and could be traced in the records of the department of gynaecology. Of the 162 patients, 29 had cervical carcinoma stage 0 as diagnosed at conisation of the cervix and five had invasive cervical carcinoma stage I-II. One hundred and seventy-two age-matched controls were selected from the registers of births, marriages, and deaths and followed up in the same way as the patients. Seven cases of carcinoma of the uterine cervix stage O were found and one case in an invasive stage. The frequency of carcinoma was thus 20% in the patients compared with 5% in the controls—that is, four times higher in the patients who had previously had infection with neisseriae.

The results are in agreement with the general opinion that genital infections predispose to cervical neoplasia. Neither in the neisseria group nor in the controls was the frequency of herpesvirus infection known. We feel that estimation of the significance of herpesvirus infection and of the importance of possibly carcinogenic metabolites of bacterial origin requires well-planned long-term studies. Attention must be given also to other micro-organisms known to be of importance in genital infections, such as *Mycoplasma hominis*[2] and *Chlamydia trachomatis*.[3]

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Epidemic myalgic encephalomyelitis

SIR,—From Dr H G Easton's letter (24 June, p 1696), I can only conclude that he ignored all the evidence at the symposium on myalgic encephalomyelitis at the Royal Society of Medicine that did not fit in with his theories. If he had stayed to the end, when a vote was taken, he would have found himself the only person present still in favour of the "conversion hysteria" theory.

Dr Pampiglione, for example, referred to the electroencephalographic abnormalities—which were quite different from those seen in an acute encephalitis or liver failure with encephalopathy. The abnormalities were also different from those in chronic psychiatric patients. The cerebral cortex appeared to be disturbed by an insidious illness which was worthy of further investigation. Dr Peter Behan said that lumbar puncture performed on different days could give different results. Abnormal lymphocytes had been found by Dr Dillon, and reference was also made to anticomplementary activity in the serum and the ability of lymphocytes to live in vitro for an extended period, as is found with lymphocytes from patients with known viral diseases.

Dr Easton's "vapour and virus" remarks are hardly worth serious attention. Failure to isolate a virus does not rule out the possibility of a viral illness, because viruses that are of low antigenicity could become non-detectable if they were incorporated into the host cell's DNA. I would suggest that before putting pen to paper again he talks to some of the nurses (who have never been adequately followed up) permanently disabled as a result of the Royal Free Hospital outbreak. He might then discover how much unnecessary anguish the "conversion hysteria" theory had added to their mental and physical suffering. Or perhaps he would prefer to talk to some of the patients affected in the recent Essex outbreak, originally diagnosed as multiple sclerosis. Your leader admirably demonstrated the similarity between the two conditions. Perhaps Dr Easton thinks that multiple sclerosis is also hysterical in origin, since many of the symptoms, like those in myalgic encephalomyelitis, cannot be proved to be of organic aetiology.

Dr Peter Behan said at the symposium that he thought the disease was an immunological reaction triggered off by a virus. It would be helpful if more doctors, instead of pursuing outdated theories, seized the ample opportunities which study of this illness offers for research, a point which you rightly make in your leader.

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Leukostasis in chronic myeloid leukaemia

SIR,—In his recent paper (6 May, p 1169) on leukostasis in acute myeloid leukaemia (AML) Dr A L Harris draws attention to an important, avoidable cause of early death which is also relevant to other types of leukaemia. We have recently seen a similar event in a patient with chronic myeloid leukaemia (CML).

The patient was a 26-year-old man who presented with sudden deterioration of vision in one eye. Examination revealed several deposits with surrounding haemorrhage in both fundi and splenomegaly of 10 cm. Blood and bone marrow examination showed CML; his haemoglobin concentration was 6·8 g/dl, leucocyte count 500×10^9/l ($500\,000/mm^3$) with a typical differential count, and platelet count 75×10^9/l ($75\,000/mm^3$). Neutrophil alkaline phosphatase activity was absent and the Philadelphia chromosome was present. He was treated initially with busulphan 4 mg daily, but his condition deteriorated, with malaise, fever, pain in the splenic area, and some confusion. It was thought that these features reflected the very high leucocyte count, now 630×10^9/l ($630\,000/mm^3$) and he was therefore transferred for leukapheresis (Hemonetics model 30). A blood count immediately before the procedure was as follows: haemoglobin 6·1 g/dl, leucocyte count 770×10^9/l ($770\,000/mm^3$), platelets 100×10^9/l ($100\,000/mm^3$). The leucocyte count immediately after leukapheresis had fallen to 560×10^9/l ($560\,000/mm^3$) and a transfusion of 5 units of blood and 2 units (10 donations) of platelets was given. The following day the leucocyte count had not changed significantly (550×10^9/l ($550\,000/mm^3$)) and a second leukapheresis was carried out. Within 4 h the clinical features of a subarachnoid haemorrhage developed. The leucocyte count at this time was 300×10^9/l ($300\,000/mm^3$). The patient's condition deteriorated and he died shortly afterwards. Permission for necropsy was not obtained.

