HTLV-III INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

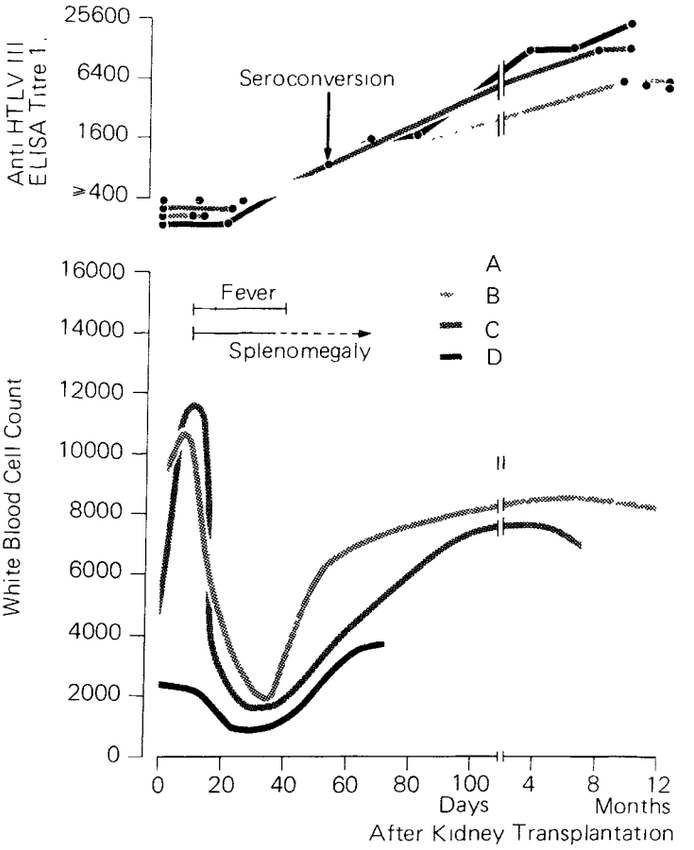
SIR,—Dr Prompt and colleagues (Sept 21, p 672) describe the transmission of AIDS virus (HTLV-III) via kidney grafts from a haemophiliac donor. While screening patients with end-stage renal disease in Berlin for antibodies to HTLV-III we found four patients who were repeatedly positive (Organon ELISA test). Antibody titres above 6400 were found in a quantitative ELISA.[1] All these sera were confirmed as positive by western blot and by indirect immunofluorescence. These four patients had received a cadaver kidney graft during 1984 from donors at high risk of AIDS. The three kidney donors had a history of intravenous drug abuse. Five of the six donated kidneys were transplanted (four in Berlin, one in Austria); the other was discarded after transport to Denmark because of prolonged cold ischaemia. The recipient in Austria is anti-HTLV-III positive 8 months after transplantation (personal communication).

Before and after transplantation sera of the four Berlin recipients were available for retrospective serological testing. Sera of all four patients before and up to 40 days post transplantation were anti-HTLV-III negative in all tests. 8 months after transplantation all four patients had HTLV-III-specific antibodies with ELISA-titres of 6400 to 25 600. For two patients sera were available for days 56 and 68; both were positive but at lower titres (C 800, D 1600) (see figure). Neither in these sera nor in sera obtained 3–5 weeks post transplantation was HTLV-III-specific IgM detectable by three different methods (preliminary results).

Post transplantation the four patients were given our standard immunosuppressive regimen, starting with prednisolone 1 mg/kg and intravenous cyclosporin 5 mg/kg.

All four patients had a similar clinical course 2–7 weeks post transplantation. Fever (up to 39°C), either recurrent and of short duration or continuing for more than 3 weeks, was observed in all four between days 12 and 47. Patients C and D had enlarged spleens at the same time, and patient D had his spleen removed because of infarction 5 months post transplantation. The most remarkable finding was pronounced leucopenia and lymphopenia in all four patients around day 12 (figure) and lasting up to day 55. An immediate rise in white blood cell count is generally seen in kidney graft recipients, as a result of massive prednisolone medication. 3–5 weeks post transplantation, WBC counts had returned to normal. No decrease in WBC below normal is usually seen after transplantation and immunosuppression with cyclosporin, except in patients with, for example, acute cytomegalovirus (CMV) infection. Such infections were not detected in the four recipients at that time and we interpret the clinical course observed as an "acute AIDS virus infection".[2]

Patient D had received five, patients A and B one and patient C two blood transfusions post transplantation. The estimated prevalence of anti-HTLV-III positivity among Berlin blood donors in 1984 was less than 0·001%, and since all four recipients got infected from three kidney donors at high risk of AIDS we must conclude that the kidney grafts were the source of all four HTLV-III infections. Two recipients of cornea grafts from one donor are negative for anti-HTLV-III 18 months after transplantation. The husband of patient B was seropositive when tested one year after his wife had received the kidney graft. Since he was not otherwise at risk



Clinical course, HTLV-III antibody titres, and white blood cell counts in four recipients of HTLV-III infected kidney transplants.

