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 cephalixin 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, mebidrolin 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 Hynes⁵ 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 cited¹⁻³ raise the strong possibility of a causal link between cephalothin and red cell aplasia in our patient.—We are, etc.,

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- 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 we¹ 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' tumour	1	1
Chronic lymphatic leukaemia	1	1

*The patient reported by Miller¹⁴ as having membranous nephropathy was later re-examined³ 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 Mardiney⁷ 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 Jarrett⁸ 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.,

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- 1 Row, P. G., *et al.*, Membranous Nephropathy: Long-term Follow-up and Association with Neoplasia. Submitted for publication.
- 2 Fromm, 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 Wochenschrift*, 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 Costleman, 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 pharmacopoeia. 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