AIDS IN AFRICA

A manual for physicians

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Foreword

Cases of acquired immunodeficiency syndrome were reported for the first time in central Africa around 1982. Since then, this viral infection has spread, at first gradually and now more rapidly, through practically all the countries of central Africa. It now also affects several countries in southern and western Africa.

For many health professionals in Africa, as elsewhere, this disease represents a new challenge, and workers are gradually gaining experience in clinical management of cases, laboratory diagnosis, epidemiological studies, and prevention. At the same time national AIDS committees have been formed and efforts are being made to accelerate public education and information without creating panic.

So far, health workers in Africa who wish to learn more about AIDS have had to rely mainly on hearsay information, published articles, and a relatively small number of seminars and workshops that have been organized by WHO and other agencies. This handbook is therefore most welcome as a reliable source of up-to-date information in this new and rapidly expanding field. I am convinced that physicians, nurses, laboratory technicians, epidemiologists, social workers, and other health professionals will find this book of great use in the fight against AIDS.

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Contents

1. Introduction

The acquired immunodeficiency syndrome (AIDS) was first recognized in 1981, in the United States of America, in young homosexual men who had Kaposi sarcoma and serious infections—predominantly *Pneumocystis carinii* pneumonia—that were unusual in men in this age group with no underlying disease. Several million individuals throughout the world are now infected with the human immunodeficiency virus (HIV), the causative agent of AIDS; of these, a large proportion (30–50%) are expected to die within 5–10 years of acquiring the infection. With the high case-fatality rate, the impact on health and society, and the lack of curative treatment or vaccine, the HIV/AIDS pandemic is one of the most serious health problems of this century.

The dramatic and well-publicized epidemic rise in the number of AIDS cases in the United States since 1981, the onset of a similar epidemic in Europe starting in 1982–1983, and the more recent awareness of AIDS as an international health concern involving all continents have generated intense interest and work by many national and international research teams in virology, immunology, clinical medicine, epidemiology, and public health.

Within a few years after the original description of the syndrome, its cause and basic immunological abnormalities were identified, and the modes of transmission of the causative virus were documented. Control programmes have been initiated in many countries, and the World Health Organization has been charged with overseeing the international efforts to combat the pandemic.

Public health and social importance

The impact of HIV infection on public health and on development programmes is only now becoming appreciated. HIV infection is

associated with often fatal illness, thereby increasing overall morbidity and mortality. Because of its chronic nature and associated life-threatening conditions, health care costs for HIV-infected patients are tremendous, putting a heavy burden on already limited budgets. These patients occupy hospital beds and consume scarce resources in palliative care that might otherwise be used for diseases that can be cured. The underlying immunodeficiency induced by HIV infection is now thought also to cause increased severity of signs and symptoms, or relapse after treatment, of other endemic infectious diseases, such as tuberculosis.

HIV-infected infants and children may put an extra burden on primary health care programmes. Immunization programmes are faced with the problem of availability of sterile needles. Family planning, maternal and child health, and diarrhoeal disease control programmes may have to cope with HIV-associated infant mortality and unmanageable chronic diarrhoea and weight loss in HIV-infected people.

Many people in African countries, as elsewhere, have reacted to AIDS with denial, panic, and stigmatization, often in response to government-imposed discriminatory measures such as compulsory HIV testing of immigrants and students.

AIDS in Africa

Infection with HIV is now endemic in several African countries; estimates of the number of infected people range in the millions. Seroprevalence rates of HIV infection vary from less than 1% up to 20% of the general adult population, and from 27% to 88% of female prostitutes in some cities of Central and East Africa. It is evident that, in many parts of the continent, HIV infection has created a major public health problem, which may have reached the same scale as malaria, diarrhoea, respiratory diseases, and malnutrition.

In one major hospital in Central Africa, up to 35% of the children and adults admitted have HIV infection, and this figure is likely to increase. Thus, many African clinicians are taking care of HIV-infected patients, and they will be confronted with an increasing number of AIDS cases in the near future.

The ability to recognize HIV-associated disease is important because of its implications for the management of the patient and the patient's environ-

ment and family. However, since this is a new disease, physicians and other health workers have not been trained in its diagnosis and management. In addition, the clinical presentation of HIV infection in Africa is somewhat different from that found in European and American patients. The overwhelming majority of publications on the clinical features of AIDS relate to patients in Europe or North America, making them sometimes less useful for African practitioners.

The major aims of this book are therefore to provide a comprehensive description of the clinical manifestations of HIV infection in Africa and give some guidelines for the management of patients. It is written primarily for physicians working in hospitals. The content is derived both from published material and from the authors' experiences with patients with HIV infection. The authors recognize that information on several aspects of HIV infection and AIDS in Africa is still very incomplete. It is hoped that a future edition will be based more on local experience and will include guidelines for case management that are more specific to the African situation.

