celiac sprue or sprue like disease. *Lab Invest* 1989;**60**:106A.
4 Hansky J, Shiner M. Gastric studies in idiopathic steatorrhea. *Gastroenterology* 1985; **45**:49–56.
5 Gillberg R, Kastrup W, Mobacken H, Stockbrügger R. Gastric morphology and function in dermatitis herpetiformis and in coeliac disease. *Scand J Gastroenterol* 1985;**20**: 133–40.

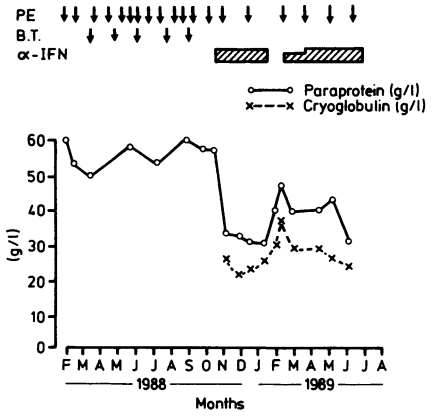
Treatment of Waldenström's macroglobulinaemia with α interferon

Alpha interferon has been shown to have some activity against B cell non-Hodgkin's lymphomas, primarily the low grade histological types.[1] It has also been used in Waldenström's macroglobulinaemia, but its activity in this disorder is not very well documented.[2] We report a patient with Waldenström's macroglobulinaemia and cryoglobulinaemia, who derived considerable benefit from treatment with α interferon.

A 68 year old Caucasian woman presented in November 1985 with a six month history of recurrent epistaxis, night sweats, and severe Raynaud's disease. She also complained of blurring of vision. On examination the fingers were blue, there was no lymphadenopathy, and the spleen was just palpable. Fundal examination showed typical changes of hyperviscosity. A full blood count showed: haemoglobin concentration of 10·7 g/dl, white cell count of 8·7 10^9/l with a normal differential, and a platelet count of 360 × 10^9/l. Urea and electrolytes and liver function tests were normal, but the total protein was raised at 126 g/l, with the presence of an IgM λ paraprotein band. There was minimal immune suppression and Bence-Jones protein was absent. The paraprotein band was quantitated at 55 g/l, of which 40 g was a cryoglobulin. The bone marrow findings were consistent with a diagnosis of Waldenström's macroglobulinaemia.

She had urgent plasmapheresis with good resolution of her symptoms, but as Bence-Jones protein became detectable within the next few months, she was started on a course of chlorambucil, 10 mg daily for seven days, repeated every four weeks. As there was no change in the paraprotein concentration, this was discontinued. She continued to have plasma exchanges every four to six weeks and remained quite well. In early 1988, however, her condition began to deteriorate and she was given cyclophosphamide, 1 g intravenously, at monthly intervals. This was discontinued after six months as the paraprotein concentration had not changed. Moreover, she was requiring regular blood transfusions.

By October 1988, despite three weekly plasma exchanges, her general condition continued to deteriorate. She had excessive gum bleeding, her visual disturbance worsened, and she had several episodes of loss of consciousness. She was therefore given α interferon (Intron A), 3 megaunits three times weekly. The figure shows the striking response of the paraprotein and cryoglobulin concentrations to treatment with α interferon. In particular, she required no further blood transfusion and needed only one plasma exchange in the ensuing three months. She experienced severe side effects from α interferon, however, and it was temporarily discontinued. The paraprotein concentration increased, with reappearance of her symptoms, necessitating an urgent plasma exchange. She was given another preparation of α interferon (Roferon A) at a lower dose (3 megaunits twice weekly), without much improvement in her symptoms. When the interferon was increased to 3 megaunits three times weekly, the cryoglobulin concentration fell to around 25 g/l and her symptoms disappeared. She remains well and has not required any further plasma exchange since June 1989.



Response of paraprotein and cryoglobulin concentrations to treatment with α interferon. PE = plasma exchange; BT = blood transfusion.

