None of them had a history suggestive of tropical spastic paraparesis, the other known syndrome associated with HTLV-1 infection. Our patient was a second generation immigrant from south China. She had never travelled to HTLV-1 endemic areas, but had received a blood transfusion for post-partum haemorrhage during delivery of her first child.

**Comment**

HTLV-1 infections have not been widely documented in east Asia outside of Japan and Taiwan. The seroepidemiological pattern of this infection in South East Asia has not been well studied. A recent serological survey of 9689 healthy blood donors and pregnant women in Singapore showed an incidence of 0.03% (unpublished data). This is close to the 0.025% seroprevalence documented in blood donors in the United States.4

The fact that both vertical and horizontal transmission of this infection can readily occur is well illustrated by this case. This ease of transmission is of concern, especially when pockets of HTLV-1 infection have been documented in unusual areas.5 At the least, seroepidemiological trends must be monitored to ensure that the problem does not take on greater proportions.

---

**Treatment of acute myeloid leukaemia in a renal allograft recipient: Implications of cyclosporin immunosuppressive treatment**

R J G Guthbert, N H Russell, P A E Jones, A G Morgan

**Abstract**

The clinical effects of cyclosporin were evaluated during cytotoxic treatment in a 61 year old man with acute myeloid leukaemia. He had received a renal transplant 18 months before presenting with acute myeloid leukaemia (FAB subtype M4). He had received cyclosporin 3.5-4.0 mg/kg daily to maintain a plasma cyclosporin concentration of 75-150 ng/ml. Cyclosporin was continued during induction chemotherapy with daunorubicin, cytarabine, and 6-thioguanine (DAT). He had fever and oropharyngeal candidiasis that was unresponsive to anti-bacterial drugs but responsive to systemic amphotericin. Bone marrow examination 14 days after chemotherapy showed complete haematological remission. Subsequently he tolerated consolidation treatment with DAT with no serious complications. Unfortunately he developed fatal septicaemia following a second consolidation with mitozantrone and cytarabine.

Inhibition of P-glycoprotein activity by cyclosporin may not significantly increase the toxicity of aggressive chemotherapeutic regimens, and as benefit may be achieved by this approach further clinical evaluation is justified.

In the management of malignant disease resistance to cytotoxic drugs often makes treatment unsuccessful. Interest has developed in studying the possible benefits of inhibiting the activity of P-glycoprotein to circumvent cytotoxic drug resistance.1 P-glycoprotein is a 170 kilodalton transmembrane glycoprotein which acts as an energy dependent pump, causing active efflux of structurally hetero-

---

Case report
In March 1988 a 61 year old man received a cadaver renal allograft for end stage polycystic disease. He was treated with cyclosporin 3.5–4.0 mg/kg daily and prednisolone 10 mg daily. The plasma cyclosporin concentration was maintained in the range 75–150 ng/ml.

In September 1989 he developed malaise and fever. The peripheral blood count showed a white cell count of $79 \times 10^9/l$ with 95% blasts. The bone marrow showed 80% AML blasts (M4) with suppression of normal haemopoiesis. Cytogenetic analysis showed a normal 46,XY karyotype. He was treated with daunorubicin 50 mg/m², for three doses on alternate days, cytarabine 100 mg/m², 12 hourly, and 6-thioguanine 100 mg/m², 12 hourly, for 10 days (DAT 3 + 10). He continued to receive cyclosporin 3.5–4.0 mg/kg daily and prednisolone 10 mg daily throughout his treatment. His fever was unresponsive to anti-bacterial drugs. He developed moderately severe oropharyngeal candidiasis which did not respond to topical antifungal treatment. He was given intravenous amphotericin 0.6 mg/kg daily with a good clinical response. Bone marrow examination two weeks after chemotherapy showed complete haematological remission.

Subsequently he received two courses of consolidation chemotherapy: daunorubicin 50 mg/m² for two doses on alternate days, cytarabine 100 mg/m², 12 hourly and 6-thioguanine 100 mg/m², 12 hourly, for seven days (DAT 2 + 7). This was followed after one month by cytarabine 1 g/m², 12 hourly, for three days and mitozantrone, 10 mg/m² daily, for five days (MidAC). The figure shows the haematological and renal responses to chemotherapy. There were no clinical complications following DAT 2 + 7. After MidAC, however, while severely neutropenic, he developed Pseudomonas aeruginosa septicaemia, and despite aggressive antibiotic and supportive treatment he died from acute renal failure and adult respiratory distress syndrome.

Discussion
Myelodysplasia and acute myeloid leukaemia have been described in renal allograft recipients treated with azathioprine.\textsuperscript{7} We know of only one previous report of the development of acute myeloid leukaemia in such patients receiving cyclosporin.\textsuperscript{8} This patient had also received azathioprine. One further unpublished case is cited in this report. Our patient had been given immunosuppressive treatment with cyclosporin for 18 months before the onset of acute myeloid leukaemia. Although a causal relation between his relatively short duration of immunosuppression and the subsequent development of acute myeloid leukaemia seems unlikely, the possibility cannot be excluded.

Remission induction was achieved relatively easily in our patient. There was no evidence that his concurrent cyclosporin treatment caused increased toxicity to normal tissues or to his grafted kidney. This suggests that inhibition of P-glycoprotein with drugs such as...
Inhibition of urease activity but not growth of Helicobacter pylori by acetohydroxamic acid

J Goldie, S J O Veldhuyzen van Zanten, S Jalali, H Richardson, R H Hunt

Abstract
The in vitro effects of acetohydroxamic acid (AHA), a potent urease inhibitor, were studied to determine the effect on the urease activity and growth of 38 strains of Helicobacter pylori. AHA in concentrations of 50-1000 mg/l had a noticeably reversible inhibitory effect on the urease activity of the organism but no effect on growth.

Helicobacter pylori has a very high urease activity which is thought to be related to its pathogenicity, allowing it to colonise and survive in the harsh gastric environment. There is a need for a more effective treatment against H pylori because currently available treatments are unsatisfactory. Acetohydroxamic acid (AHA) is a potent inhibitor of the enzyme urease. AHA has been used in the treatment of urinary tract infections, associated with struvite stone formation, in which urea splitting organisms are important. AHA prevents alkalisation of the urine by inhibiting urease, thus preventing hydrolysis of urea and subsequent production of ammonia.

The high urease activity of H pylori might be inhibited by AHA and we therefore studied this in vitro to determine whether AHA inhibits urease activity and the growth of H pylori.

Methods
Thirty three recent clinical isolates and five reference strains (obtained from LCDC, Ottawa) of H pylori were grown microaerobically at 35°C for five days. Dense suspensions were made in 3 mmol monobasic sodium phosphate buffer (NaH2PO4) containing a concentration of AHA to approximate a final concentration of 10⁸ organisms/ml when