hurts, whereas if the anterior (subscapularis) or posterior (infraspinatus) part of the cuff contains the lesion pain occurs on resisted medial or lateral rotation respectively. The importance of accurate anatomical location of the lesion is that it enables one to know in which tissue to seek a tender area before giving a steroid infiltration. Merely injecting "the tender spot" is haphazard, since it may be misleadingly placed.

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¹ Cyriax, J., *Textbook of Orthopaedic Medicine*, 6th edn, p 213. London, Baillière Tindall, 1975.

Prolonged malaria prophylaxis

SIR,—Your expert's answer (17 September, p 757) to a question concerning antimalarial drugs suitable for prolonged prophylaxis in airline pilots calls for dissenting comments on several points.

There is no evidence that chloroquine taken at the dose of 300 mg base once a week causes any visual impairment, let alone blindness. Neuroretinal changes have been observed in a small number of persons whose cumulative dosage of this drug over a period of years was of the order of 100 g. This would require in theory some eight years of continuous taking of 300 mg of chloroquine base once a week or four years of a regimen at double this dosage. It is inconceivable that the postulated "extra chloroquine" for occasional treatment of malaria could significantly increase the risk of visual impairment in persons on the usual chloroquine dosage. On the other hand, chloroquine is the most reliable antimalaria prophylactic, precisely in Africa where no resistance of plasmodia to this compound has been proved to exist. Both proguanil at 100-200 mg daily and pyrimethamine at 25 mg once a week produce fewer side effects than other drugs but are less certain to protect from malaria infection in Africa and elsewhere, as areas of plasmodial resistance to antifolate compounds are much wider and less well known.

Maloprim (pyrimethamine 12.5 mg with dapsone 100 mg) is a reasonably effective prophylactic but not "against malaria anywhere in the world," since areas of resistance to antifolates with sulphones have been reported, especially in south-east Asia. Unfortunately the dosage of two tablets a week quoted by your expert is excessive. Side effects of Maloprim at two tablets a week have been reported from some parts of the world. Haemolysis in certain subjects and agranulocytosis are particularly to be guarded against and the manufacturers of this otherwise valuable drug combination stress that the dosage of one tablet a week should not be exceeded.

Your expert's unqualified condemnation of alcohol, apparently "increasing the susceptibility to malaria and many other diseases," is overstated and not quite fair to the acceptable, moderate, social "sundowner" with minimal if any side effects.

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*Our expert replies: "(1) Professor Bruce-Chwatt states that neuroretinal changes have been observed in a few people who have taken a cumulative dosage of 100 g chloroquine,

equivalent to 300 mg weekly for eight years, which is not long, since an airline pilot might fly to malarious areas for about 30 years and take 300 mg chloroquine weekly on Professor Bruce-Chwatt's advice. This is equivalent to about 400 g of chloroquine—well over the dangerous amount. Many airline pilots are aged between 40 and 55, a time of life when increasing impairment of vision is common, and long-term consumption of chloroquine might have an additive effect. Further evidence of chloroquine retinopathy has been the recent study of five patients from West Africa with visual impairment and a history of chloroquine ingestion for several years.¹

"(2) Airline pilots have the duty to fly planes safely, and presumably this requires perfect physical health and above all perfect vision. Thus the preservation of vision and, arguably, the avoidance of chloroquine might take precedence over the relative risk of acquiring malaria, especially since there are other drugs available for prophylaxis. Proguanil 100-200 mg is a safer chemoprophylactic than chloroquine, and, although it may be less effective than chloroquine, breakthroughs of malaria do occur with any of the drugs used. Therefore ideally facilities to examine blood films for malaria should be available at all international airports that receive travellers from areas endemic for malaria. Examination of blood films for malaria should be made on all pilots who feel unwell and have been in an endemic area.

"(3) Maloprim has proved to be an effective chemoprophylactic against malaria in both chloroquine-resistant² and chloroquine-sensitive³⁻⁴ areas and is marketed in Britain and many other countries. The manufacturer's recommended dose in adults is, as Professor Bruce-Chwatt indicates, one tablet weekly. This may be the optimum dose for tropical people weighing 50 kg, but possibly not for airline pilots weighing on average 80 kg, in whom two tablets weekly might be a more appropriate dose. Also diformyl dapsone (a chemical congener of dapsone) 400 mg with pyrimethamine 25 mg weekly for six months has been given to villagers in Thailand without toxicity.⁵ Fansidar (pyrimethamine 25 mg with sulfadoxine 500 mg in each tablet) is the most effective chemoprophylactic against chloroquine-resistant falciparum malaria⁶⁻⁷ and is available in most endemic areas, although it is not marketed in Britain. The drug is effective given once a month (three tablets) or every two weeks (two tablets), but one tablet weekly is a convenient regimen.

