported more fully in the

near future, and we are at present carrying out a further double-blind trial of benoxaprofen in psoriasis of varying degrees of severity to assess its overall place in the management of this condition.

The significance of these observations on our understanding of psoriasis may be great. All non-steroidal anti-inflammatory drugs inhibit the cyclo-oxygenase pathway of arachidonic acid metabolism to prostaglandins, but benoxaprofen also inhibits the lipoxygenase pathway to the highly leucotactic "leucotrienes" including leucotriene B₄ (LTB₄), which is one of the most potent stimulators of leucocyte migration yet identified. One of the characteristic features of psoriasis histologically is the infiltration of polymorphonuclear leucocytes into the epidermis, frequently with the formation of microabscesses. It is probable that by reducing LTB₄ formation benoxaprofen is reducing migration of polymorphonuclear leucocytes into the epidermis. If so it gives a clear pointer to the fact that the polymorphonuclear leucocytes themselves are responsible for at least some of the symptoms of psoriasis. This would explain many puzzling aspects of the condition such as the improvement caused by peritoneal dialysis, the simultaneous improvement in joints and skin when cytotoxic drugs are used, and the lack of response to razoxane and hydroxyurea until a demonstrable and often profound leucopenia is induced.

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Radiation-induced leukaemia in spondylitics: dose-response relationships

SIR,—Mr P G Smith and Sir Richard Doll (13 February, p 449) have tested whether the risk of leukaemia in patients treated with x-rays for ankylosing spondylitis is given by bD, bDe^{-λD}, or bD²e^{-λD}, where D is the mean absorbed dose in active bone marrow.¹ Only part of the marrow was irradiated and the dose to marrow cells within the irradiated field might have been greater than the mean by a factor of 2 or more. Because of this the authors acknowledge that the validity of the two models incorporating an exponential function to allow for cell sterilisation is questionable. In fact, the use of mean dose to test any non-linear dose-response relationship can be very misleading as will be evident from the following extreme example.

Equations such as $y = bDe^{-\lambda D}$ are often found to provide a satisfactory fit to observations on the yield of tumours following various absorbed doses D to the cells at risk. In this case, the graph of tumour yield y against dose is a hump-backed curve. Suppose the peak incidence occurs at D_M. Now consider an individual in whom half the relevant cells are not irradiated and the other half receive a dose 2D_M for which the probability of a transformed cell is very small. Clearly the tumour yield from this irradiation is much smaller than that corresponding to the mean dose D_M which is at the peak of the curve. In this case, relating tumour yield to the mean dose would give a very misleading impression of the shape of the dose-response curve. The difficulty arises because of the