2. Etiology and pathogenesis

Human immunodeficiency virus (HIV)

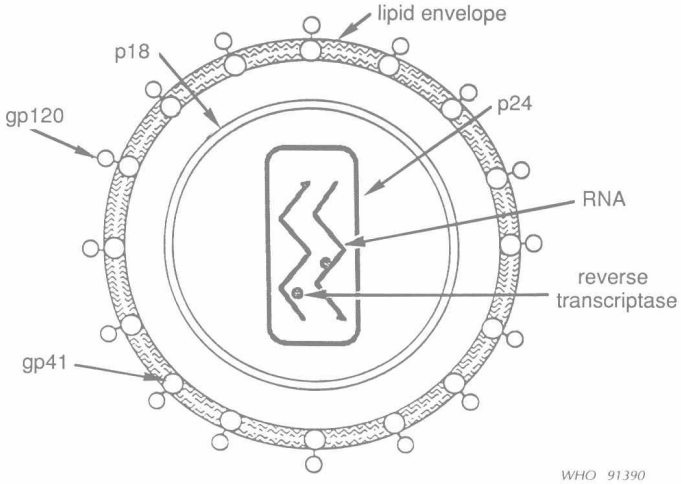
Only 2 years after AIDS was first described, in the United States of America, scientists in France isolated its causative agent, which they called lymphadenopathy-associated virus (LAV). The virus was independently isolated by two groups of research workers in the USA, who called it human T-lymphotropic virus type III (HTLV-III) and AIDS-related virus (ARV). The virus is now generally known as the human immunodeficiency virus (HIV).

HIV belongs to a group of retroviruses, more specifically to the family Retroviridae, subfamily Lentivirinae. Other retroviruses cause disease in animals, including feline leukaemia virus, equine infectious anaemia virus, caprine arthritis-encephalitis virus, and visna virus. The diseases they produce share immunological and pathological characteristics with AIDS in humans; however, these retroviruses are genetically and phenotypically strikingly different from HIV. Different isolates of HIV exhibit genomic diversity, particularly in the *env* region, which codes for the major exterior glycoprotein of the virus. It is not clear whether this variability has any implication for the pathogenesis of disease.

HIV has an outer membrane or envelope that is about 0.014 μm thick (Fig. 1). Because of its glycoprotein content, this envelope has been found to be extremely susceptible to destruction by heat, household detergents, bleach, and alcohol.

Inside this outer glycoprotein coat are the "core" proteins and genes—the genome of the virus. These have been designated the *gag* gene, the *env* gene, the *pol* gene, and the *tat* gene. The internal "core" proteins are encoded by the *gag* gene, the envelope of the virus (glycoproteins with relative molecular mass of 41 000 and 120 000) is encoded by the *env* gene,

Fig. 1. Structure of HIV



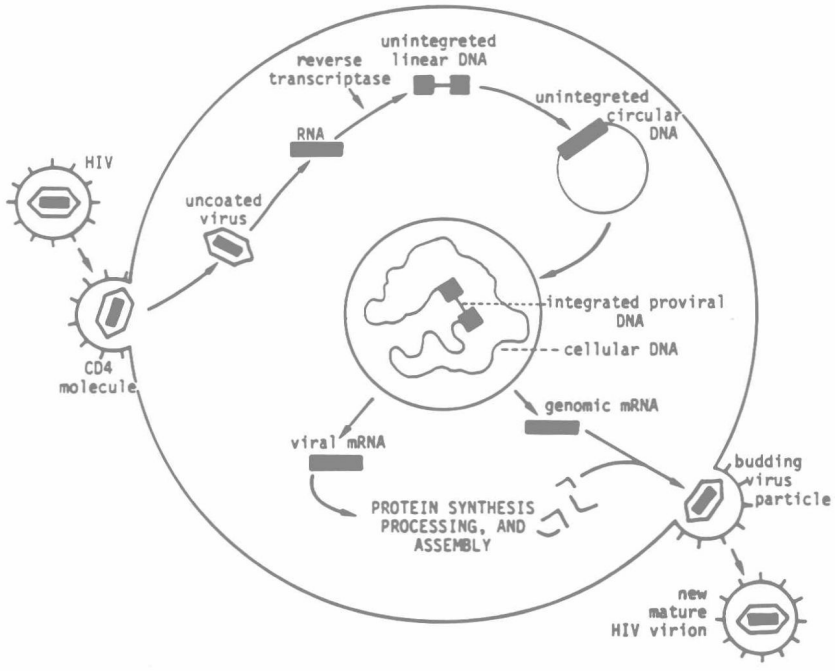
while the *pol* gene is responsible for the production of an important enzyme, reverse transcriptase, which enables the virus to manufacture DNA from RNA. The *tat* gene appears to play a critical role in the regulation of viral replication and possibly in the pathogenesis of AIDS.

