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Introduction to AIDS

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AIDS has become a matter of increasing concern in a number of countries, particularly in North America and Europe. Since the first recognition of the AIDS in 1981, over 17,000 cases have been reported to WHO up to 15 November 1985, mainly from the industrialized countries. Approximately half of these cases were reported in 1985 and over 75% were reported during the 1984-1985 biennium. More than 80% of cases recorded to date have been reported from the USA. There have been relatively few cases from countries in Asia and Oceania (except Australia). Recent information indicate that AIDS may be a serious public health problem in tropical Africa, estimated incidence rates in some central African cities are comparably to those in the USA, and cases have been identified in residents or migrants from over a dozen of African countries. In North America, Europe and Australia, homosexual men account for at least 70% of the total detected AIDS cases. The disease has been noted in intravenous drug abusers, hemophiliacs, recipients of blood transfusion, and the heterosexual partners or infants of patients or members of groups at increased risk of infection.

The etiological agent of AIDS is a retrovirus described as LAV (Lymphoadenopathy-associated virus), HTLV-III (human T-lymphotropic virus, type III), or ARV (AIDS-related virus). The LAV was first reported from the Pasteur institute group in 1983 and then about one year later the NCI group isolated the retrovirus similar to LAV and called HTLV-III. Soon Dr. J. Levy and his co-workers reported the isolation of AIDS-related virus from patients in San Francisco. In this introduction, the virus will be referred to as AIDS virus for the sake of simplicity only.

The AIDS virus infects peripheral T-lymphocytes of a particular type, called “helper” or “inducer” subset; the cells are expressing the OKT4 /Leu 3 antigen on the surface. Either the virus infected or the viral antigen-coated T cells may lose their ability to function, and dies prematurely, leading to the depletion of the cellular immune system that is characteristic of AIDS. Both seroepidemiological and in vitro data strongly suggest that the retrovirus isolated from patients in fact the causative agent of AIDS. In addition, there is compelling evidence that the AIDS virus may infect cells in the central nervous system (CNS), although which cells in the brain became infected is still unclear. Infection of the CNS may occur at early stage in infection with the AIDS virus, perhaps simultaneously with infection of peripheral T-lymphocytes. This potential reservoir of virus in an immunologically privileged site—beyond the blood-brain barriers—has important implications for treating AIDS.

The immune suppression induced by the retrovirus triggers to generate the opportunistic infections with many kinds of microbes which include pneumocystis carinii, candida or cryptococcus, mycobacterium, cytomegalovirus or Epstein-Barr (EB) virus etc. The immune deficiency of the patients induces not only the severe microbial infections but also malignant tumors i.e. Kaposi’s sarcoma and or B-cell lymphoma. The B-cell lymphoma in AIDS may be a resultant of transformation of cell by EB virus grown vigorously in the patients. However, it has been not
proven yet that the induction of Kaposi's sarcoma is really related to the potential oncogenic activity of cytomegalovirus. It is obvious that such the severe opportunistic infections or tumors lead to the fatal consequence of AIDS patients.

The DNA sequence of the AIDS virus has been derived from molecular clones of both unintegrated and integrated proviruses in 1985. The sequences of LAV, HTLV-III and ARV show general agreement in the size and organization of the AIDS virus genome. The AIDS virus is the longest retrovirus sequenced to date. The AIDS virus contains many characteristic features of replication competent retroviruses: LTRs, group specific antigens (gag), a gene region (pol) encoding reverse transcriptase as well as putative endopeptidase and integrase enzyme, and a gene encoding the virus envelope glycoprotein (env).

Retroviruses have been traditionally classified on the basis of their biology, electron microscopic morphology, and genomic structure. Biological classifications have divided retroviruses into three groups: 1) the oncovirus, many of whose members are naturally oncogenic, producing leukemias, lymphomas, and mammary cancers; 2) the spuma virus or foamy virus, which produce vacuolization of tissue culture cell but no known decrease; and 3) the lentivirus, or slow virus, which produce cytopathic effect on tissue culture cells and slowly progressive disease in animals.

In biological, morphological and genetic grounds, the AIDS virus, with its capacity to produce cytopathic effect on cultured cells and slowly progressive disease in man, seems to have many features of a lentivirus. Although AIDS virus shares its target cell tropism and ability to form syncytia in the cells with adult T-cell leukemia virus (ATLV) or HTLV which cause ATL. The ATLV/HTLV is definitely in a family of oncogenic retrovirus, and it is etiologic agent of ATL which is particularly endemic in Japan and possibly in Africa.

A very important problem in understanding the epidemiology and pathogenicity of AIDS, as well as developing therapy and vaccine, is the question of the heterogeneity of the virus. How variable is one isolate from another? Where do the variations occur and how will they affect viral pathogenicity and antigenicity? Although the restriction maps of HTLV-III, ARV, and LAV proviral DNAs have not been formally compared, superficial inspection of published cleavage maps and Southern blots suggests that HTLV-III and LAV are closely related to one another, whereas ARV and many other isolates are substantially different.

At present, it is unclear why AIDS virus infection of man results in a slow progressive immunosuppressive disease, some models of lentivirus persistence are consistent with structural difference observed between LAV/HTLV-III and ARV. Neutralization studies indicates that periodic nature of disease caused by equine infectious anemia virus (EIAV), a lentivirus, is due to sequential appearance, in an infected animal, of novel antigenic viral variants that temporarily escape host immune surveillance. The different antigenic strains of EIAV responsible for sequential febrile episodes contain alterations confind to virion glycoproteins. Similar antigens variants have been reported for visna virus, although the relationship of env glycoprotein antigenic variations and viral pathogenesis is unclear. If the substantial variability in env glycoproteins, reflecting genetic alterations attending AIDS virus infection in man, in different AIDS virus strains isolated from different patients is verified, then preventive and therapeutic strategies may have to be directed to less viable regions of the viral genome.

While the number of cases of AIDS continues to rise relentlessly not only in USA and Europe, but also in Australia, South America, Central Africa and other countries including Japan, no
particular drug currently holds great promise. However, there is the possibility of achieving the stopping of viral replication by inhibiting reverse transcriptase. Further, in conjunction with the therapy to modulate the immune system, the treatment of AIDS in very near future looks more realistic.

I have not a too pessimistic but not too optimistic view of the fight against the AIDS. I believe that to minimize the victims of AIDS, the highly efficient international collaboration is absolutely necessary not only in the information exchange and public education but also in the development of diagnostic procedures, therapeutic agents and vaccine for this serious disease.