NEONATAL DEATH AND PREVALENCE OF HANDICAPPED SURVIVORS IN RESIDENT GROUP (1959–78) AND NON-RESIDENT GROUP (1970–78)

	Resident				Non-resident	
	A	B	C	D	C	D
Neonatal deaths	143	81	45	23	15	37
Normal	81	54	68	57	11	45
"Handicapped"	27 *(28%)**	25 *(27%)*	17 *(20%)*	3 *(5%)*	0	11 *(20%)*
Spasticity	8	6	10	1	0	6
Deaf	14	15	4	1	0	0
RLF	0	0	0	0	0	1
Epilepsy	4	1	2	0	0	2
Hydrocephaly	1	0	1	1	0	3
Retardation	8	6	10	3	0	6
Total live births	251	160	130	83	26	93

*As % of total neonatal survivors.
RLF = retrolental fibroplasia
(A) 1959–64; (B) 1965–69; (C) 1970–74; (D) 1975–78.

"resident" babies becomes all the more striking—a shift opposite in direction to that envisaged by Sinclair et al.

We conclude that there has been a steady reduction both in perinatal mortality and in long-term morbidity of very immature infants in our clinic during the last twenty years. It is hard to avoid the conclusion that this change is related to improvements in the care of these very vulnerable infants.

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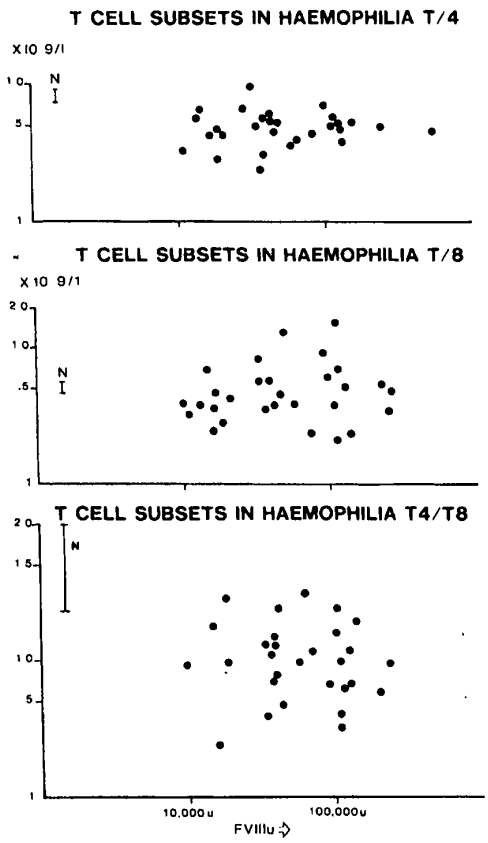
ABSENCE OF AIDS IN HAEMOPHILIACS IN AUSTRALIA TREATED FROM AN ENTIRELY VOLUNTARY BLOOD DONOR SYSTEM

SIR,—We know of no instances of acquired immunodeficiency syndrome (AIDS) in haemophiliacs in Australia. Since its inception the Blood Transfusion Service in Australia has had a policy of attempted self-sufficiency in blood and blood products. All blood donations in Australia are collected from voluntary unpaid HBsAg screened donors. Despite the HBsAg screening there is still a hepatitis hazard among haemophiliacs in this country,[1] but, according to a statement from the Australian Red Cross Society printed in the *Sydney Morning Herald* of June 3, 1983, to date AIDS has not been seen in any haemophilic recipient of Australian blood products.

In the context of the present worldwide interest in AIDS, its possible relationship to T cell subset perturbations and particularly the occurrence of AIDS in haemophiliacs who are the recipients of commercial blood products, we wish to mention briefly our T cell findings in a group of Australian haemophiliacs studied in Sydney. None of these patients have received any commercial blood products. The possible relevance of these observations has been mentioned by Dr Gordon (April 30, p 991). All the patients studied have been treated over the past three years with either cryoprecipitate, Margolis product,[2] standard antihaemophilic factor produced by the Commonwealth Serum Laboratories, or combinations of two or three of these products. None of the patients in this study have been treated exclusively with cryoprecipitate.

25 (73%) of the 35 patients studied had T_4/T_8 ratios less than those of their age and sex matched controls. 23 (67%) of the 34 had



T4 and T8 values and T4/T8 ratios against total units of FVIIIc received over the past three years in a group of haemophiliacs.

absolute T_4 values less than their age and sex matched controls. Only 6 patients (17%) had raised T_8 values while 7 patients (20%) had T_8 values less than normal. Only 4 patients were lymphopenic. In this population of haemophiliacs it appears that the deficiency of helper T cells is the more important factor in the production of a lowered T_4/T_8 ratio. We have plotted the relationship of the T_4/T_8 ratio and T_4 and T_8 values in these haemophiliacs to total units of factor VIII received over the previous three years. There is no positive correlation in these graphs (figure) suggestive of a direct relationship between the amount of FVIII received and alterations in T_4 and/or T_8 values. Cytomegalovirus antibody titres in all these patients were normal, unlike the situation in patients with AIDS. Immunoglobulin levels were normal. Only 1 of the patients in this study had an antibody to FVIII; his T_4/T_8 ratio was normal. None of these patients have had opportunistic infections.