Fig. 2 shows the replication cycle of the virus. Important biological properties of HIV include the presence of reverse transcriptase; the ability of viral DNA to integrate into the genome of the host cell; the preferential infection of T lymphocytes with the helper phenotype (CD4/OKT4/Leu 3a+—hereafter referred to as CD4+) and the ability to infect monocytes/macrophages, which are probably responsible for spreading the virus throughout the human body, including the brain.

HIV infection of CD4+ cells may result in cell destruction. However, the virus may also remain in a state of latency in the lymphocytes or macrophages, or replicate without causing clinical disease. The mechanism responsible for the dramatic cytopathic effect on infected cells (Fig. 3) is not precisely known. It is thought that once an individual has become infected with this virus, he or she remains infected for life.

HIV has been isolated from blood (including serum, CD4+ cells, and cell-free plasma), semen, vaginal/cervical secretions, bone marrow, saliva, brain tissue, cerebrospinal fluid, tears, urine, amniotic fluid, and breast milk, but only blood, sexual secretions, and breast milk have been shown to

Fig. 2. Replication cycle of HIV

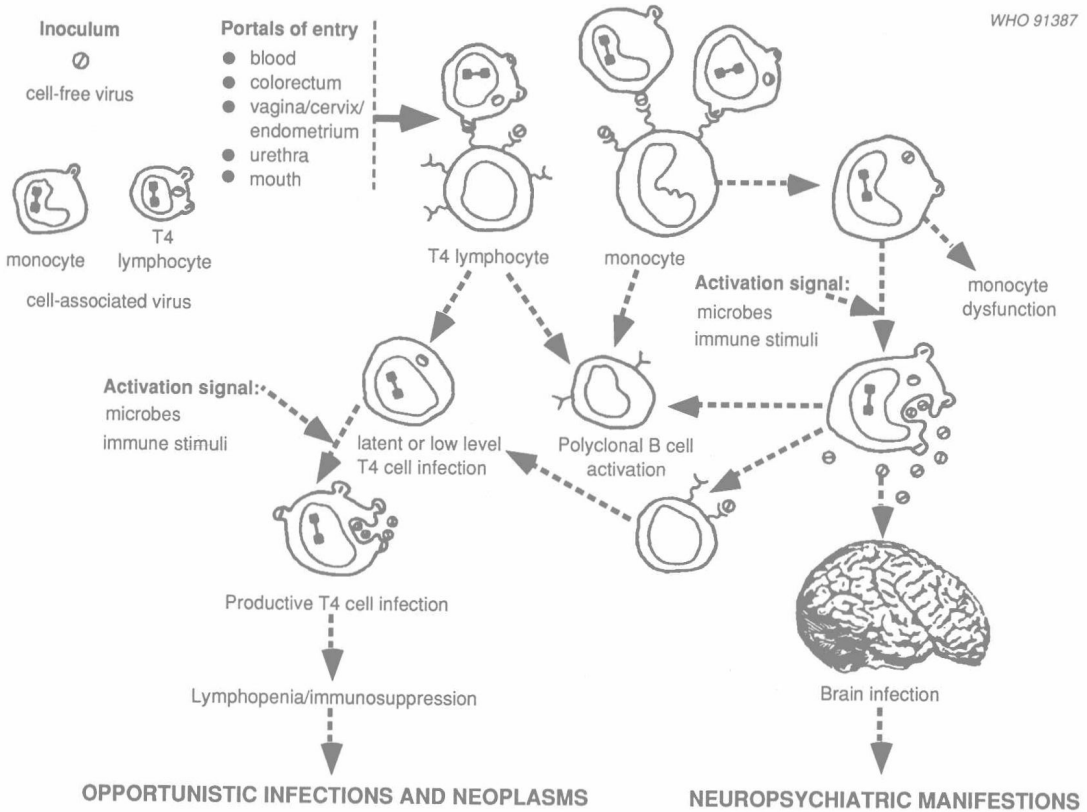


transmit the virus. Although HIV can now be isolated by several laboratories throughout the world, this is a technically demanding and costly procedure and is not done on a routine basis.

HIV-2

In 1985 retroviruses that caused immunodeficiency but were different from the original HIV were isolated from individuals residing in West Africa. Similar isolates, designated HIV-2, have been recovered from asymptomatic individuals and from patients with AIDS and AIDS-related complex (ARC). They cross-react serologically with isolates of simian immunodeficiency virus (SIV), a retrovirus found in some monkey species. HIV-2 also infects preferentially CD4+ cells. Serological evidence of human infection with these viruses has been found not only in West and Central Africa, but also in Europe. HIV-2 also seems to be new and to be spreading slowly over the continent of Africa, apparently through the same mechanisms of transmission as HIV-1.

