We report here the development of severe anaemia due to erythroblastopenia in a patient receiving high doses of cephalothin.

A 67-year-old man had bilateral total hip prostheses for osteoarthritis, the right hip having been replaced in 1969 with a McKee-Farrar prosthesis and the left hip in 1970 with a Charnley prosthesis. In February 1974 an abscess developed in the anterolateral aspect of his right hip. Surgical exploration indicated that the abscess extended into the cavity of the hip joint and alongside the shaft of the femur. A heavy pure growth of green-zone streptococci was cultured.

The patient was initially treated with benzylpenicillin 5 megaunits intravenously six hourly. During the fourth week of treatment he developed a diffuse maculoerythematous skin rash which was thought to be due to penicillin allergy. As a result treatment was changed to lincomycin 0·5 g together with fusidic acid 1 g six-hourly by mouth. At the same time oral cephalexin was given, starting with small doses which were gradually increased to 4 g daily up to a total of 28 g until the skin rash had completely faded. As there was no clinical evidence of cross-allergenicity these antibiotics were ceased and cephalothin intravenously 4 g six-hourly was given with probenecid 2 g daily for a total of 22 days. The only other drug administered concurrently was diazepam, 2 mg thrice daily.

His blood picture had been normal at the time of admission on 27 February. On 26 April his haemoglobin level had fallen to 8 g/100 ml and the reticulocyte count was less than 1%. Bone marrow biopsy showed normal megakaryocytes and granulocytic series, but there were no red cell precursors. A diagnosis of pure red cell aplasia was made and all medications ceased.

The patient was transfused and six days later erythromycin was started. Reticulocytosis heralded bone marrow recovery and on 11 May, 15 days after the haematological diagnosis had been made, a repeat bone marrow biopsy showed a return of vigorous normoblastic erythropoiesis. The peripheral blood picture was completely normal 27 days after ceasing cephalothin. The direct Coombs antiglobulin test was first performed 3 months after the aplastic episode and proved negative. It remained negative after incubation of the patient's red cells with varying concentrations of cephalothin.

The offending prosthesis was removed later and convalescence was uneventful. His renal function was normal throughout and appropriate radiological studies excluded thymoma. During the 10 weeks prior to the first bone marrow biopsy the only other drugs he had received and not mentioned in the above history were clindamycin 300 mg six-hourly for three days approximately five weeks previously, mebhydrolin 1 g daily for three days for the skin rash, and three Doloxene (aspirin with dextropropoxyphene) capsules given eight weeks previously.

Pure red cell aplasia is a rare condition and was reviewed recently by Teoh *et al.*,[4] who described three new cases, in one of which there was an associated thymoma. In another review Recker and Hynes[5] noted an association between pure red cell aplasia and drug therapy in 40 patients; 21 cases occurred after treatment with chloramphenicol, and other drugs incriminated were sulphathiazole, arsphenamine, penicillin, phenobarbitone, isoniazid, chenopodium, phenylbutazone, tolbutamide and chlorpropamide, and phenytoin.

In our patient the return of erythropoiesis within 15 days of withdrawing cephalothin, diazepam, and probenecid strongly suggests that one of these three drugs was responsible for the erythroblastopenia. We have been unable to find any previous record of pure red cell aplasia being associated with any of these drugs. The clinical history and the references already cited[1-3] raise the strong possibility of a causal link between cephalothin and red cell aplasia in our patient.—We are, etc.,

D. MACCULLOCH
J. M. JACKSON
J. VENERYS

Departments of Microbiology, Haematology, and Orthopaedics,
Royal Perth Hospital, Perth, Western Australia

1 Davis, A., *et al.*, *Antimicrobial Agents and Chemotherapy*, 1963, **3**, 272.
2 Sheiman, L., Spieloogel, A. R., and Horowitz, H. J., *Journal of the American Medical Association*, 1968, **203**, 601.
3 Molthan, L., Reidenberg, M. M., and Eichman, M. F., *New England Journal of Medicine*, 1967, **277**, 123.
4 Teoh, P. C., *et al.*, *Medical Journal of Australia*, 1973, **2**, 373.
5 Recker, R. R., and Hynes, H. E., *Archives of Internal Medicine*, 1969, **123**, 445.

