# THE ACQUIRED IMMUNODEFICIENCY SYNDROME — A REVIEW OF THE GLOBAL SITUATION

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ABSTRACT

The Acquired Immunodeficiency Syndrome (AIDS) was first recognised in the United States in 1981. Since then, a pandemic had occurred worldwide. This article reviews the events leading to the discovery of the Human Immunodeficiency Virus (HIV), the clinicoepidemiological aspects of the disease, and international and national programmes to curb its spread.

In Singapore, an AIDS Programme was set up in 1985 to control the spread of HIV infection in the Republic. The programme included health care delivery, education of health care workers and the community, surveillance and counselling of high-risk individuals, as well as screening of blood donors for HIV. As at 30 April 1988, 22 Singaporeans with HIV infection have been detected. Of these, four had AIDS.

Key words: AIDS, review

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## RECOGNITION OF A NEW DISEASE

AIDS was first recognised in the United States in 1981. In June 1981, the Centres for Disease Control (Atlanta, Georgia, United States) reported the unusual occurrence of 5 cases of Pneumocystis carinii pneumonia among previously healthy male homosexuals in Los Angeles (1). By July 1981, 10 additional cases had been identified in Los Angeles and San Francisco. This brought the total number to 15 since September 1979.(2). At the same time, Kaposi's sarcoma, an uncommonly reported malignancy in the United States, had been diagnosed in 26 young gay men in New York and California (2). These 26 patients ranged in age from 26 to 51 years (Mean 39 years). These cases were identified retrospectively, as far back as 1978.

Until then, Pneumocystis carinii pneumonia had been observed only in severely immunocompromised patients; and Kaposi's sarcoma, a rare and indolent type of skin cancer in the United States, seen primarily in elderly men (2).

By late 1981, AIDS had been reported in heterosexual intravenous drug abusers (IVDAs). An estimated 200,000 IVDAs were found in the New York Metropolitan area and 750,000 nationwide in the United States. By 1986, reports indicated close to 60% seropositivity among IVDAs in New York (3, 4). As at 15 June 1987, 4798 IVDAs with AIDS has been reported (5). Indiscriminate needle sharing among narcotic addicts had been implicated in the spread of the disease (4).

In January 1982, the occurrence of AIDS in a haemophiliac was first reported. This strengthened theories of a transmissable agent in the etiology of the disease, as haemophiliacs had long been known to be at risk for the transmission of specific viral agents, such as hepatitis B, non-A, non-B hepatitis, and cytomegalo-virus. There are an estimated 12,000 to 17,000 haemophiliacs in the United States and the incidence of AIDS is 3.6 per 1000 haemophilia A patients and 0.6 per 1000 haemophilia B patients (4). 327 cases of AIDS among haemophiliacs had been reported (5).

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Shortly afterwards, transfusion-associated AIDS was documented as was the transmission from infected male IVDAs to their female sexual partners. The first cases suggestive of an AIDS-like illness in children were reported by the Centres for Disease Control in 1982 (4). Since then, there had been 280 cases of AIDS in children in the United States (5).

## DISCOVERY OF THE HUMAN IMMUNODEFICIENCY VIRUS

The sequence of events since 1981 led to hypotheses about an infectious etiology, through a blood-borne, transmissible agent. These hypotheses were strengthened in 1983 by the discovery and characterization of a pathogenic retrovirus found in AIDS patients.

In late 1983 and early 1984, Luc Montagnier at the Pasteur Institute in Paris, and Robert Gallo at the National Institute of Health in the United States independently isolated what is now believed to be the same virus from patients with AIDS. Montagnier named it Lymphadenopathy-Associated Virus (LAV), Gallo called it Human T-Lymphotropic Virus Type III (HTLV-III). It is now commonly called the Human Immunodeficiency Virus (HIV) by the scientific community.

The live virus has now been isolated from blood, semen, urine, vaginal secretions, bone marrow, lymph nodes, spleen, cerebrospinal fluid, brain and neural tissues. The virus has also been isolated from saliva although there is no evidence to suggest transmission of the virus through contact with saliva.