This case shows that α interferon may be useful in the treatment of refractory Waldenström's macroglobulinaemia, especially in association with cryoglobulinaemia. It may also be worth exploring its use in cases of cryoglobulinaemia from other causes.

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1 Wagstaff J, Loynds P, Crowther D. A phase II study of human and rDNA alpha-2 interferon in patients with low grade non-Hodgkin's lymphoma. *Cancer Chemother Pharmacol* 1986;**18**:54–8.
2 Ozer H, Ratanatharathorn V, Leavitt R, *et al. Proceedings of the American Society of Clinical Oncology*, 1985;**4**:214.

Apoptotic cell death during renal transplant rejection

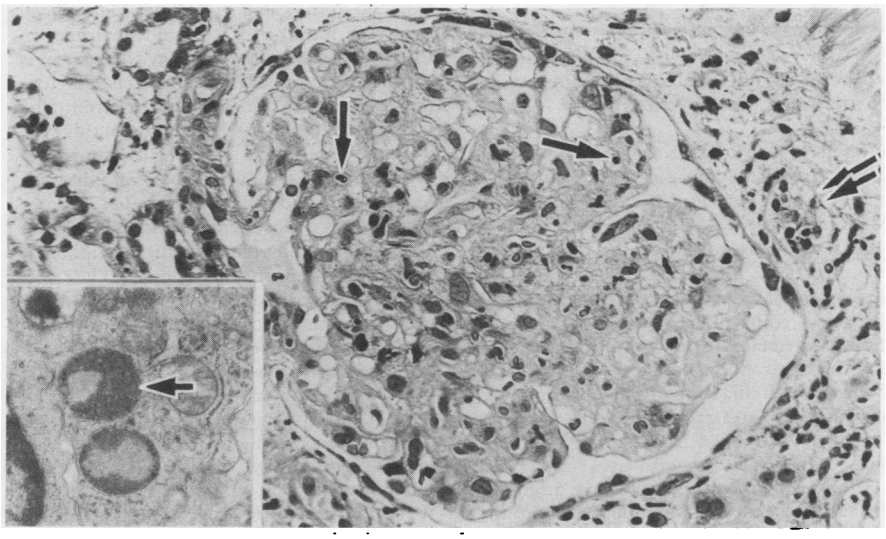
Apoptosis is a form of intrinsically programmed cell death described in a wide range of physiological and pathological states.[1] Its occurrence has been documented in several renal disorders.[2] Acute rejection of renal transplants produces widespread damage, principally in tubules and vasculature, but glomerular abnormalities have been reported.[3] Although well described, the pathogenesis of much of this damage is unclear. We describe a case of acute renal transplant rejection in which cell death by apoptosis was striking within the glomeruli and tubules.

A 45 year old woman who had had a functioning renal transplant for nine months presented with a pronounced decline in renal function. Rejection was clinically confirmed by biopsy and the patient responded slowly to increased doses of immunosuppressive drugs. A second biopsy specimen two and a half weeks later showed diminished but continuing active rejection which eventually responded to immunosuppression. Four and a half months after that, however, a further decline in renal function occurred with a third biopsy specimen showing chronic rejection.

The first biopsy specimen showed acute rejection with a prominent interstitial lymphocytic infiltrate and a "tubulitis" with tubular necrosis. Endothelial swelling, foam cells, lymphocytic infiltration and oedema were present in the intima of medium and large sized arteries. A variable expansion in mesangial matrix was seen, but striking cell death by apoptosis was identified, principally in endothelial cells but also in the mesangium (figure). Review of the tubular damage showed, focally, a similar mode of cell death. Electron microscopic examination showed characteristic apoptotic nuclear fragments with condensed, featureless chromatin. Some had been phagocytosed by other cells (figure; inset).

The second biopsy specimen was similar but the rejection process was milder. Apoptotic cell death persisted in the glomeruli. Arterial narrowing, tubular atrophy, and interstitial fibrosis typical of chronic vascular rejection were seen in the third biopsy specimen.