Nephrotic Syndrome in Chronic Lymphatic Leukaemia

SIR,—We were interested to see the recent paper by Dr. J. R. E. Dathan and others on this subject (14 September, p. 655) since we have recently had two such patients under our care. Both, like the patients described by Dr. Dathan and his colleagues, were middle-aged men. The first patient was aged 64 and presented with a nephrotic syndrome. During investigations of this the diagnosis of chronic lymphocytic leukaemia was established. Renal biopsy showed typical membranous nephropathy on both electron microscopy and immunofluorescent study. He was treated with chlorambucil, and though proteinuria has diminished and he no longer has oedema, proteinuria persisted and therapy was stopped after one year. This patient is discussed in more detail elsewhere.[1] The second patient was a man of 57 years when chronic lymphocytic leukaemia was diagnosed. Because heavy proteinuria and ankle oedema were also present he was referred for renal biopsy. This showed sclerosing proliferative glomerulonephritis on light and electron microscopy; immunofluorescent studies were not done. Three years later his nephrotic syndrome persisted with a reduced glomerular filtration rate (48 ml/min). He received no specific treatment.

There is no doubt that the association between neoplasia and a nephrotic syndrome with evidence of immune complex disorders is a strong one and that the commonest histological appearance in this association is membranous nephropathy. To date we[1] have noted 27 patients whose nephrotic syndrome and neoplasm were diagnosed within one year of one another and who showed membranous nephropathy on renal biopsy (see table). Only a small number of patients have been reported with proliferative glomerulonephritis, though a number of patients with Hodgkin's disease and minimal changes have been described.[2 3]

Sites and Types of Neoplasia Associated with Membranous Nephropathy

Neoplasm	No. of Patients Reported	References
Carcinoma of bronchus	10	1, 9-13
Carcinoma of colon or rectum	4	1, 5, 6
Hodgkin's disease*	4	1, 2, 14, 15
Carcinoma of mouth or pharynx	2	9
Carcinoma of breast	1	10
Carcinoma of skin	1	9
Carcinoma of ovary	1	9
Carcinoma, origin unknown	1	9
Wilms's tumour	1	1
Chronic lymphatic leukaemia	1	1

*The patient reported by Miller[16] as having membranous nephropathy was later re-examined[3] and the section considered to show minimal changes.

The possibility most investigated is that tumours might release antigens which in turn lead to circulating soluble complexes.[4-6] In the leukaemias, particularly, the possibility of complexes formed with oncogenic virus antigen also arises. In addition to the evidence from mice that Dr. Dathan and his colleagues quote, the work of Sutherland and Mardiney[7] is of interest. In a series of 90 patients dying from leukaemias and lymphomas, 10% showed granular IgG and C3 in their glomeruli, suggesting soluble complex deposition. Further, in two patients with chronic myelocytic leukaemia antigen consistent with the interspecies gs-3 portion of the feline leukaemia virus was demonstrated in kidney homogenates. Anderson and Jarrett[8] have also shown appearances resembling membranous nephropathy in feline leukaemia, though electron microscopy and immunofluorescence were not done in this study.

We would like to endorse Dr. Dathan's plea that patients with carcinomas, leukaemias, and lymphomas should be investigated for proteinuria regularly and, if it is found, that full investigation including renal biopsy should be performed.—We are, etc.,

STEWART CAMERON
C. S. OGG

Guy's Hospital,
London S.E.1

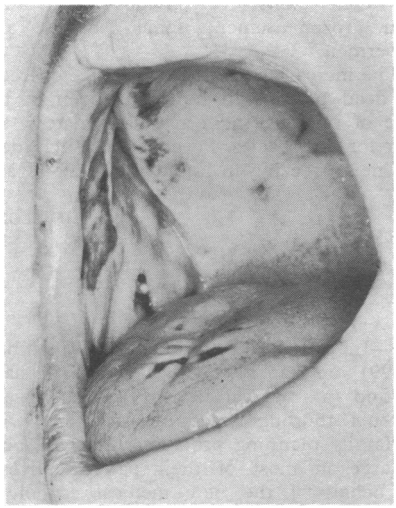
1 Row, P. G., *et al.*, Membranous Nephropathy: Long-term Follow-up and Association with Neoplasia. Submitted for publication.
2 Froom, D. W., *et al.*, *Archives of Pathology*, 1972, **94**, 547.
3 Sherman, R. L., *et al.*, *American Journal of Medicine*, 1972, **52**, 699.
4 Lewis, M. G., Loughridge, L. W., and Phillips, T. M., *Lancet*, 1971, **2**, 134.
5 Costanza, M. E., *et al.*, *New England Journal of Medicine*, 1973, **289**, 520.
6 Couser, W. G., *et al.*, *American Journal of Medicine*. In press.
7 Sutherland, J. C., and Mardiney, M. R., *Journal of the National Cancer Institute*, 1973, **50**, 633.
8 Anderson, L. J., and Jarrett, W. F. H., *Research in Veterinary Science*, 1971, **12**, 179.
9 Lee, J. C., Yamauchi, H., and Hopper, J., *Annals of Internal Medicine*, 1966, **64**, 41.
10 Loughridge, L. W., and Lewis, M. G., *Lancet*, 1971, **1**, 256.
11 Richard, D., *et al.*, *Journal d'Urologie et de Nephrologie*, 1973, **79**, 745.
12 Asamer, H., Stuhlinger, W., and Dittrich, P., *Deutsche medizinische Wochenshrift*, 1974, **99**, 573.
13 Higgins, M. R., Randall, R. E., and Still, W. J. S., *British Medical Journal*, 1974, **3**, 450.
14 Hardin, J. G., Coker, A. S., and Blanton, J. H., *Southern Medical Journal*, 1969, **62**, 1111.
15 Castleman, B., Scully, R. E., and McNeely, B. U., *New England Journal of Medicine*, 1973, **289**, 1241.
16 Miller, D. G., *Annals of Internal Medicine*, 1967, **66**, 507.

