HIV infection except possibly a blood transfusion in 1986, when the blood supply was regarded as "safe" in Australia.

Initial investigations of cell-mediated immunity revealed a negative delayed-type hypersensitivity skin test for candida and a negative candida blastogenesis assay; both results persist. Investigations have now included T cell subsets by cytofluorographic analysis:

Date	*CD4+ (/μl)*	*CD8+ (/μl)*
Jan, 1985	160	90
May, 1988	250	320
March, 1989	80	120

Normal. CD4+, 120–600; CD8+, 400–750.

All measurements of CD4+ cells were reduced and in 1988 and 1989 the CD4:CD8 ratio inverted. Repeated HIV antibody testing by two ELISAs,[1] western blotting ('Novapath', Biorad Laboratories), and HIV p24 antigen assay ('HIV Antigen EIA', Abbot) have been negative. The patient is currently well on ketoconazole 200 mg per day, but, as in Parkhurst and Peakman's case, she has low peripheral CD4+ cells in the absence of HIV infection. These findings provide further support to the previous warning about overinterpretation of low CD4+ counts in the presence of candidiasis.

Department of Clinical Immunology,
Royal Prince Alfred Hospital,
Camperdown, New South Wales, 2050 Australia — PAUL A. GATENBY

1. Reesink HW, Lelie PN, Huisman JG, et al. Evaluation of six enzyme immunoassays for antibody against human immunodeficiency virus. *Lancet* 1986; ii. 483–86

REMOVAL AND REPLACEMENT OF TENCKHOFF CATHETER AT SINGLE OPERATION

SIR,—Paterson et al[1] reported the successful treatment of refractory peritonitis complicating continuous ambulatory peritoneal dialysis (CAPD) in 12 patients by the removal and immediate replacement of the Tenckhoff catheter at a single operation.[1] This approach spares the patient several weeks of haemodialysis in hospital and a second operation for reinsertion of a new catheter. Although Morton et al[2] reported a satisfactory outcome in a further 12 cases, others have been less successful. Marichal et al[3] experienced failure in 3 of 18 cases, and the recurrence of peritonitis in 3 of the 13 cases treated by Grefberg[4] led him to abandon the technique.

We have treated 12 consecutive cases of refractory peritonitis by a modification of the technique of Paterson et al. The indications for catheter removal were persistent peritonitis in 4 cases (*Staphylococcus aureus* 3, *Pseudomonas aeruginosa* 1), and recurrent peritonitis in 8 cases (*Staph aureus* 2, coagulase-negative staphylococci 2, *Ps vesicularis* 1, *Ps stutzeri* 1, *Acinetobacter anitratus* 1, *Achromobacter* sp 1). The cases of peritonitis caused by *Staph aureus* and *Ps aeruginosa* were associated with a pre-existing infection of the Tenckhoff catheter exit site with the same strain. Antibiotics that had failed to eradicate the organisms were continued during the operation and for 7 days thereafter (all doses administered intraperitoneally). In the cases of recurrent peritonitis, antibiotic therapy was started 24 hours before the operation to ensure adequate tissue levels at the time of replacement. There has been no recurrence of infection (mean period of observation 16 months, range 4–24).

We attribute our success to two factors. Firstly, our modification of the replacement technique. Paterson et al fashioned a new subcutaneous tunnel and exit site for the replacement catheter, but used the same peritoneal insertion site. We chose to regard the procedure as two separate operations: the infected catheter was removed and the surgeon then changed gown, gloves, and instruments before inserting the replacement catheter at a different site from the previous catheter throughout its subcutaneous length, including the site of entry into the peritoneum. Secondly, we impress upon our patients the importance of aseptic bag exchange and exit site care (especially important in cases associated with exit site infection).

Our modification of the single operation catheter technique has ensured a successful outcome in all cases of refractory peritonitis so far treated. We consider this to be a major advance in the management of infection in CAPD, yielding considerable savings for both patient and hospital.

