HAEMOPHILIA AND TUBERCULOSIS

SIR,—Impaired cell-mediated immunity and opportunistic infections have been described in patients with haemophilia A.[1] We describe here an unusual outbreak of tuberculosis amongst children with bleeding disorders—including haemophilia A, christmas disease (factor IX deficiency), and von Willebrand's disease.

During a one month period at the end of 1981, a patient on a ward at our hospital was regularly visited by her mother, who was later found to have pulmonary tuberculosis. The ward is used for inpatient haematology, oncology, and general paediatric conditions and also an outpatient haemophilia service.

X-ray screening of at-risk patients revealed a high incidence of pulmonary lesions consistent with pulmonary tuberculosis (table).

X-RAY EVIDENCE OF TUBERCULOSIS

Inpatients	Exposed (at risk)	With tuberculosis
Leukaemia/solid tumours	21	10 *(48%)*
Bleeding disorders	16	6 *(38%)*
Other paediatric conditions	78	3 *(4%)*

The children with leukaemia and solid tumours would be expected to have a significant degree of immunosuppression due to chemotherapy. The surprising finding was the frequency of pulmonary tuberculosis amongst the patients with bleeding disorders. This was approaching the level found in the chemotherapy group and was considerably greater than that in the patients with other paediatric conditions. None of the children with bleeding disorders acquired miliary tuberculosis.

Abnormalities of lymphocyte T-cell subpopulations have been reported in patients with haemophilia A, and related to treatment with lyophilised factor VIII concentrates but not with cryoprecipitate infusions.[2,3] We have yet to complete detailed immunological studies of these children, but it is interesting that 1 received only cryoprecipitate and another only prothrombin complex infusion. Preliminary analysis of treatment in the year before tuberculosis exposure, has indicated that those patients with bleeding disorders who had pulmonary disease received about twice as many units of factor replacement as did those in whom the disease did not develop. Whilst development of disease related to duration of exposure and proximity to the index case, the higher attack rate in the bleeding disorder patients was confirmed even when these factors were allowed for. (1 patient, not included in the table, had pulmonary tuberculosis after one brief outpatient visit.)

The results suggest an unusual susceptibility to an opportunistic organism amongst our patients with bleeding disorders, possibly related to abnormal cell-mediated immunity.[1-3]

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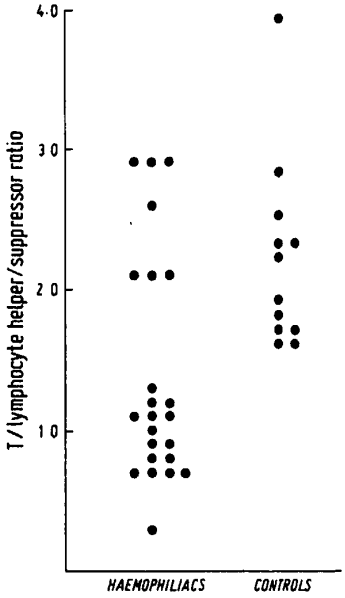
DISORDERED IMMUNE REGULATION IN HAEMOPHILIACS NOT EXPOSED TO COMMERCIAL FACTOR VIII

SIR,—Dr Gordon, in his stimulating letter (April 30, p 991), wondered whether T-lymphocyte abnormalities in haemophiliacs result solely from infusion of foreign proteins or whether they are due to contamination of the factor VIII concentrates by an AIDS (acquired immunodeficiency syndrome) virus, and he appealed for data to differentiate between these two mechanisms. The preliminary results of a study of haemophiliacs in South-East Scotland may serve to distinguish between them.

Concentrates of factor VIII and factor IX and cryoprecipitate used to treat most of our patients are manufactured by the Scottish National Blood Transfusion Service (SNBTS) from plasma voluntarily donated in Scotland. So far AIDS has not been reported amongst Scottish blood donors. We have studied twenty-three patients with severe haemophilia and von Willebrand's disease who have received exlusively SNBTS factor VIII, factor IX, or cryoprecipitate in the past five years. Most of these patients have never received commercial or non-Scottish factor VIII. All were clinically well.



Lymphocyte helper/suppressor ratios in Edinburgh haemophiliacs.

Helper and suppressor/cytotoxic T-lymphocytes were identified by indirect immunofluorescence with commercial monoclonal antisera, and the results were scored either by eye (on a Leitz 'Ortholux' microscope with Ploems incident fluorescence illumination) or on a Becton Dickinson FACS IV flow cytopherometer. The mean helper/suppressor T cell ratio in the patients was 1·4 (range 0·3–2·9) and this was clearly different from that of twelve non-haemophiliac controls (mean 2·2, range 1·6–3·9). Two-thirds of our patients had helper/suppressor ratios below the lower limit of our normal range (see figure). On retesting eight haemophiliacs the results were found to be reproducible. Absolute lymphocyte counts were normal in all haemophiliacs and controls.

Our results confirm other reports of low helper/suppressor ratios in haemophiliacs.[1-3] Since there are no known cases of AIDS in our blood donor population it seems likely that the immunosuppression observed in haemophiliacs, as reflected by reduced T lymphocyte helper/suppressor ratios, results from infusion of foreign protein or a ubiquitous virus rather than a specific AIDS virus in the factor VIII concentrates.

Supported by a grant from the Scottish Home and Health Department

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NUTRITIONAL SUPPLEMENTS IN CROHN'S DISEASE

SIR,—Dr Harris and his colleagues (April 23, p 887), in a group of malnourished patients with Crohn's disease of widely differing age, duration of disease, and disease activity, and with an appreciable

1. Centers for Disease Control *Pneumocystis carinii* pneumonia among persons with hemophilia A *MMWR* 1982; **31**: 365–7.
2. Lederman MM, et al. Impaired cell-mediated immunity in patients with classic hemophilia. *N Engl J Med* 1983; **308**: 79–83.
3. Menitove JE, et al T lymphocyte subpopulations in patients with classic hemophilia treated with cryoprecipitate and lyophilized concentrates *N Engl J Med* 1983; **308**: 83–86

1. Lederman MM, Ratnoff OD, Scillian JJ, Jones PK, Schacter B Impaired cell-mediated immunity in patients with classic hemophilia. *N Engl J Med* 1983, **308**: 79–83
2. Menitove JE, Aster RH, Casper JT, Lauer SJ, Gottschall JL, Williams JE, Gill JC. Wheeler DV, Piaskowski V, Kirchner P, Montgomery RR T-Lymphocyte subpopulations in patients with classic hemophilia treated with cryoprecipitate and lyophilized concentrates. *N Engl J Med* 1983; **308**: 83–86
3. Luban NLC, Kelleher JF, Reaman GH. Altered distribution of T-lymphocyte subpopulation in children and adolescents with haemophilia. *Lancet* 1983; i 503–05