Mouth Ulceration and Slow-release Potassium Tablets

SIR,—Oral potassium supplements are one of the most commonly used medications in the pharmacopoiea. However, the ulcerogenic potential of high concentrations of potassium chloride in contact with mucosal surfaces is well known; both stenosis and perforation of the small intestine have been described.[1 2] As a result of this, slow-release preparations of potassium chloride have been devised; these incorporate the active agent in a slow-release wax core. I report a case of mouth ulceration in a patient who sucked slow-release potassium tablets.

A 69-year-old European insulin-dependent diabetic was admitted to hospital in May 1974 with ischaemic heart disease, peripheral vascular disease, congestive cardiac failure, and pulmonary oedema. She responded to treatment with digoxin, insulin, diuretics, and potassium supplements in the form of slow-release tablets.

Two weeks after admission she was noticed to have developed multiple, well-demarcated, deep ulcers on the mucosa of her tongue, gums, and



cheeks (see fig.). These were entirely painless, and in fact the patient herself was initially completely unaware of them. There was no associated lymphadenopathy. Examination of other mucous membranes showed no evidence of ulceration. Swabs sent for bacteriological studies revealed no yeasts or organisms of Vincent's angina, and grew nothing on culture. Her white blood cell count and temperature remained within normal limits.

The patient denied any trauma but did admit to sucking her slow-release potassium tablets; she apparently swallowed all her other medications. The potassium supplements were changed to an effervescent form, and over the course of the next 7-10 days the ulcers healed completely.

Slow-release tablets of potassium chloride have been formulated because it is thought that rapid release of potassium chloride over a short segment of intestine is the precipitating factor in the ulceration produced by enteric-coated supplements.[3] With these preparations the solubility of potassium chloride is reduced by partially coating the crystals with an inert insoluble wax and with a sugar rather than enteric coating. The tablets release potassium chloride over a period of four hours compared with 15 minutes for those that are enteric-coated.[3] Studies with slow-release potassium preparations have shown that the potassium chloride is effectively absorbed and does not produce side effects.[4] However, under the unusual circumstances of the tablets being sucked it seems that high concentrations of potassium chloride are in contact with relatively small areas of mucosa and can thus induce ulceration.

I would like to thank Dr. Andrew Allison for his help and encouragement and for his permission to report this case.

—I am, etc.,

B. R. McAvoy

Department of Medicine,
Southern General Hospital,
Glasgow

1 Baker, D. R., Schrader, W. H., and Hitchcock, C. R., *Journal of the American Medical Association*, 1964, **190**, 586.
2 Lindholmer, B., Nyman, E., and Räf, L., *Acta Chirurgica Scandinavica*, 1964, **128**, 310.
3 Martindale, *Extra Pharmacopoiea*, 26th edn., ed. N. W. Blacow. London, Pharmaceutical Press, 1972.
4 Wynn, V., *Lancet*, 1965, **2**, 1241.

Post-herpetic Pruritus

SIR,—In September 1973 a 35-year-old man developed pain in his right upper arm and shoulder. A few days later he developed typical lesions of herpes zoster on the inner aspect of the right upper arm and the right side of the upper trunk. The rash was severe but eventually settled and apart from the scars of shingles he was left with severe intractible irritation around the right axilla and right upper inner arm, together with some pain in the right shoulder region. Clinical examination revealed scars of herpes zoster predominantly in the dermatomes of T2 and T3 and there was hypoaesthesia in the region of T2 on the inner upper arm. Haemoglobin, full blood count, and erythrocyte sedimentation rate were all normal and no abnormality was seen on *x*-ray of his chest and right shoulder. *X*-ray of his upper spine merely showed degeneration of the eighth dorsal disc. Despite treatment for almost a year with various local preparations (including steroid creams) and systemic therapy with various antihistamines, sedatives, analgesics, and carbamazepine the severe pruritus has persisted, overshadowing his shoulder pain.