As far as we know, this is the first description of apoptosis during acute renal trans-



Glomerulus with prominent apoptotic bodies in characteristic scattered distribution (single arrow). Interstitial infiltration and tubulitis are also seen (double arrow) (Haematoxylin and eosin). Inset: apoptotic body in tubular epithelial cell.

plant rejection. The absence of staining for leucocyte markers and the characteristic electron microscopic findings show that the light microscopic appearances do not merely represent inflammatory cell fragmentation. The pathogenesis of this finding is uncertain. Mild ischaemia and cytotoxic T lymphocyte mediated killing can both cause apoptosis.[4] Clinically important ischaemia must have occurred in this case because of the severity of vascular damage. Lymphocytic infiltration was seen in tubules but was absent in glomeruli. In rats perfusion of kidneys with Lyl antibody, which binds to mesangium, induces "mesangiolysis", changes morphologically similar to apoptosis.[5] Antibody dependent mechanisms are thought to be important in vascular rejection with endothelial cells the principal target. Interestingly, apoptosis was most prominent in glomerular endothelial cells.

The importance of apoptosis in transplant rejection is unclear. It may represent a specific form of cell killing or be a reflection of ischaemia. Further studies are underway to assess its clinical importance in various patterns of rejection and its prognostic value, if any.

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1 Wyllie AH. What is apoptosis? *Histopathol* 1986;10:995–8.
2 Harrison DJ. Cell death in the diseased glomerulus. *Histopathol* 1988;12:679–83.
3 Porter KA. Renal transplantation. In: Heptonstall RH, ed. *Pathology of the Kidney*. Vol. 3. 3rd Edition. Boston: Little, Brown & Co, 1983:1455–547.
4 Ucker DS. Cytotoxic T lymphocytes and glucocorticoids activate an endogenous suicide process in target cells. *Nature* 1987;327:62–4.
5 Yamamoto T, Wilson CB. Quantitative and qualitative studies of antibody induced mesangial cell damage in the rat. *Kidney Int* 1987;32:514–25.

MATTERS ARISING

Value of throat swabs from index cases of meningococcal meningitis

We believe that Jewes, Norman, and McKendrick[1] may have misinterpreted our comments in Broadsheet 121 (Investigation of Meningococcal disease)[2] on the value of throat swabs as an aid to the diagnosis of meningococcal meningitis. They point out that strains of meningococci isolated from the throats of contacts are often different from the strain isolated from the index case, and that throat swabbing contacts is of no value. We agree with this contention; large numbers of contact isolates received at the reference laboratory show just how diverse these can be.

In the Broadsheet, however, we discussed the value of a throat swab obtained from the *index* case as an aid to diagnosis. Meningococci can be isolated from throat swabs in about half the cases of invasive meningococcal disease, and the isolation rate seems to be unaffected by parenteral antibiotic treatment administered within three or four hours of the collection of the throat swab (Cartwright KAV, unpublished observations). While in theory it may be possible for a case to yield different strains from cerebrospinal fluid, blood, and throat cultures, in practice this situation has never been encountered among the many "sets" of such strains received at the reference laboratory each year. If a meningococcus is isolated from a throat swab in addition to a deep site (blood or cerebrospinal fluid) the strains are always of the same group and type (though strains from the throat are often less well endowed with capsular polysaccharide and are therefore occasionally non-groupable).

We therefore reiterate our belief in the value, both clinical and epidemiological, of throat swabs collected from the index case, especially when the patient has been given parenteral penicillin by the general practitioner or when a lumbar puncture has not been performed.

We are currently preparing data for publication on the pattern of meningococcal carriage in contacts of cases of meningococcal disease.

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1 Jewes L, Norman P, McKendrick MW. Value of throat swabs in meningococcal meningitis. *J Clin Pathol* 1989;42:1229.
2 Cartwright KAV, Jones DM. Investigation of meningococcal disease. *J Clin Pathol* 1989;42:634–9.