Although no positive proof was obtained the clinical features and course of this patient were sufficiently similar to those described by Dr Harris to make cerebral leukostasis and haemorrhage the likely cause of death. It is evident that transfusion must be approached cautiously in any patient with a very high leucocyte count and preferably postponed until the count has been reduced to a level which does not significantly affect whole-blood viscosity. This can be achieved within a few days in AML but may take several weeks in CML with traditional treatment. In these circumstances more vigorous chemotherapy or leukapheresis may be needed. Although in this case each leukapheresis produced a fall of over 200×10^9/l ($200\,000/mm^3$) the leucocyte count still remained high enough for leukostasis to result from the combined haemodynamic effects of transfusion and the rapid blood volume changes inherent in the leukapheresis technique.

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Treatment of ulcerative colitis

SIR,—We wish to reply to the remarks made by Mr P G Bevan about the problems of colitis patients being treated in fever hospitals (3 June, p 1459). As a group associated with a so-called "fever hospital" we feel that the discipline of infectious diseases has a contribution to add to the subject of inflammatory bowel disease (IBD).

It is not widely appreciated that salmonella infection by itself can produce a severe inflammatory colitis with persistent bloody diarrhoea[1] and even, on occasions, toxic dilatation of the colon,[2] so it would be true to say that the distinction from IBD on clinical grounds is not possible. In fact the differentiation between IBD and salmonellosis in an acutely ill patient may not be readily solved by sigmoidoscopic or barium *x*-ray appearances or even by biopsy findings.[3] We find that it is only by repeated assessment and repetition of the major investigations over a period of time that the diagnostic puzzle can be resolved, with all its implications for the management of the patient. To make matters worse, there are occasional patients in whom IBD of acute onset and salmonella infection coexist, and in these all the problems are compounded.

We feel that the specific bowel infections should be considered as part of the spectrum of IBD and, as in the case of ulcerative colitis and Crohn's disease, to produce good results it is necessary to have close co-operation at senior level between physicians and surgeons with experience of the problem.

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Spontaneous remission of nephrotic syndrome in amyloidosis

SIR,—I have read with interest the article by Drs J Michael and N F Jones on spontaneous remissions of nephrotic syndrome in secondary renal amyloidosis (17 June, p 1592). Spontaneous remission can also occur in primary amyloidosis. Indeed I have observed

spontaneous remission of the nephrotic syndrome after a course of 6 months in a Sepharad Jewish boy affected with renal amyloidosis associated with familial Mediterranean fever. The patient then remained free of any renal symptom, including proteinuria, for the next 5½ years until he experienced a dramatic relapse with a full-blown nephrotic syndrome and severe renal failure.[1] A renal biopsy performed after 3½ years of remission showed the persistence of amylotic deposits with a distribution and intensity similar to those seen when the first biopsy was performed, when the nephrotic syndrome was present.

The importance of such spontaneous remissions must be stressed in view of several recent articles ascribing to various drugs the disappearance of the nephrotic syndrome in renal amyloidosis.[2-5]

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Snakes and snake bite

SIR,—I was interested in the review by Dr David A Warrell of the book *Snakes and Snakebite* by John Visser and David Chapman (13 May, p 1269). As I have a special interest in this subject I would like to make one or two comments on the review which may be pertinent.

Dr Warrell has already made a number of observations about the book and its contents. However, the implication of the "futility of local interference at the site of the bite" is that pressure-relieving incisions play no part in the treatment of snake bite. I believe it has been amply demonstrated in several disciplines of medicine that pressure-relieving fascial incisions can prevent necrosis. A particularly good example of this is the anterior tibial compartment syndromes. The use of tourniquets is only controversial in as far as the dangers in the hands of lay people are concerned. If they are not applied within a few minutes of the bite they are unlikely to do any good at any time.

