

### SEROCONVERSION FOR HTLV-III SINCE 1980 IN BRITISH HAEMOPHILIACS

SIR,—Three UK cases of acquired immunodeficiency syndrome (AIDS) in haemophilic patients and several reports of a pre-AIDS-like syndrome have been recorded. Human T-lymphotropic virus type III (HTLV-III) is intimately associated with AIDS and can be transmitted by transfusion of whole blood and blood products, including factor VIII concentrate.<sup>1</sup> Cheingsong-Popov et al<sup>2</sup> found that about 33% of British haemophiliacs are seropositive for antibody to HTLV-III and had presumably been exposed to and infected by the virus. A similar study in West Germany revealed a 53% seropositivity rate in haemophiliacs.<sup>3</sup>

During studies to determine the source of infection we have been able to test sera from a cohort of 20 severe haemophiliacs with factor VIII:C levels below 0.02 IU/ml. Sera were collected in 1980–81, in September, 1982, and again in September, 1984. All these patients had received regular prophylactic home therapy with factor VIII concentrate, with an average annual treatment rate of 29 000 units. Between 1982 and 1984 60% (9/15) of these haemophiliacs seroconverted for HTLV-III antibody: only 1 was seropositive in 1980–81, 5 had antibody in 1982, and 14 were seropositive in 1984. These patients had received both NHS and commercial non-heat-treated factor VIII concentrates, and had had 44–80% of their treatment requirements as commercial product. All these patients remain well although mild thrombocytopenia and lymphopenia have developed lately in 1.

We have also tested sera collected in September, 1984, from another group of 13 moderate and mild haemophiliacs who had received cryoprecipitate and/or NHS factor VIII concentrate only. These patients have had an average treatment rate of 12 500 units per year since 1982. All 13 have remained well and are seronegative for anti-HTLV-III.

These results confirm the increasing seropositivity of British haemophiliacs exposed to regular infusions of factor VIII concentrate over the past four years. We do not know what proportion of seropositive patients will acquire AIDS or other HTLV-III related disease. All 16 who are seropositive are well, including the 6 who were seropositive in 1982, and only 1 has thrombocytopenia and lymphopenia.

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1. Editorial. Blood transfusion, haemophilia and AIDS. *Lancet* 1984; ii: 1433–35.
2. Cheingsong-Popov R, Weiss RA, Dalgleish A, et al. Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain. *Lancet* 1984; ii: 477–80.
3. Gurtler LG, Wernicke D, Eberle J, et al. Increase in prevalence of anti-HTLV III in haemophiliacs. *Lancet* 1984; ii: 1275–76.

### HAEMOPHILIA AND AIDS

SIR,—Dr Bird and his colleagues (Jan 19, p 162) draw timely attention to the possible side-effects of heated blood products, but their arguments for the continued use of non-heated factor VIII concentrates are debatable. At least two contaminated batches of British factor VIII concentrate have already been identified and it is unlikely that screening for antibody to human T-lymphotropic virus type III (HTLV-III) will be available routinely at all regional transfusion centres for several months. Even then antibody-negative viraemic donors will not be excluded. Furthermore, the prevalence of HTLV-III infection in British homosexuals seems to be increasing. Experience with hepatitis B indicates that even with sensitive and reliable donor antigen screening tests, most haemophiliacs treated with large pool products eventually seroconvert. Although American concentrates pose the most risk, untreated factor VIII concentrates of any type must be considered potentially to be infected with HTLV-III. The Advisory Committee

on Dangerous Pathogens has published stringent interim guidelines for handling dangerous samples in the laboratory. It seems unreasonable therefore to recommend that the risks from spillage of patients' blood during intravenous therapy should be compounded by preparing and injecting infected materials in hospital or domestic practice.

Whilst attempts are often made to restrict viral exposure by reserving batches for individual patients, rapid turnover and lack of stocks of British concentrates often makes this logistically impracticable. Plans sometimes fail after hours when treatments are administered by inexperienced staff. The proposals of Bird and colleagues could lead to infection of previously uninfected patients or family members.

Heated factor VIII concentrates have been used for over a year without immunological complications being reported. All the manufacturers, including the National Health Service, look for altered proteins and neoantigens by immunoradiometric and other methods. Licensed products are also checked by the control agency at the National Institute for Biological Standards and Control. Factor VIII is a trace protein and the specific activity of several commercial concentrates is higher and general protein content lower than those of current NHS concentrates. Even in the heated state high purity commercial concentrate could induce less general immune response than unheated NHS concentrate. If immune stimulation is relevant to retroviral replication one could envisage a relation between acquired immunodeficiency or related syndromes and factor VIII inhibitor after treatment even with unheated factor VIII, and we have some unpublished data to support this. On a theoretical, non-specific immunological basis, current heated British concentrate is one of the less desirable products but data on these aspects are not available.

In the end the complications and efficacy of heat-treated concentrates will depend upon clinical and serological follow-up, and the preliminary results of Dr Rouzioux and colleagues (Feb 2, p 271) concerning HTLV-III (LAV) antibody are encouraging. Nevertheless, Bird and his colleagues are right to draw attention to the possible immunological risks because these, as well as the degree of protection from HTLV-III, may be dose-related. A hierarchical assignment of risks from single donor cryoprecipitate and various heated concentrates together with different patient characteristics such as age, previous treatment, and HTLV-III serology should be made before each lesion is treated. The use of coagulation factor concentrates in the UK is still increasing by arithmetic progression. It may be wise, now, to take stock of the situation so that treatment intensity at least levels out until the possible risks can be more rationally assessed.

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### ANTIBODY TO HTLV-III IN BLOOD DONORS IN CENTRAL AFRICA

SIR,—With acquired immunodeficiency syndrome (AIDS) in Africans in Europe<sup>1</sup> or central Africa,<sup>2,3</sup> heterosexual contact is the principal mode of transmission of the AIDS virus. The relative importance of other routes in this population is unknown. In the United States AIDS is sometimes transmitted through blood transfusions.<sup>4</sup> We report here an African case of AIDS probably transmitted by this route.

In November, 1983, a healthy female student, aged 17, was delivered of a normal baby after a full-term, uneventful pregnancy, in the Centre Hospitalier, Kigali, Rwanda. Severe post partum bleeding necessitated the transfusion of 6 units of whole blood. The patient recovered and remained well until April, 1984, when generalised lymphadenopathy, fever, a 12 kg weight loss, fatigue, and diarrhoea developed. In May her baby died at home from dehydration related to gastroenteritis. In July a 7 cm cervical lymph node was studied by biopsy and *Mycobacterium tuberculosis* adenitis was diagnosed. The patient complained of nausea and dysphagia. Oesophagoscopy, biopsy, and culture disclosed massive oesophageal candidiasis. Delayed hypersensitivity skin testing was