Departments of Medical Microbiology,
Surgery, and Renal Medicine,
St Thomas' Hospital,
London SE1 7EH — H. A. LUDLAM, A. E. YOUNG, A. J. WING

1. Paterson AD, Bishop MC, Morgan AG, Burden RP. Removal and replacement of Tenckhoff catheter at a single operation: successful treatment of resistant peritonitis in continuous ambulatory peritoneal dialysis *Lancet* 1986; ii: 1245–47.
2 Morton AR, Waldek S, Holmes AM. Removal and replacement of Tenckhoff catheters. *Lancet* 1987, i: 229.
3. Marichal JF, Faller B, Mengus C, Wagner JD, Frey G. Le remplacement du catheter de dialyse peritoneale au cours des peritonites persistantes en dialyse peritoneale continue ambulatoire. *Nephrologie* 1985; **6:** 7–10.
4. Grefberg N Renewal of Tenckhoff catheters *Lancet* 1986; ii: 1467.

VP-1 ANTIGEN IN CHRONIC POSTVIRAL FATIGUE SYNDROME

SIR,—Yousef et al[1] reported that an enterovirus group specific protein, the VP-1 antigen, was found in 51% of a series of patients with the postviral fatigue syndrome (PVFS). No antigen was demonstrated in any of 36 neighbourhood controls. The VP-1 antigen is claimed to be specific for chronic enterovirus infection and to facilitate the clinical diagnosis of PVFS.[2] More than 10 000 samples have now been tested.[3] The clinical relevance of these findings has been questioned.[4] The selection of patients from members of a self-help organisation for people with postviral fatigue may also have led to overestimation of the association. The choice of normal neighbourhood controls is also questionable.

We report the frequency of the VP-1 antigen in patients with chronic unexplained fatigue and in controls who were general neurological cases. The clinical characteristics of the 47 cases of PVFS have been described.[5] Intensive neurological investigation was normal in all cases. All were assessed on a variety of measures, including general health questionnaire (GHQ), hospital anxiety and depression scale (HAD), somatic discomforts questionnaire, visual analogue scales recording functional impairment, a new questionnaire concerning fatigue, and the schedule for affective disorders and schizophrenia. The controls were 50 randomly chosen inpatients on a general neurological ward. They had a variety of neurological diagnoses. None were admitted for investigation of fatigue, and all but 2 were given a definitive diagnosis. All blood samples were labelled "? PVFS", and were sent to the pathology laboratory at St Mary's Hospital, London, with other routine samples.

Of the 47 cases of "PVFS", samples were obtained from 38, since 9 patients were seen before the test became available. Results were received on 30; the other samples were destroyed during a postal strike or during a machine failure. 7 control samples were similarly destroyed.

9 out of 30 (30%) of the cases were positive for VP-1 antigen (confidence interval 13·6–46·4%) compared with 5 of 43 (12%) of the controls (2·0–21·2%). The diagnoses in the positive controls were: multiple sclerosis (2), glioma (1), hemichorea (1), and cerebrovascular disease (1). The 2 patients for whom no definitive diagnosis could be made were both negative. The difference in proportions possessing the antigen between cases and controls was just significant ($\chi^2 = 3{\cdot}848$, $p = 0{\cdot}05$; 95% confidence limits for difference in proportions, 0·001–0·36). There were no differences between cases with or without VP-1 antigen on all measured variables including illness duration, self-ratings of physical and mental fatigue, number of somatic symptoms, GHQ score, HAD score, and visual analogue scales of functional impairment. There were no differences between the proportions receiving psychiatric diagnoses or reporting muscle pain, post-exercise myalgia, or an initial infective illness.

Our results confirm that the VP-1 antigen is associated with the chronic fatigue syndrome, but at a lower frequency than previously reported. However, as our sample came from a specialised centre, selection bias remains possible. Furthermore the antigen was found in a few neurological conditions that are not aetiologically related to

enterovirus infection. Enteroviral antigenaemia may have been fortuitous or a consequence of the initial illness. Either conclusion poses problems in the interpretation of a positive result in chronically fatigued patients. We conclude that at present VP-1 antigen status remains of research interest but its sensitivity and specificity are unsuitable for routine clinical use.