The virus is spherical and comprises of a outer lipid envelope enclosing the core protein, RNA genome and an unique enzyme called reverse transcriptase. The envelope consists of glycoprotein molecules which bind to specific glycoprotein receptors of the helper/inducer T4 lymphocytes of the host, which is the main target of the HIV. In the host cell, viral RNA is transcribed into DNA, gets inserted into the host cell genome, resulting in chronic infection. When the infected T4 lymphocytes are activated, the virus multiplies, leading to death of the lymphocytes. Lymphopenia, due to a decreased absolute number of T4 cells, increases host susceptibility to a wide range of opportunistic infections and neoplasms. The ratio of T4 to T8 lymphocytes in the blood is lowered in patients with AIDS, often to 0.5 or less (3).

The African green monkey (Cercopithecus aethiops) had been implicated to have haboured the ancestor of the AIDS virus: Simian T-Lymphotropic Virus III (STLV-III). STLV-III does not usually cause disease in its simian host, but it might infect humans and give rise to HTLV-III after several genetic mutations. The monkey virus was isolated from sera obtained from African green monkeys in 1985 by Myron Essex and Phyllis J Kanki of the Harvard Medical School (6).

Tests on stored blood sera from the 1960s and 1970s from many parts of the world detected no antibodies to HTLV-III anywhere except in a small region in Central Africa, where the earliest signs of infection had been found in serum samples taken in the 1950s. The subsequent occurrence of AIDS in Haiti and Haitian immigrants to the United States, and the increasing number of cases of AIDS in Central Africa then suggested the spread of the disease had occurred from Africa (3, 6).

## EPIDEMIOLOGY

AIDS has reached pandemic proportions with cases reported from all continents. As at 31 March 1988, 85273 cases were reported worldwide (7). The majority of these cases were reported by the United States, totalling 55167 cases. These represent only a fraction of the total number of AIDS cases, as current World Health Organisation (WHO) estimates put the total number of AIDS cases in excess of 100,000 with between 5 and 10 million persons infected with HIV. By 1991, WHO estimates that at least one million new cases of AIDS could develop in people already infected with HIV (8).

The largest number of reported cases came from the Americas, totalling 62536 cases. This represents 73% of the total reported cases worldwide. Europe had reported 10677 cases from 28 countries; Africa 10995 cases from 50 countries; Oceania 834 cases from 14 countries, and Asia 231 cases from 37 countries (7).

**Three patterns of AIDS worldwide could be recognised:**

**(1) PATTERN 1 (Western Pattern)**

AIDS in the United States, Europe and Australia had been predominantly a disease of young men. Most (89%) of the patients were between 20 and 49 years of age, and 93% were males (3). The male-to-female AIDS case ratios have been reported as between 13 and 15:1 (4). The majority of affected persons were male homosexuals with multiple partners, bisexuals, IVDAs who shared needles, and receipients of infected blood and blood products.

**(2) PATTERN 2 (African Pattern)**

The male-to-female AIDS case ratios were observed to be between 1.1 and 1.9:1 in Africa. This suggested bi-directional transmission due to frequent heterosexual contact among both male and female patients (4). The use of unsterilized injection equipment and spread through infected blood and blood products were also important factors in the transmission of HIV.

**(3) PATTERN 3 (Asian Pattern)**

The incidence of AIDS in Asia is low compared to that of the United States, Europe, Australia or Africa. The pattern is as yet not clear. A small number of AIDS cases had been reported from India, China, Taiwan, Hong Kong, Japan, Thailand and Singapore (7). These cases had either been related to imported blood and blood products or to sexual transmission through sexual contact with men or women from countries where AIDS was more prevalent (9).

Epidemiological studies worldwide have documented three modes of HIV transmission (4, 10, 11):

(a) Sexual intercourse (homosexual or heterosexual)
(b) Contact with HIV infected blood, blood products, donated semen or transplanted organs. The majority of contacts with HIV infected blood involved transfusion of unscreened blood or the use of unsterilized syringes and needles by IVDAs.
(c) Infected mother to child (transplacental acquisition)

There is no evidence to suggest viral spread by casual contact with infected individuals or by exposure to tears and saliva. Household contacts, siblings of infected individuals do not acquire the disease (4).

