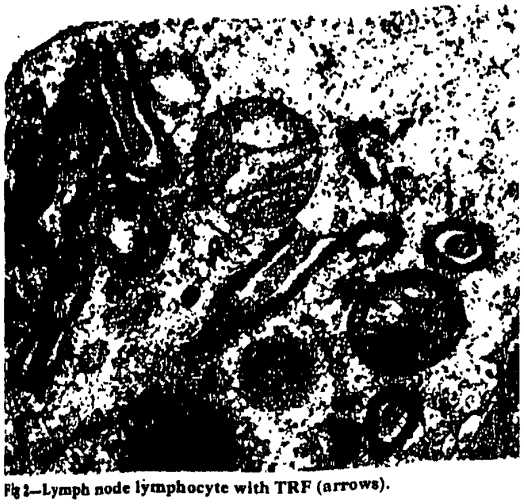

Fig 2—Lymph node lymphocyte with TRF (arrows). (×20 000.)

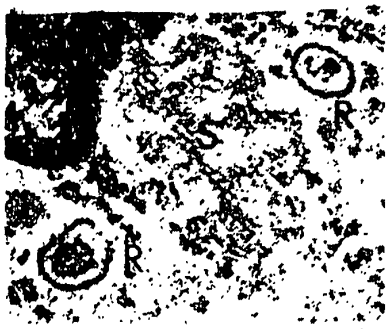

Fig 3—Tissue retrieved from paraffin-embedded lymph node.

Note a TRS (S) and two TRF (R). (×35 750.)

TRF have been described only once before, in a Japanese case with adult T cell leukaemia.[7] Patients with this disease harbour the human T leukaemia virus (HTLV).[8] The nature of TRF and their relation to this or any other agent is unknown.

TRS and TRF appear to be ultrastructural markers of AIDS.

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FACTOR VIII PRODUCTS AND DISORDERED IMMUNE REGULATION

SIR,—Altered distribution of T-lymphocyte subpopulations in young haemophiliacs under treatment with factor VIII concentrate in Washington, DC, has lately been reported in *The Lancet*.[1] Similar observations in other haemophiliacs in Ohio and Wisconsin were reported earlier this year[2,3] and a recent report from Iowa describes similar observations.[4] By March 3, 1983, eleven cases of clinical acquired immunodeficiency syndrome (AIDS) in haemophiliacs had been reported to the Centers for Disease Control; all had received factor VIII concentrate. These observations are consistent with the hypothesis that AIDS is caused by a transmissible agent, presumably a virus, that can be included in blood products, and that some recipients of the agent have not (at least not yet) developed the complete clinical syndrome with its devastating complications. They are also compatible, however, with the possibility that repeated administration of factor VIII concentrate from many varied donors induces a mild disorder of immune regulation by purely immunochemical means, without the intervention of an infection. Such a mild immunosuppression could predispose to subsequent infection with a biological agent.

These alternative hypotheses might be distinguished through a study of T-lymphocyte subpopulations among similarly treated haemophiliacs in a geographical area to which AIDS has not yet been introduced. The resolution of this question by a timely investigation in some country, where cases of AIDS have not yet been reported would be an immense help to public health workers worldwide. In this situation "negative results" would be of great significance.

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ABNORMAL T-LYMPHOCYTE SUBPOPULATIONS ASSOCIATED WITH TRANSFUSIONS OF BLOOD-DERIVED PRODUCTS

SIR,—The T-lymphocyte abnormalities which accompany the acquired immunodeficiency syndrome (AIDS) have also been observed in some patients with haemophilia A, in the presence or absence of opportunistic infections.[5-8] Because homosexuality and intravenous drug abuse were not associated with these cases, repeated exposure to lyophilised factor VIII concentrates[7,8] with possible transfer of an undefined blood-borne agent(s)[9] has been an implicated aetiological factor for these patients' immune dysfunction. Menitove et al[7] and Lederman et al[8] suggest that the risk of developing impaired T-lymphocyte function may be negligible in haemophiliacs treated only with cryoprecipitate or fresh frozen plasma.

We have studied groups of patients repeatedly exposed to lyophilised FVIII concentrates or to other blood products (table). All the patients had a good performance status and were evaluated in the absence of concurrent illnesses. T-lymphocyte subpopulations were counted by flow cytometry and indirect immunofluorescence with monoclonal antibodies OKT3 (pan T cell), OKT4 (helper/inducer T-cells), and OKT8 (suppressor/cytotoxic T-cells).

Haemophiliacs treated with lyophilised FVIII concentrates had a significantly reduced mean T4/T8 ratio compared with age and sex-matched controls. Similarly, T4/T8 ratios were much depressed in von Willebrand's disease, mild haemophilia A, and in hypertransfused patients with sickle cell anaemia. These groups received cryoprecipitate, fresh frozen plasma, or packed red cells exclusively. Mildly decreased T4/T8 ratios have been noted in hypertransfused subjects with β-thalassaemia (P. Gaseon, N. S. Njaung, and others, unpublished), Diamond-Blackfan syndrome, and congenital dyserythropoietic anaemia (table), but numbers are too small for statistical testing. In contrast, those treated with prothrombin

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