National Hospital for Nervous Diseases,
London WC1N 3BG

DAVID HALPIN
SIMON WESSELY

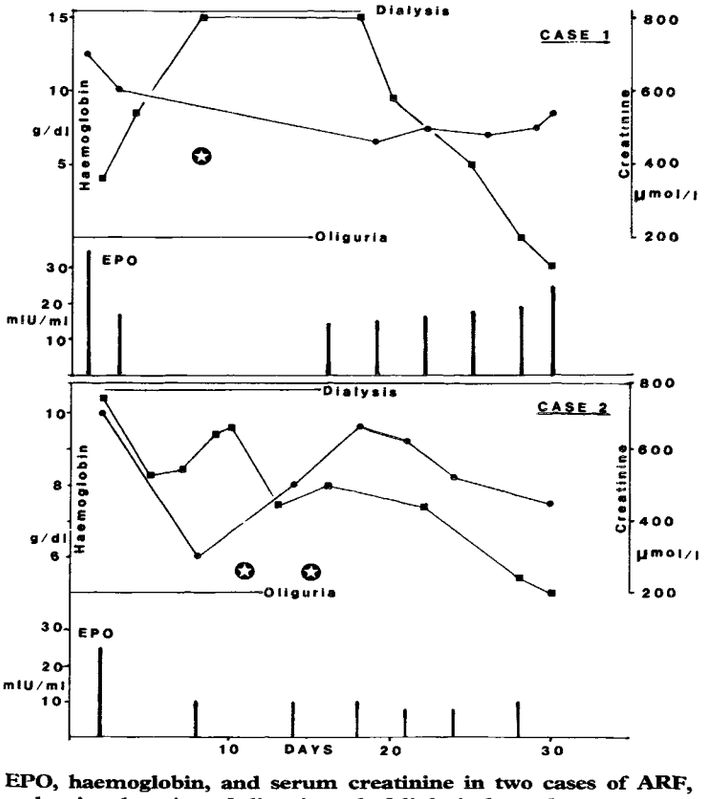
1. Yousef G, Bell E, Mann G, et al. Chronic enterovirus infection in patients with postviral fatigue syndrome. *Lancet* 1988; i: 146–50.
2. Yousef G. Postviral fatigue syndrome. *Update* 1989; Jan 1, 33–37.
3. Mowbray J. Data presented at the Clinical Virology Section, Society for General Microbiology, Cambridge, April 6, 1989.
4. Wright D. Postviral syndrome. London: CIBA Foundation. *CIBA Foundation Bull* no 22, 1989: 10.
5. Wessely S, Powell R. Fatigue syndromes: a comparison of chronic "postviral" fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg Psychiatry* (in press).

ERYTHROPOIETIN IN ACUTE RENAL FAILURE

SIR,—Dr Nielsen and Dr Thaysen (March 18, p 264) report erythropoietin (EPO) levels in acute renal failure (ARF). We have measured EPO concentrations serially in five patients with oliguric ARF. Two examples illustrate the trend (figure), in a 21-year-old man (crush syndrome) and a 67-year-old woman (gram-negative septicaemia). EPO concentrations fell rapidly within 2–3 days of onset and remained very low throughout the course of ARF and for some time after normal renal function had been regained.

EPO is produced in the peritubular cells of the kidney. In acute tubular necrosis a precipitous fall in EPO followed by a rapid rise on recovery of tubular function might be expected. However, appropriate EPO levels are not achieved for at least three weeks after serum creatinine and renal tubular concentrating power have returned to normal. This suggests that the manufacture or control of production of EPO does not recover with other aspects of tubular function.

Haemoglobin concentrations fall rapidly in the first few days of ARF. Even allowing for shortened red-cell survival, EPO deficiency cannot be a major factor in the development of anaemia unless ARF is unduly prolonged. Haemoglobin concentrations often take weeks to return to normal, and inappropriately low EPO production in the recovery phase may account for the slow rise. Treatment with recombinant EPO could hasten complete recovery from ARF.