Dr Warrell correctly points out that puff adder bites can cause significant delayed hypotension and concealed blood loss, but his suggestion that the antivenom can help in preventing local necrosis appears unfounded in view of the fact that the antivenom does not contain any local cytotoxin-effective antibodies. The point to be emphasised is that antiserum need never be given for puff adder bites except in controlled circumstances and after admission to hospital. In my own experience the incidence of reaction to intravenous antivenom is low except in snake handlers who have previously been bitten and treated. Neither the authors nor the reviewer make any mention of prevention of serum sensitivity by the use of high-dosage cortisone. Although adrenaline is highly effective in the treatment of serum sensitivity, it is in itself a dangerous drug which should not be handled by lay persons, and if treatment with antivenom is always preceded by a bulk injection of a pharmacological dose of cortisone antiserum sensitivity can be expected to disappear completely; this has been our experience. Finally I would like to re-emphasise Dr Warrell's point that the doses of antivenom administered in most hospitals are quite inadequate and should not be used routinely.

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SIR,—It would be interesting to know the evidence on which Dr D A Warrell (13 May, p 1269) makes the assertion that venom from a spitting cobra spat into the eye "frequently causes corneal ulceration, and may be absorbed . . . causing hypopyon and anterior uveitis."

There is no doubt that in travellers' tales the severity of such incidents has been repeatedly asserted, but my own limited experience[1] suggests that such sequelae are rare and that the consequences of such an event are relatively mild and unlikely to occasion permanent damage. Duke-Elder's comprehensive *System of Ophthalmology*[2] makes only limited reference to this particular problem. This again would tend to confirm one's impression that this particular snake's venom in the eye is perhaps no worse a mishap than accidental contamination with, say, neat washing-up liquid or one of the quaternary ammonium compounds—painful and discomfiting but not the major event suggested by the quotation.

It is a little difficult to envisage in a case of a simple "spit" a more effective treatment than local lavage and analgesia. One surely would be very reluctant in such a case to add the potential risk of necrosis by use of antivenom.

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Alcohol and the blood

SIR,—Your leading article (10 June, p 1504) provides a fine historical review of the blood changes that may be related to excess alcohol consumption. However, it gives little information about which of these abnormalities are common and which are rare, and no guidance in their use for the detection of alcoholism. Most of the studies referred to were made on "skid-row" alcoholics, who are not typical of patients with alcohol-related diseases seen in the UK.

The majority of our alcoholic patients with macrocytosis are well nourished,[1 2] are in regular employment, and have normal vitamin B_{12} and folate stores. Unger and Johnson[3] found that 3% of an insurance company's employees were macrocytic on routine blood count and, of 17 examined, 16 were probably consuming excessive amounts of alcohol. A low serum folate concentration was found in only one subject, and although the remainder were treated with large doses of first folic acid and then B_{12} their mean cell volume (MCV) did not fall. In addition, there have been several other recent reports on macrocytosis of alcoholism from the UK and France which give a similar picture.[4-8]

Further evidence that the rise in MCV may be unrelated to folate deficiency has been provided by the deoxyuridine (dU) suppression test,[9] which is a sensitive biochemical test for folate or B_{12} deficiency performed on short-term bone-marrow culture. All eight of the alcoholic patients with macrocytosis studied by Wickramasinghe and Longland[10] gave normal results in this test, and their erythrocyte folate and serum B_{12} levels were subsequently found to be normal. This implies that the alcohol effect could not be attributed to an interference with B_{12} or folate metabolism and we believe that alcohol has some other direct effect on the developing erythroblast. When folate deficiency does occur in alcoholics it is almost always due to associated nutritional folate deficiency, a feature universally present in the "skid-row" alcoholic but seen in only one-third of our patients, who are more likely to be spirit than beer drinkers.

Finally we would suggest that British practitioners are unlikely to see many alcoholic patients with sideroblastic anaemia, thrombocytopenia, or Zieve's syndrome but will often see patients with a normal haemoglobin concentration, a normoblastic bone marrow, normal B_{12} and folate levels, and a raised MCV that returns to normal after three or four months of abstention from alcohol.

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Nutrition and the brain

SIR,—Your leading article (17 June, p 1569) presents an informative analysis of the present state of knowledge and uncertainty as to the relationship between nutrition and cerebral development. The general approach is factually based, with a brief review of some of the relevant data. In sharp contrast is your curt dismissal of "unscrupulous" attempts to link malnutrition to "mental retardation in its usual sense."

Severer degrees of mental handicap (profound, severe, and moderate) occur at about 4 per 1000 in populations aged 10-16 years in Britain, as shown by a number of careful surveys. While it seems improbable that such severe mental handicap can be specifically or commonly due to malnutrition in a relatively developed country, the sources which you quote, and others, still leave open the possibility in cases of prolonged maternal or severe infant malnutrition elsewhere. However, the majority of the mentally retarded singled out for help from the special services in Britain or the USA are the mildly retarded, as defined by the International Classification of Diseases or the American