Stored serum samples (●) of recipients A–D were diluted and tested at the same time by quantitative ELISA. White blood cell counts were done daily up to day 30–50 after transplantation and two or three times weekly thereafter.

of HTLV-III infection he became infected through sexual contact with his wife. All four children (4 to 14 years) of this couple are seronegative.

Three patients are now on daily cyclosporin maintenance doses designed to achieve blood drug levels of 200–400 ng/ml.

Patient C is becoming leucopenic and lymphopenic 10 months after infection, with a T-helper cell count of only 93/μl (normal 600–1200) and an OKT_4/OKT_8 ratio of 0·3. Patients A and B have ratios of 0·7–1·6, with T-helper cell counts of 300–750/μl. Patient D (splenectomy, graft failure by chronic rejection, and no longer on cyclosporin) had generalised lymphadenopathy 18 months post transplantation with a T_4/T_8 ratio of 0·9 and a T-helper cell count above 750/μl.

We conclude that HTLV-III infection was transferred via kidney grafts from three German donors with a history of intravenous drug abuse to four recipients in Berlin and one in Austria (see table). The Berlin patients had clinical signs of acute AIDS virus infection that had disappeared by the time HTLV-III antibody was first detected. One case suggests female-to-male transmission of the virus.

A WHO working group[3] has recommended that all potential donors of blood, semen, organs, and tissue be tested for HTLV-III

FINDINGS IN THREE DONORS AND FIVE RECIPIENTS OF HTLV-III INFECTED KIDNEYS

Graft donors			Graft recipients					
						HTLV-III Ab		
Sex, age	Cause of death	Date and place of death	Place of transplant	Patient	Sex, age	Before	8 mo after transplant	Graft function
M, 38	IV drug abuse until 1982, death after alcohol intoxication; splenomegaly at necropsy	Jan, 1984; Berlin	Berlin	D	M, 28	−ve	+ve	Failure (chronic rejection)
			..*	..	..	..	.	..
M, 27	IV drug abuse; death after heroin overdose	Sept, 1984; Berlin	Berlin	A	F, 48	−ve	+ve	Stable
			Berlin	B	F, 31	−ve	+ve	Stable
F, 31	IV drug abuse until 1981; SA	Dec, 1984; Frankfurt	Berlin	C	M, 39	−ve	+ve	Stable
			Austria	E	F, 40	NT	+ve	Stable

*Other kidney not transplanted (see text) NT = not tested SA = subarachnoid haemorrhage.

antibodies and that members of groups at high-risk of AIDS be excluded as donors. This recommendation should be followed strictly.

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1. Pauli G, Vettermann W, Marcus U, et al. Riskgroups for AIDS. *Münch Med Wschr* 1985; **127:** 42–44
2. Cooper DA, Maclean P, Finlayson R, et al. Acute AIDS retrovirus infection. *Lancet* 1985; i: 537–40.
3. Anon. The acquired immunodeficiency syndrome (AIDS). Memorandum from a WHO meeting. *Bull WHO* 1985; **63:** 667–72.

PREVENTION OF AIDS

SIR,—We must take issue with your Nov 16 editorial's statement about emergency blood donor panels. In this region we discourage such panels and aim to provide a service which renders them unnecessary. However, in other areas where these panels are still used we would strongly recommend that the donors should be subjected to the same screening and testing procedures as those used by the National Blood Transfusion Service. Every donor should be asked to sign a consent form stating that he/she is in good health and is free of the conditions which would disqualify him/her as a donor (these conditions are listed on the form). Donors should state that they had read the literature explaining about AIDS and defining those individuals at high risk of contracting it. Every blood donation should be tested on every occasion for HBsAg, syphilis, and anti-HTLV-III because testing once a year is not acceptable. We have experience of acute hepatitis B infection transmitted by untested blood given by "emergency donors", and there is every reason to believe that HTLV-III transmission could occur in a similar fashion.

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SIR,—Your Nov 16 editorial reviews AIDS in the UK. However, the screening of antenatal women warrants further consideration.

The population incidence of HTLV-III antibody positivity, though low, is inexorably doubling about every eight months, greatly outnumbering females. However, heterosexual spread can occur.[1,2] Selected women may constitute reservoirs of infection: such women include drug addicts and prostitutes elsewhere[3,4] (if not in the UK[5]). In some areas where the disease has been established for a long time (eg, equatorial Africa) affected women are now about as common as men, though other, as yet ill-defined co-factors may operate in those areas.