Thus it seems that Australian haemophiliacs treated with locally produced blood products have T cell subset changes similar to those reported from other countries,[3,4] but the AIDS problem has not been seen. One might speculate that the frequent use of factor VIII products induces changes in T cell subsets but that this alone does not lead to the development of AIDS. Perhaps for AIDS to occur there needs to be the introduction of an infectious agent in addition to these T cell perturbations. Such an agent may not be present in non-commercial blood products collected in an entirely voluntary donor system as in Australia. Perhaps reactivation of cytomegalovirus infections in persons with T_4/T_8 abnormalities may be a trigger mechanism for AIDS. On the other hand CMV reaction may be a result of the immunodepression of AIDS. Despite

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the absence of AIDS in Australian blood recipients there is no room for complacency, and the blood transfusion centre directors are taking positive steps to discourage individuals at high risk for AIDS from contributing blood within the voluntary donor system in Australia—and physicians caring for haemophilia patients in Australia will maintain their vigilance.

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INTESTINAL PROTOZOAL INFECTIONS AND AIDS

SIR,—Several theories have been put forward to explain the cellular immune dysfunction that is the hallmark of acquired immunodeficiency syndrome (AIDS). Overlooked, however, has been the possible association between intestinal protozoal infection and host immunosuppression.

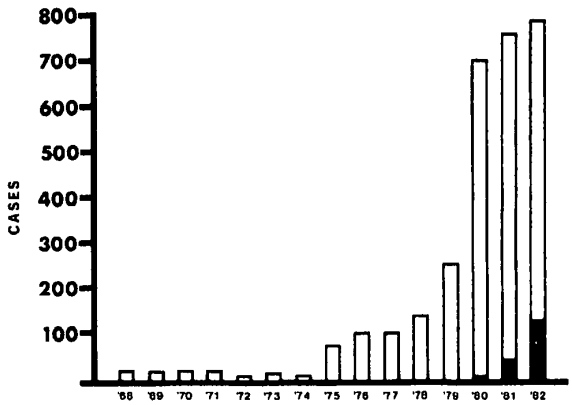
Among homosexual men aged 20–39 living in San Francisco, the incidence of reported symptomatic intestinal amoebiasis has jumped 8000% in the past ten years (figure). Non-opportunistic enteric pathogens are found more frequently in AIDS cases than in clinic controls,[1] and Haitians with AIDS[2] and rhesus monkeys with an AIDS-like syndrome[3] harbour the pathogens that are most prevalent among "healthy" homosexual men—namely, *Entamoeba histolytica* and *Giardia lamblia*.

Not widely known is the fact that *E histolytica* trophozoites have an associated lectin activity[4] and that the aqueous extract of *E histolytica* is mitogenic for human T-lymphocytes.[5] Lectins such as concanavalin A (con A) alter immune effector responses in vivo and when added to lymphocyte cultures induce proliferation of cells with demonstrable suppressor activity.[6] Both *G lamblia* and *E histolytica* infections in laboratory animals depress phytohaemagglutinin reactivity and abrogate other T-cell-mediated immune responses.

A soluble suppressor factor has been found in the blood of AIDS patients and male homosexuals with lymphadenopathy.[7] The factor apparently resembles a lectin-induced murine macrophage suppressor factor. A similar factor, which acts like an "endogenous" non-mitogenic lectin and which blocks mitogen-induced T-cell proliferation, has been isolated from supernatants of con-A-stimulated peripheral blood mononuclear cells.[8] If the lectin associated with *E histolytica* has an action similar to that of con A it is conceivable that sera of individuals chronically infected with such (or similar) parasites would also contain a soluble, lectin-like, immunosuppressor factor.

Factor VIII has a lectin binding site[9] that might transfer mitogen to type A haemophiliacs or to patients receiving platelets which have surface-associated factor VIII molecules.

It has been suggested that human T-cell leukaemia virus (HTLV), a T-lymphotropic retrovirus originally isolated from adults with lymphoid malignancies, may be responsible for T-cell abnormalities



Annual incidence of amoebiasis *(E histolytica)* (□) and AIDS (■) reported to the San Francisco Department of Health.

associated with early stages of AIDS, although a similar isolate is endemic in Southern Japan apparently without the appearance of AIDS.[10] I suggest that mitotic activation of T-lymphocytes by *E histolytica* or other parasites, especially where there are multiple or recurrent infections, sets the stage for viral infection and replication of a putative AIDS virus. Chronic or multiple parasitic infections alone could account for the immunosuppression associated with AIDS, but in either case what may predispose groups to AIDS is a pre-existing "pan-immunosuppression" less severe than that seen in fulminant AIDS. Consistent with this idea is the identification of AIDS in groups with altered inducer-helper/cytotoxic-suppressor T-cell ratios but with no AIDS prodrome or life-threatening diseases—eg, opioid addicts and haemophiliacs receiving lyophilised factor VIII preparations.

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INCREASED FREQUENCY OF HLA-DR5 IN LYMPHADENOPATHY STAGE OF AIDS

SIR,—An increased frequency of the HLA-DR5 allotype was found in male homosexuals with the epidemic form of Kaposi's sarcoma associated with the acquired immunodeficiency syndrome (AIDS).[1] This observation provided evidence that genetic factors related to the major histocompatibility complex are associated with the emergence of this malignancy. Unexplained persistent lymphadenopathy, frequently associated with fever and weight loss, has been reported in homosexual men without evidence of malignancy or opportunistic infection.[2] We wondered if patients with the lymphadenopathy syndrome uncomplicated by Kaposi's sarcoma or opportunistic infection exhibited an alteration in the frequency of DR allotypes similar to that in patients with fully developed AIDS.

We studied thirty-four homosexual White males living in New York City who had persistent unexplained adenopathy 1 cm or more in size that had been present for at least three months and affected two or more anatomical regions exclusive of the inguinal region.

Analysis of T lymphocyte phenotypes[3] revealed that the median absolute number of T lymphocytes bearing Leu3 or T4 was 419/μl (range 131–1050), compared with a normal control median of 1300/μl (range 1050–1680). The median ratio of cells positive for T4 or Leu3 to those positive for T8 or Leu2 was 0·42 in the patient

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