EPO, haemoglobin, and serum creatinine in two cases of ARF, showing duration of oliguria and of dialysis dependence.

●—● = haemoglobin (g/dl); ■—■ = creatinine (µmol/l); stars indicate blood transfusion.

General Infirmary at Leeds,
Leeds LS1 3EX

G. W. LIPKIN
R. KENDALL
P. HAGGETT
J. H. TURNEY
A. M. BROWNJOHN

LIPID-LOWERING DRUGS IN TREATMENT OF HYPERLIPIDAEMIA ASSOCIATED WITH NEPHROTIC SYNDROME

SIR,—Rabelink et al[1] compared the efficacy of cholestyramine, a bile-acid binding resin, with simvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor, in the treatment of hyperlipidaemia in patients with nephrotic syndrome. Simvastatin inhibits the rate-limiting step in the intracellular biosynthesis of cholesterol and reduces low-density lipoprotein (LDL) cholesterol in plasma. We[2,3] and others[4] have suggested that HMG-CoA reductase inhibitors are the therapy of choice since the underlying mechanism for the hyperlipidaemia in nephrotic syndrome is essentially increased synthesis and not defective catabolism. It may be wise, however, to proceed with caution in this form of therapy, at least with regard to dosage. Before our use of lovastatin, another HMG-CoA reductase inhibitor, in patients with nephrotic syndrome, we evaluated the drug in a rat model.

Nephrotic syndrome was induced in 24 male Sprague-Dawley rats (180–270 g) by daily intraperitoneal injection of three doses of puromycin aminonucleoside 80 mg/kg, which is sufficient to produce overt nephrotic syndrome.[5] The animals were then randomly divided into a treatment group (n = 12), which received a daily oral dose of lovastatin 25 mg/kg (a dose slightly below the minimum toxic dose for rats indicated by the manufacturers); the other group was the controls.

Lovastatin reduced the elevated LDL cholesterol levels associated with nephrotic syndrome, but between days 14 and the end of the experiment (day 20) 6 of the 12 lovastatin-treated rats died. Necropsy revealed extensive hepatocellular necrosis and vacuolar degeneration. The 6 surviving animals, compared with the controls, showed no hepatic abnormalities that were inconsistent with puromycin-induced nephrotic syndrome; renal histological findings in all the rats were compatible with minimal change disease.

We are investigating whether the deaths resulted from the induced nephrosis (although this is a well established model), from the toxicity of lovastatin in combination with puromycin, or whether the dosage of the lipid-lowering agent needs to be reduced in nephrotic syndrome. This condition predisposes to hepatic and renal dysfunction, and reduced plasma albumin levels may result in increases in uncomplexed (and consequently toxic) circulating drug levels.

Lipid Research Unit,
Hospital de Sant Joan de Reus,
43021 Reus, Spain

J. JOVEN
L. MASANA
E. VILELLA
P. R. TURNER

1. Rabelink AJ, Hené RJ, Erkelens DW, Joles JA, Koomans HA. Effects of simvastatin on lipoprotein profile in hyperlipidaemia of nephrotic syndrome. *Lancet* 1988; ii: 1335–38.
2. Joven J, Villabona C, Masana L, Vallés M. Increased low density lipoprotein synthesis in patients with nephrotic syndrome. *Med Sci Res* 1987; **15:** 847–48.
3. Joven J, Masana L, Villabona C, et al. Low density lipoprotein metabolism in rats with puromycin aminonucleoside induced nephrotic syndrome. *Metabolism* (in press).
4. Vega G, Grundy SM. Lovastatin therapy in nephrotic hyperlipidemia: effects on lipoprotein metabolism. *Kidney Int* 1988; **33:** 1060–68.
5. Messina A, Davies DJ, Dillane PC, Ryan GB. Glomerular epithelial abnormalities associated with the onset of proteinuria in aminonucleoside nephrosis. *Am J Pathol* 1987; **126:** 220–30.