

THE ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

Between June 1981 and January 13th 1982 the Communicable Disease Centre at Atlanta, Georgia, U.S.A. became aware of an increase in the occurrence of Kaposi's sarcoma (KS), Pneumocystis carinii pneumonia (PC), and other serious opportunistic infections among promiscuous homosexual men in the U.S.A.<sup>(1)</sup> In all these cases, there were none of the well known predisposing causes of immunosuppression, such as cytotoxic drug therapy, steroid treatment, malignancy or other predisposing cause. There were 216 cases (81 of KS, 91 of P. carinii pneumonia, 18 of both and 18 of other infections). At least 88 (40.8%) of these patients have died.

Other serious infections included progressive or disseminated herpes simplex virus (HSV) infections, particularly of the colon or rectum, toxoplasmosis of the central nervous system, cryptococcus meningitis and 24 patients with disseminated cytomegalovirus (CMV) infection. Over 40% of patients with KS, P. carinii or both had other serious opportunistic infections (10 of 73 patients with KS alone, 42 of 61 with P. carinii alone, and 12 of 15 with both KS and P. carinii pneumonia).

A considerable delay was noted between the occurrence of initial symptoms and diagnosis (KS 1-30 months: median 5.5; P. carinii pneumonia 1-18 months: median 3.5). This meant that there was an average 3-6 months delay between the onset of symptoms and diagnosis. The signs and symptoms were in most cases insidious and non-specific in nature. They were as follows:-

	Kaposi's syndrome (n = 73)	P. carinii pneumonia (n = 61)	Both (n = 15)
	per cent	per cent	per cent
Skin or mucosal lesions nodule, ulceration etc.	80.0	8.2	86.7
Lymphadenopathy	43.8	23.0	40.0
Fever	23.3	93.4	86.7
Weight loss	19.2	70.5	53.3
Diarrhoea	17.8	34.4	40.0
Dyspnoea	5.5	88.5	100.0
Oral thrush	6.8	41.0	26.7

The frequency of weight loss, fever and lymphadenopathy illustrates the generalised nature of this disease.

The overall mortality was highest in those patients with P. carinii pneumonia only (60.7%) compared with 15% with KS only. In patients with both KS and PC the mortality was 46.7%.

The age range was 15-57 years (median 35). There was no association with ethnic origin. One hundred and thirty six of 158 (86%) were homosexuals; 12 were heterosexuals.

#### LABORATORY DATA

The most interesting feature of the laboratory findings was the broad impairment of cell mediated immunity (CMI) as demonstrated by the variety of opportunistic infections with a normal humoral immunity. The laboratory features were; severe lymphopenia, failure to respond to skin test antigens used in the assessment of CMI, a decreased ability of the patients lymphocytes to respond to stimulation with mitogens; T lymphocyte depletion, with a depleted ratio of helper to suppressor T cells.

The severe illness was preceded by an insidious non-specific illness characterised by malaise, fever, weight loss,

lymphadenopathy and oral thrush for several months. It was possible that this was due to an immunosuppressive virus infection. Since then reported cases of a similar syndrome have been noted in promiscuous heterosexuals<sup>(2)</sup> who are mainline drug addicts, immigrants from the Island of Haiti<sup>(3)</sup> (with no obvious association with drugs or sexual promiscuity) and recently in 7 haemophiliacs, 6 of whom also have no association with drugs or sexual promiscuity.<sup>(4)</sup> Three cases have been described in the U.K. and one in Spain. All probably acquired their disease in the U.S.A. However, 4 cases were recently observed in Denmark<sup>(5)</sup> and there was evidence suggesting that person to person transmission had occurred in that country.

Clustering of cases has been found in the homosexual population in California.<sup>(6)</sup> The disease shows a progressive course with little or no tendency to resolve spontaneously. KS usually causes a disease in elderly men and renal transplant recipients in the U.S.A. and occurs in young men in some parts of Africa.

#### AETIOLOGY

Several theories have been advanced. It seems likely that this is a 'new' syndrome.

- 1) The effect of drugs such as amyl nitrate taken by homosexuals to heighten sexual experience. This is not a factor as the disease has been described in patients who do not use the drug.
- 2) The immunosuppressive effect of cytomegalovirus infection which has been suggested as a cause of KS. This seems unlikely, as CMV infection is rarely the primary cause of profound immunosuppression such as is described here, though a lesser degree can be

demonstrated in patients with CMV associated infectious mononucleosis, etc.<sup>(7)</sup>

- 3) The association with sexual promiscuity, intravenous drug abuse and possibly the transfusion of commercial blood concentrates, together with evidence of clustering and a prodromal phase suggest an infectious agent with a similar epidemiology to that of hepatitis B, possibly specific for human T. cell populations. The presence of this syndrome in Haitian immigrants to the U.S.A. suggests that this agent may have spread from one previously unidentified ecological niche, perhaps situated in the tropics.

If (3) is the most likely cause, then it is possible that such an agent might be present in the plasma pools used to prepare commercial factor VIII and IX concentrate manufactured from donor plasma collected in the U.S.A. Presumably this would have been obtained from homosexuals who donated plasma for fractionation when in the incubation period of the disease.

Three patients have acquired the disease where the most likely mode of transmission was blood or platelet transfusions. The incubation period was between six months and two years. The most recent information (8) suggests that at least ten haemophilia A patients have been reported with clinical features of the syndrome. All but one of these patients had no other predisposing factors such as intravenous drug abuse or homosexuality and resided in areas of the U.S.A. such as Alabama or Ohio where cases of the AIDS syndrome had not been previously found. Five of these patients have so far died.

There is also some evidence that female sexual partners of drug addicts can acquire the disease and of the existence of a

carrier state. It is also possible that the initial phase of the disease characterised by enlarged lymph nodes which is associated with a proliferation of lymphoreticular cells, the onset of autoimmune disease e.g. thrombocytopenia or haemolytic anaemia, loss of weight and malaise may not always progress to the final syndrome where marked depletion of the lymphoid cells is the most obvious appearance on histology of lymph nodes. It is therefore evident that the disease is not universally fatal and some patients may recover. All the epidemiological evidence is consistent with the existence of a transmissible agent whose mode of spread is remarkably similar to that of hepatitis B. Precautions against cross infection should therefore be based on those taken for hepatitis B.

It is thought likely that batches of factor VIII concentrate which might contain the AIDS agent came into use since January 1st 1980 in the U.S.A. The Communicable Disease Centre of the U.S. Public Health Service at Atlanta, Georgia, therefore has requested the U.K. Haemophilia Centre Directors to co-operate with them in a survey by reporting cases of AIDS possibly associated with transfusion of U.S. commercial factor VIII concentrate. Cases will also be notified to the Communicable Disease Surveillance Centre in the U.K. at the Central Public Health Laboratory, Colindale, London. The total number of AIDS cases reported in the U.S.A. up to 10.12.82 was just under 800.

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## REFERENCES

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