Post-herpetic neuralgia is rare in young people, and though severe itching can occur as a troublesome sequel to herpes zoster,[1] it is by no means common. This young man has been unfortunate on both counts. The zoster-varicella virus causes acute inflammation at some point in the course of the first sensory neurone, the dorsal root ganglia and corresponding sensory ganglia of cranial nerves being the commonest sites. Microscopic changes include haemorrhage and infiltration with mononuclear cells, and in severe cases fibrosis and secondary degeneration can occur. These changes can lead to persistent post-herpetic symptoms. This man has post-herpetic neuralgia, hypoaesthesia, and severe pruritus in the root distribution.

It is generally accepted that post-herpetic neuralgia is very resistant to therapy and this case report illustrates that post-herpetic pruritus can be just as aggravating to the physician as well as the patient.—I am, etc.,

KEITH LIDDELL

Department of Dermatology,
Royal South Hants Hospital,
Southampton

1 Brain, W. R., and Walton, J. A., *Brain's Diseases of the Nervous System*. 7th edn. London, Oxford University Press, 1969.

La Condition Humaine

SIR,—Sympathy must of course be given to a number of Dr. S. Bradshaw's views (14 September, p. 682), but somewhere his tocsin has become intoxicated and his carillon most definitely cracked. It seems that the blind villain and its skivvy arrived from outer space after Queen Victoria died. Just how did science and technology arise? Slowly and gradually and basically of God; Christians must believe this. Can Adam now replace the fruit and tiptoe through the unmown grass again with Eve, ignorant even of their nakedness? Science means knowledge, and unless Dr. Bradshaw is a fundamentalist he will probably agree that total ignorance is not necessarily the most blessed state for human beings. When we knew little we were not so far from the animals. As knowledge has advanced so have our capacities for evil and the worship of false gods; so also, I firmly believe, has our capacity for collective good. It is not science and technology that is the anti-Christ but our own faults, and this has been so from the time of Herod.—I am, etc.,

JAMES MILLAR

Oxford

Value of Hospital Case Notes

SIR,—During the course of a broadcast presentation on "Family Practice" on B.B.C.4 on the evening of 1 October a general practitioner referred to the fact that on certain hospital notes were printed the words, "Not to be seen by the patient." He commented that the reason for this was not to avoid the patient's embarrassment by finding out what might be the matter with him, but because the content of the notes was "rubbish." He repeated this statement and in spite of a telephone call to the B.B.C. to ask that this wholesale criticism of the hospital service should be withdrawn, no further comment was made.

It is most regrettable that any member of our profession should allow himself to make such sweeping condemnatory statements of other sections of the profession at a time when we are trying to overcome the barriers which still exist still between those responsible for primary care and those working under similarly difficult conditions in the hospital service. If this public statement is allowed to go unchallenged it remains as a sad indictment of literally thousands of overworked hospital residents who have insufficient secretarial assistance and whose notes on the whole are comprehensive and dependable. One wonders whether this particular practitioner considered that the notes that he himself wrote during his resident posts were worthy of such a description.—I am, etc.,

D. F. ELLISON NASH

London S.E.19

Lead and Intelligence

SIR,—Your leading article (28 September, p. 761) is acceptable as a grudging admission that a problem exists in relation to the effects of lead on behaviour. As a review of the recent work on this important subject, however, it is inadequate on several counts.

There is now a great deal of evidence that lead can adversely affect behaviour, most often by the production of hyperactivity. On this account the correlation between I.Q. and educability does not always hold in the children affected because of their poor attention span. It is curious that this observation was not commented upon since it is one of the most significant made by Byers and Lord in their classic paper which appeared in 1943.[1]

Again, in addition to the negative findings of Lansdowne *et al.*,[2] which were criticized by a number of authors[3-5] as to both methodology and conclusions, one would have wished to see some of the more recent reports included which show clearly that behavioural changes can be induced by relatively modest body burdens of lead. A study from El Paso[6] states unequivocally that "children with blood lead levels ≥ 40 μg/100 ml have diffuse and subtle impairment of the fine motor, perceptual, and visual perceptual skills." When it is realized that in many American cities 25-30% or more of the children examined in large screening programmes have blood lead levels greater