Leukaemic phase of mantle zone lymphoma

The article, "Leukaemic phase of mantle zone (intermediate) lymphoma: its characterisation in 11 cases,"[1] was very informative. Intermediate lymphocytic lymphoma (ILL) can pose problems with regard to correct diagnosis and therefore treatment. In their introduction the authors mention that in the Working Formulation most cases would be assigned to the category of small cleaved cell type with intermediate prognostic grade. In their discussion, however, they state that it is a form of low grade lymphoma. It is therefore not clear from this paper or from the literature as to the proper grading of this type of lymphoma in the Working Formulation. Weisenburger *et al*, on the basis of immunophenotyping and cytogenetic studies, suggest that there is a close lineage relation between ILL and small lymphocytic lymphoma/chronic lymphocytic leukaemia.[2] They feel that on the basis of their differing clinical, cytological, and architectural features, cases of ILL should be considered a separate category of lymphocytic lymphoma of the Working Formulation. On the other hand, the median survival of less than 24 months in the series reported by Pombo de Oliveira, Jaffe, and Catovsky,[1] and 22 months (leukaemic patients) in the series reported by Weisenburger *et al*,[3] would tend to suggest that it may be more appropriately classified into the intermediate prognostic grade. In the latter series, even in cases without leukaemic phase, the median survival was only 35 months.

Perhaps a multi-institutional study comprising a large number of cases, which also incorporate immunological and cytogenetic data, would result in a better understanding and therefore a more appropriate categorisation of this non-Hodgkin's lymphoma.

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1 Pombo de Oliveira MSI, Jaffe ES, Catovsky D. Leukaemic phase of mantle zone (intermediate) lymphoma: its characterisation in 11 cases. *J Clin Pathol* 1989;42:962–72.
2 Weisenburger DD, Sanger WG, Armitage JO, Purtilo DT. Intermediate lymphocytic lymphoma: immunophenotypic and cytogenetic findings. *Blood* 1987;69:1617–21.
3 Weisenburger DD, Nathwani BN, Diamond LW, Winberg CD, Rappaport H. Malignant lymphoma, intermediate lymphotic type: a clinicopathologic study of 42 cases. *Cancer* 1981;48:1415–25.

HPV or human parvovirus?

A short while ago a letter in this Journal commented on the inappropriateness of the designation "HPV" for human parvovirus, stating that HPV had been the denominator for human papillomaviruses for many years.[1]

At the risk of the subject becoming tedious, I would like to expand on this issue. Earlier this year I expressed concern regarding the use of the abbreviation "HCV" for a newly identified non-A, non-B hepatitis virus designated C. As far back as 1975 a report by the Study Group of Coronavirus, Vertebrate Virus Subcommittee, International Committee on the Taxonomy of Viruses (ICTV) proposed a list of abbreviations for the species of coronavirus, including HCV for human coronavirus.[2] This and abbreviations for other coronaviruses were again stated in the second report of the ICTV Coronavirus Study Group 1978.[3]

The use of the abbreviation HCV for a hepatitis C virus in man could cause considerable confusion, and matters could get worse should another candidate non-A, non-B hepatitis virus be designated hepatitis E virus (HEV). This abbreviation already exists for porcine haemagglutinating encephalitis virus – by chance another coronavirus! In my opinion it is therefore inappropriate to use the abbreviation HCV for anything other than human coronavirus. If it is necessary to classify viruses causing hepatitis in man as A, B, C, D, etc, then the name should surely be prefixed with the word human—human hepatitis C virus HHCV.

I have been informed that abbreviations of virus names have no formal or official status. Why, then, are they acceptable as key words on papers? Literature searches can be difficult enough without further avoidable complications! Clearly, virus name abbreviations need to be regulated by the appropriate virus study group – now.

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1 Vermeer-De Bondt PE, Van Elsacker-Niele AMW. Designation of "HPV" for human parvovirus. *J Clin Pathol* 1989;42:780.
2 Tyrell DAJ. Coronaviridae. *Intervirology* 1975;5:76–82.
3 Tyrell DAJ. Coronaviridae: Second Report. *Intervirology* 1978;10:321–8.