Fig. 3. Potential mechanisms of pathogenesis of HIV infection (from: Fauci, A. S. The human immunodeficiency virus: infectivity and mechanisms of pathogenesis. *Science,* **239**: 620 (1988)).



Importantly, individuals infected with HIV-2 often do not give a positive reaction in commonly used serological tests for HIV-1, such as commercially available enzyme immunoassays. In particular, antibodies against the envelope glycoprotein gp41 of HIV-1 are usually not produced. In contrast, most individuals with HIV-2 infection have antibodies that cross-react with the core proteins of HIV-1 in a Western blot assay. However, currently used serological tests increasingly incorporate antigens capable of eliciting antibodies to both HIV-1 and HIV-2.

Immunological abnormalities

The clinical manifestations of AIDS and ARC result primarily from the critical injury to the immune system caused by the selective infection of CD4+ cells. The central role of T4 lymphocytes (including CD4+ cells) in the human immune system is illustrated in Fig. 4.

Because of the selective destruction of the CD4+ cells, functional defects can be identified in virtually every part of the immune system, including humoral and cellular immunity (Table 1). Infected macrophages play an important role in spreading HIV all over the body and may be responsible for directly infecting the brain cells. It should be noted that the immunological laboratory findings are neither diagnostic nor specific for AIDS or associated syndromes (see Chapter 7).

Fig. 4. The central role of the T4 lymphocyte in the human immune system

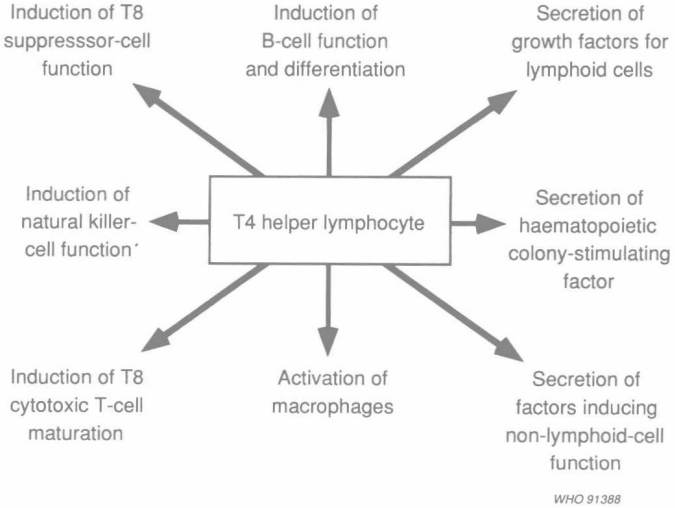


Table 1. Immunological abnormalities associated with HIV infection

Characteristic abnormalities
Depletion of CD4+ T lymphocytes
Polyclonal B-cell activation with increased spontaneous proliferation and IgG production—predominantly IgG, IgG_3, IgA, and IgD
Decreased γ-interferon production in response to mitogens and antigens
Decreased humoral response to certain immunogens
Decreased helper function for pokeweed mitogen-induced B-cell IgG production
Decreased proliferative response to soluble antigens
Impaired delayed-type hypersensitivity
Consistently observed abnormalities
Lymphopenia
Decreased proliferative response to T-cell mitogens and alloantigens
Increased immune complex formation
Decreased monocyte chemotaxis
Decreased interleukin-2 production
Decreased proliferative response to B-cell mitogens
Decreased major histocompatibility complex class-II antigen expression on monocytes/macrophages
Increased acid-labile α-interferon levels
Decreased cytotoxicity to virus-infected cells
Decreased natural killer-cell activity despite normal binding to target cell
Decreased proliferative response to autologous mixed lymphocyte reaction and to anti-T3

Persons infected with HIV develop IgG serum antibodies to specific viral antigens 4–18 weeks after becoming infected. IgM serum antibodies have also been found in some patients. IgG antibodies to HIV detected in the currently available serological assays (see Chapter 7) do not neutralize the virus. However, low concentrations of specific neutralizing serum antibodies can be demonstrated. This finding may have important implications for understanding the pathogenesis of AIDS as well as for vaccine development. IgG antibody to HIV is also synthesized in the central nervous system.

It is noteworthy that HIV can be isolated from the overwhelming majority of seropositive individuals. This implies that for practical purposes, seropositive persons should be considered infective.

Natural history of HIV-1 infection

Soon after becoming infected with HIV-1, some people have an acute self-limiting illness, indistinguishable from many other mild viral illnesses. After