No health care worker in the world had contracted AIDS although there were reports of exposure to blood or body fluids of patients infected with HIV, and needle-stick and sharp injuries. In a serological study of 1758 health care staff in the United States who had directly or indirectly been in contact with AIDS patients, 26 (1.5%) were found to have HIV antibody in their blood but 23 of these were homosexual men (4, 12, 13).

## CLINICAL DIAGNOSIS

The rapid growth of knowledge about HIV had resulted in a need for a system of classifying patients within the wide spectrum of clinical and laboratory findings attributable to HIV infection (14, 15).

In 1986, the Centres for Disease Control, United States, presented a classification system primarily applicable for public health purposes (16):

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| GROUP 1 | Acute Infection |
| GROUP 2 | Asymptomatic |
| GROUP 3 | Persistent generalized lymphadenopathy |
| GROUP 4 | Other diseases |
| Subgroup A | Constitutional disease |
| Subgroup B | Neurologic disease |
| Subgroup C | Secondary infectious disease |
| Category C1 | Specified secondary infectious diseases listed in the CDC Surveillance Definition for AIDS |
| Category C2 | Other specified secondary infectious diseases |
| Subgroup D | Secondary cancers |
| Subgroup E | Other conditions |

In 1987, a revised case definition for AIDS was developed by the Centres for Disease Control, United States (17). Major changes included the inclusion of (a) HIV encephalopathy, HIV wasting syndrome and a broader range of specific AIDS-indicative diseases; (b) inclusion of AIDS patients whose indicator diseases were diagnosed presumptively; and (c) elimination of exclusions due to other causes of immunodeficiency.

### Case Definitions

**(1) AIDS**

AIDS is defined as occurring in people with both:

(a) A reliably diagnosed disease moderately indicative of underlying cellular immune deficiency (e.g. Kaposi's sarcoma in a patient aged less than 60 years old, or an opportunistic infection).
(b) No underlying cause for the immunodeficiency or of any defined cause for reduced resistance to the disease. This diagnosis is excluded if all laboratory indicators of immune deficiency or HIV infection are negative.

**(2) ARC (AIDS-RELATED COMPLEX)**

ARC is diagnosed in a patient with two or more findings in each of the following categories:

(a) Clinical findings (present for more than 3 months):
Pyrexia more than 38°C.
Chronic diarrhoea
Weight loss more than 10% body weight
Malaise and lethargy
Persistent generalised lymphadenopathy
Night sweats
Oral candidiasis
Hairy leukoplakia
Herpes zoster

(b) Laboratory findings:
HIV antigen or antibodies
Leucopenia and lymphopenia
Thrombocytopenia
Anaemia
Raised ESR
Immunological abnormalities
Cutaneous anergy

In a review of the literature, Taylor et al noted that estimates of between 5 and 20% have been given for the proportion of virus-infected individuals who will eventually develop AIDS. They studied 177 young homosexuals in Los Angeles, and statistical analysis using an adaptation of the Kaplan-Meier scheme, showed that the probability of developing AIDS within two years of infection is 2% and within four years, about 11% (18).

**Testing for HIV**

The HIV antibody assays allow improved surveillance of virus transmission. Generally three techniques have been employed worldwide as well as locally (19):

(1) Enzyme-linked immunoabsorbant assay (ELISA)
(2) Particle-agglutination test
(3) Western Blot procedure

The first two methods are extremely sensitive but relatively non-specific. They are used as screening tests. The Western Blot procedure is more specific and is used as a confirmatory test. It is more labour intensive and expensive to perform. Currently, detection of viral antigen in infected sera has become possible.

## THERAPY

Despite intensive research, hitherto, it has not been possible to provide specific treatment for HIV infection. Strategies aimed at elimination of the virus and restore immune competency had failed.

Interferon, interleukin -2, thymic hormones, bone marrow and thymus transplantations had been used with disappointing results in an attempt to enhance the compromised immune functions of those infected. Anti-viral agents, such as suramin, antimoniotungstate (HPA 23), ribavirin and foscarnet sodium had been used unsuccessfully because of their toxic side effects (20).