"(4) Alcoholism (here defined as evidence of physical or mental disease caused by alcohol) is a common problem and its prevalence in doctors or airline pilots has not yet been determined. But three pilots, who had all regularly passed their official six-monthly physicals, showed biochemical and physical evidence of alcoholic hepatitis when seen by an independent examiner last year.⁸ Alcohol impairs driving ability and presumably flying ability as well. A liver function test, the determination of serum gamma-glutamyl transaminase (GGT) activity, gives raised values in two-thirds of alcoholics.⁹ The prevalence of alcoholism could be determined with a view to treatment if the GGT and blood alcohol levels were determined randomly at six-monthly intervals on all people with crucial jobs, such as doctors and airline pilots. It should be remembered that most airplane accidents are due to pilot error.¹⁰⁻¹²

"(5) It is therefore desirable that airline

pilots avoid alcohol, tobacco, and other toxic substances, and drugs. However, pilots flying to malarious areas in Africa should probably take an antimalarial drug regularly for prophylaxis. Proguanil 100-200 mg daily is the least toxic drug. Pilots who fly to malarious areas outside Africa are very unlikely to contract malaria, but one tablet of Fansidar weekly should be considered."—ED, *BMJ*.

¹ Kelsey, J H. In preparation.

² Segal, H E, et al, *Journal of Tropical Medicine and Hygiene*, 1973, **76**, 285.

³ Lucas, A O, et al, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1966, **63**, 216.

⁴ Weber, M C, et al, *Central African Journal of Medicine*, 1975, **21**, 177.

⁵ Pearlman, E J, et al. In press.

⁶ Pearlman, E J, and Hall, A P, *Annals of Internal Medicine*, 1975, **82**, 590.

⁷ *British Medical Journal*, 1976, **2**, 1215.

⁸ Hall, A P. In preparation.

⁹ Spencer-Peet, J, Wood, D, and Glatt, M M, *Lancet*, 1972, **1**, 1122.

¹⁰ Beatty, D, *The Human Factor in Aircraft Accidents*. New York, Tower Publications, 1969.

¹¹ Power-Waters, B, *Safety Last*. London, Dial Press, 1972.

¹² Godson, J, *Papa India: The Trident Tragedy*. Salisbury, Compton Press, 1974.

Megaloblastic anaemia associated with sulphasalazine treatment

SIR,—The report by Drs Robert E Schneider and Linda Beeley of megaloblastic anaemia associated with sulphasalazine therapy (25 June, p 1638) and the subsequent correspondence (16 July, p 190; 27 August, p 580) were most interesting and prompt this report of a similar case.

A woman, now 40 years old, presented in 1969 with bloody diarrhoea. Ulcerative proctitis was diagnosed on the basis of positive sigmoidoscopic findings and a normal barium enema. Repeated radiological examinations of both small and large intestines have since failed to show any abnormalities proximal to the rectum. In July 1976 routine haematological investigation revealed a haemoglobin concentration of 12.6 g/dl and a mean cell volume (MCV) of 108 fl (108 μm^3). On examination of the blood film occasional macrocytes and hypersegmented neutrophils were seen. At this time her therapy was codeine phosphate 30 mg twice daily, ferrous sulphate 200 mg thrice daily, diazepam 4 mg each night, acetarsol suppositories 250 mg each night, and sulphasalazine 2.5 g daily. She had been on varying doses of this last drug since 1969 and her serum total sulphapyridine levels were repeatedly in the therapeutic range of 20-50 mg/l. Her proctitis was in remission and she ate a normal diet. Further investigations were: serum vitamin B₁₂ 600 ng/l; serum folate 0.8 $\mu\text{g/l}$ and RBC folate 43 $\mu\text{g/l}$ (microbiological assay); and serum folate 0.8 μg and RBC folate 88 $\mu\text{g/l}$ (radioassay). Small-intestinal biopsy showed microscopically normal appearances. Her sulphasalazine therapy was continued, since on several past occasions her disease had relapsed on lowering the dosage of this drug, and she was started on oral folic acid 5 mg daily. After one month her haemoglobin level was 13.8 g/dl and her MCV 92 fl (92 μm^3). Serum and RBC folate levels by microbiological assay were high in the normal range (16.5 and >275 $\mu\text{g/l}$ respectively). On continuing this therapy she has remained well and haematologically normal.