Whereas people in the usually defined high-risk groups self-exclude as donors, antenatal women come from all walks of life and all countries regardless of known, unknown, or undeclared risk factors. Sooner or later, more will be infected and will be at least intermittently viraemic, most with demonstrable HTLV-III antibody. Should not antenatal screening therefore include tests for this antibody?

Changes in management should result from finding positives, even if only the "booking sample" is tested: any further venepunctures would require extraordinary precautions; obstetric, midwifery and other staff would arrange delivery with due regard to dissemination of infected blood; more especially, termination may be indicated because about 50% of fetuses would be infected (many later dying of AIDS) and because maternal AIDS-related complex or AIDS may deteriorate with continued pregnancy.

Antenatal serological screening in the UK is usually done at regional transfusion centres, and in many areas tests for syphilis and hepatitis B are included. HTLV-III screening, now done on all donor blood, could be extended to antenatal samples, but is informed consent obligatory? Very few antenatal women are told that their blood is screened for syphilis or hepatitis B; could not the same also apply to HTLV-III? Most women will prove negative and have nothing to fear; nothing need be said to anyone found "positive" until this has been confirmed, when management would need modifying anyway. Whilst I do not suggest that screening must necessarily be clandestine, screening with or without consent will reveal progressively more positives, proper management of which should improve containment of the virus.

Thus, further thought should be given to this introduction of antenatal screening for antibody to HTLV-III, if only on an epidemiological research basis at first, before the virus becomes more prevalent and spreads into the heterosexual population at large.

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1. Goldsmith M. More heterosexual spread of HTLV-III seen. *JAMA* 1985; **253:** 3377–79.
2. Redfield RR, Markham PD, Salahuddin SA, et al. Frequent transmission of HTLV III among spouses of patients with AIDS-related complex and AIDS. *JAMA* 1985; **253:** 1571–73.
3 Papaevangelou G, Roumeliotou-Karayannis A, Kallinikos G, et al. LAV/HTLV-III infection in female prostitutes. *Lancet* 1985; ii: 1018.
4. Clumeck N, Robert-Guroff M, van de Perre P, et al. Seroepidemiological studies of HTLV III antibody prevalence among selected groups of heterosexual Africans *JAMA* 1985; **254:** 2599–602.
5. Peutherer JF, Edmond E, Simmonds P, et al. HTLV-III antibody in Edinburgh drug addicts *Lancet* 1985; ii: 1129–30.

SIR,—Your Nov 16 editorial will encourage many more medical personnel to screen for antibodies to HTLV-III groups at risk of HTLV-III infection. The following case-history illustrates an avoidable pitfall that caused much distress.

A middle-aged bisexual man attended an outpatient department of another hospital under an alias. He was married with children and in stable employment. His family did not know he was homosexual and he had gone to great lengths to conceal this. There was a background of depressive illness with previous attempts at suicide. His blood was checked for HTLV-III antibodies and at his next visit he overheard two doctors discussing the result. On inquiring about this he was told that a test had demonstrated that his blood contained the antibody to the AIDS virus and that, while further tests would be done, he would be referred to our hospital for further counselling and long-term follow-up. He was very upset by this result and felt compelled to tell his family about his homosexuality and that he "had AIDS". At his subsequent attendance at this hospital he said that it was only his wife's decision not to leave him that had prevented him from committing suicide.

He had had new symptoms of night sweats and diarrhoea after he had been told of the result of the first antibody test but physical examination was normal. We checked his serum for HTLV-III antibodies and found it negative by enzyme-linked immunosorbent assay (ELISA) (Abbott) and by immunofluorescence. We contacted the referring hospital and found that the first blood sample had been "reactive" by ELISA (Abbott); this result had been reported by telephone as "equivocal" and interpreted as "weakly positive". A second sample had been requested and had subsequently been found to be negative, again by Abbott ELISA and a negative laboratory report had then been issued. The patient was promptly informed of these negative results.

This history shows the need for improved communication between laboratory, doctors, and patient. The laboratory may often be asked for a preliminary result—because, for instance, of the need to time an outpatient appointment—before an HTLV-III antibody test can be repeated and confirm by other test systems.[1] Phrases such as "reactive", "weakly positive", or "equivocal" may be used interchangeably and lead to misunderstanding. Doctors should be aware of the possibility of false positives with the more rapid screening tests and should not tell patients until HTLV-III antibodies have been confirmed by more specific tests. A further blood sample may be needed where test responses are inconclusive.