Only one drug, azidothymidine (AZT), has so far been promising. AZT inhibits replication of HIV. Its efficacy was demonstrated in a double-blind, placebo-controlled trial in 1987 (21). In that study, 145 patients received AZT, and 137 received placebo. Nineteen placebo recipients and one AZT recipient died during that study. Since then, the drug has been used extensively in a hope to prolong survival.

A cure for AIDS is still lacking. There is still no vaccine or an effective, curative mode of treatment.

## CURBING THE SPREAD OF THE DISEASE

International collaboration is needed to stop AIDS from spreading in all countries. The WHO Special Programme on AIDS (SPA) was established on 1 February 1987 to achieve this aim. The goals of the SPA are to prevent virus transmission, care for the infected people, and to unify national and international efforts against AIDS. 127 countries are collaborating with SPA to achieve these aims. The global AIDS strategy of this programme has been endorsed by the World Health Assembly and the United Nations General Assembly in 1987 (8).

National AIDS Committees have been established in 151 countries, including Singapore (8). In Singapore, the National Advisory Committee on AIDS was set up in October 1987. One of its roles is to provide a two-way communication between the Government and the Singapore community on AIDS.

At the World Summit of Ministers of Health on Programmes for AIDS Prevention, delegates from 148 countries recognised that AIDS is a global problem and also the need for a concerted effort by governments and peoples of all countries to combat the disease (21).

## THE AIDS PROGRAMME IN SINGAPORE

In 1985, an AIDS programme was set up for AIDS control in the Republic (10). The strategy was a multi-pronged approach:

(1) AIDS was made a notifiable disease under the Infectious Diseases Act 1976 on 17 April 1985 to empower the Health Ministry to control the spread of the disease (23).
(2) A Health Plan and a Contigency Plan to deal with all aspects of clinical management of the disease was formulated. These included the formation of the Advisory Committee on AIDS and the provision of an AIDS Ward at the Communicable Disease Centre of Tan Tock Seng Hospital to admit patients who are infected. The AIDS Ward was commissioned in April 1986 and admitted the first patient with AIDS in September that year. Further provision for an operating theatre solely for AIDS patients was made in 1988.
(3) All medical and paramedical personnel were issued guidelines on precautions to be taken in handling HIV infected persons and laboratory specimens.
(4) Routine screening of blood donors was carried out since October 1985 and the use of autologous blood transfusion was recommended. From October 1985 to December 1987, 145,149 blood donations were screened for HIV at the Blood Transfusion Service. Three infected donors were discovered in 1985 and another two in 1987 (24).
(5) Surveillance and counselling of persons with AIDS and their sexual contacts.
(6) A screening programme for individuals in high risk groups (e.g. prostitutes) was started in late 1986. Male and female prostitutes were tested three-monthly and six-monthly respectively. Homosexuals from the Central Manpower Base and inmates of the Drug Rehabilitation Centre were tested as well. So far, none were found infected (25).
(7) Health education programmes on AIDS for the community, organisations, and the young and sexually active were carried out. Seminars and workshops on AIDS were organised for medical and paramedical personnel and the public.

In November 1987, the existing programme on AIDS was reorganised to enable swifter action and wider dissemination of information on the disease. An AIDS Task Force was formed to replace the Advisory Committee. The functions of this Task Force are related to management of HIV infected persons, epidemiology of the disease, development of services and support for infected individuals, and provide information on the latest developments of the disease (26).

In addition, a new National Advisory Committee on AIDS was formed. Comprising representatives from var-

ious Ministries, the media and corporations, its prime role is to disseminate information on the disease to the community (27).

The first case of HIV infection in Singapore surfaced on 16 May 1985. As at 30 April 1988, 22 Singaporeans with HIV infection have been detected in Singapore. Of these, four had clinical AIDS and all have died.

## CONCLUSION

The AIDS era is upon us. In the absence of a vaccine or curative treatment, education and dissemination of information of how to avoid AIDS remain the key factors in controlling its spread.


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