In this case assays of serum and RBC folate concentrations by both microbiological and radioassay methods gave comparable results, making it most unlikely that the low levels were due to any in-vitro effect of the absorbed sulphapyridine or any other drug. None of her medications has reported associations with folate deficiency, her diet did not lack sources of folate, and there was no radiological or histological evidence of small-intestinal disease. As a trial of sulphasalazine withdrawal was

clinically less appropriate than the addition of folate supplements the apportioning of blame for folate deficiency to the sulphasalazine treatment must remain tentative.

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Anxieties and fears about plutonium

SIR,—Dr R H Mole's article (17 September, p 743) is an understandable reaction to criticism. Yet if the criticisms of official studies on plutonium toxicity are to be met we need to feel that they are being dealt with impartially and competently.

Two points in Dr Mole's article are disquieting. One is his comment on the interaction between smoking and uranium mining, where he quotes one paper¹ that suggests no interaction but not another paper² that suggests that there is one. Experts in a field are not usually so selective.

The second point is the quotation from Ide *et al*³ where Dr Mole harshly suggests that Gofman⁴ misrepresented the paper in saying that "Ide and co-workers showed 30% of ciliated cells to be denuded of their cilia among smokers." Dr Mole goes on, "If the reported evidence has to be misrepresented in this way to make a case, then the case is likely to be worthless." It so happens that at the Windscale Inquiry Dr Dolphin, an assistant director of the National Radiological Protection Board, was cross-examined on this point. In response to the question of what proportion of cilia are damaged by smoking (day 50, p 20, letter G of the official transcript) Dr Dolphin replied, "I have no first-hand knowledge of this obviously, but reports which have been quoted in the literature, for instance by Ide, indicate in his particular observations that about 30% of the cells in the bronchial epithelium had lost their cilia compared with non-smokers. That was a paper by Ide. It was published in 1959." Now I cannot imagine Dr Mole accusing Dr Dolphin of misrepresentation; presumably Gofman was thought unworthy of the normal courtesies of scientific debate because he has opposed the nuclear power industry in the past. In fact I have checked the paper by Ide *et al* and consider both Gofman and Dr Dolphin justified in their interpretations, though the paper is perhaps not very clearly written.

After three months at the Windscale Inquiry I came away more worried than when I went, because the monitoring authorities do not seem to be doing an adequate job on the Windscale effluents. The letter by Dr Mole, written apparently under the aegis of the MRC Radiobiology Unit, increases my concern still further.

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¹ Sevc, J, Kunz, E, and Plaček, V, *Health Physics*, 1976, **30**, 433.

² Archer, V E, Gillam, J D, and Wagoner, J K, *Annals of the New York Academy of Sciences*, 1976, **271**, 280.

³ Ide, G, Sultzzeff, V, and Cowdrey, E V, *Cancer*, 1959, **12**, 473.

⁴ Crofman, J W, *Journal of the American Medical Association*, 1976, **236**, 284.

* * * We sent a copy of this letter to Dr Mole,

whose reply is printed below, together with a comment on a previous letter from Dr Jacqueline Orman (8 October, p 959).—Ed, BMJ.

SIR,—Dr Blackith quite wrongly assumes that my article was a reaction to criticism. Actually it was an attempt to explain some of the background to the Windscale Inquiry which might interest busy doctors. I haven't been near the inquiry or read any of the transcripts of evidence. In my article I quoted Ide *et al*'s own words and what Gofman made of them ("... the bronchi will have sizeable regions free of cilia") and must leave Dr Blackith with his own personal assessment. Has he read Gofman's articles? In these smokers are said to be 125 times more sensitive than non-smokers to lung cancer induction by inhaled radioactive particles because the virtual absence of cilia from (parts of) the respiratory epithelium in smokers prevents the normally rapid removal of particles from the airways. Neither Ide *et al* nor Auerbach *et al*¹ said they had observed sizeable regions free of cilia in smokers but not non-smokers. I would not regard it as misrepresentation for Dr Dolphin to describe what Ide *et al* or Gofman wrote as "in the literature."

Clearly my article was not, and could not have been, a substantial review of any scientific evidence. The USA monograph on lung cancer in uranium miners² showed that there was an association between cigarette smoking by the miners and an enhanced lung cancer frequency. Possible explanations were considered—for instance, that cigarette smoking potentiated the effect of uranium mining (against which serious arguments were adduced) or that it made mining-induced lung cancer appear earlier than otherwise. Within a few years the number of lung cancers trebled in Indian uranium miners³ (who rarely smoke⁴) and the overall frequency for a 14-year follow-up ($11/780 = 1.4\%$) was as high as one-third of that for White miners (most of whom smoked) after a 24-year follow-up ($144/3366 = 4.3\%$).⁴ What need disentangling are the differential effects of two age-related phenomena, the rapidly increasing age-specific lung cancer incidence in smokers, and the much less rapidly increasing radon exposure of the lungs with increasing duration of occupation as a miner. The Czech authors (Sevc *et al*) whose words I cited surveyed more miners, found a higher risk per rad than in the US, and concluded that their dosimetric errors were lower. Was it so wrong of me to limit myself to the one reference (which cited the US work) and its conclusion that smoking as a major causal agent could be excluded?

Much of Dr Orman's letter repeated what I wrote as if I had said the opposite. However, her emphasis on hereditary damage in relation to plutonium exposure is misplaced, as I had already explained.

R H MOLE

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¹ Auerbach, D, *et al*, *New England Journal of Medicine*, 1961, **265**, 253.

² Lundin, F E, Wagoner, J K, and Archer, V E, *Radon Daughter Exposure and Respiratory Cancer: Quantitative and Temporal Aspects*. NIOSH and NIEHS Joint Monograph No 1. Washington, DC, US Department of Health, Education and Welfare, 1971.

³ Wagoner, J K, Archer, V E, and Gillam, J D, *Proceedings of the XIth International Cancer Congress*, 1975, **3**, 102.

⁴ Archer, V E, Gillam, J D, Wagoner, J K, *Annals of the New York Academy of Sciences*, 1976, **271**, 280.

Human tick infestation in Britain

SIR,—Dr J A Slater (29 October, p 1158) describes his experience of tick infestation while picnicking beside Coniston Water and would like to hear of other cases in Britain. Oddly enough, a friend recently described to me the removal of a tick from her scalp when, as a child, she lived on the shore of Coniston Water.

I have seen two cases of tick infestation in London caused by *Rhipicephalus sanguineus*, a parasite of dogs. One patient, a Scandinavian visitor, found the tick in her pubic hair. The other, an administrator at a London teaching hospital, had stayed at a cottage in Norfolk and his wife discovered the tick on his back when he was in the bath. In neither case did the tick draw attention to itself, nor was there any history of direct contact with dogs.

Ticks are common parasites of household pets, though human infestation in this country appears uncommon. The risk of transmission of serious microbial diseases, such as occurs in many other countries, must be remote. Some years ago you discussed in a leading article¹ the bites of parasites acquired from pets, but ticks were not mentioned; they deserve a place as an unusual cause of arthropod bites from this source.

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¹ *British Medical Journal*, 1971, **4**, 640.

SIR,—Dr J A Slater asks for information on human tick infestation in Britain (29 October, p 1158). Our experience in Shropshire suggests that this is uncommon but not rare.

We have seen two such incidents this year, the first for over six years. A 6-year-old boy who had been playing in the fields presented with a tick attached to the shaft of penis. An attempt to dislodge the tick by covering it with petroleum jelly to obstruct its airway was unsuccessful and traction together with the application of the hot end of a matchstick proved more satisfactory. The local lesion was then treated with magnesium sulphate dressings and a five-day course of oral penicillin was prescribed as a prophylactic measure. The second patient, seen by a colleague, was an adult with a tick on his arm; this was dislodged successfully by traction alone. Unfortunately the trauma of removal distorted the mouth parts of the parasites so that their detailed identification was impracticable but circumstantial evidence suggests that both were derived from sheep. During the last war one of us (GBR) had a tick attached to the chest wall; this was dislodged by applying a burning cigarette end to the back of the parasite.

C A MORRIS

Director,
Public Health Laboratory
G B ROSS
General practitioner

Shrewsbury, Salop

SIR,—In response to Dr J A Slater (29 October, p 1158), there are several hard ticks which may attach themselves to man in Britain. The most frequent is the sheep tick, *Ixodes ricinus*. In parts of Scotland bites by the sheep tick are accepted as a natural minor hazard of rural life and a doctor would not normally be consulted. After walking through bracken on the island of Mull I have picked, on one