World Health Organization
Regional Office for Europe
Copenhagen

Guidelines on AIDS in Europe

First revised edition

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The guidelines on AIDS contained in this book were drafted by Dr H. Zoffmann, Statens Seruminstitut, Copenhagen, Denmark and amended and approved by the participants in the Consultation on AIDS Policies in Europe (see Annex 5). This first revision incorporates data up to 30 September 1985.

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FOREWORD

The etiological agent of the acquired immune deficiency syndrome (AIDS), at present threatening the health of the European population, has only recently been identified independently by Dr Luc Montagnier (Institut Pasteur, Paris) and then by Dr Robert Gallo (National Institutes of Health, United States). AIDS is caused by a retrovirus, termed lymphadenopathy-associated virus (Montagnier) or human T lymphotropic virus type III (Gallo). The name has yet to be finalized by the International Committee on Taxonomy of Viruses.

The origin of this virus is not yet clearly understood. The number of registered AIDS cases in the European Region at present is approaching 1600 and the epidemiological situation is disturbing; experts have estimated that about 100 000 Europeans may already be infected with the virus.

The following facts about the disease indicate the need for immediate joint action directed at the protection of the European population.

1. The case fatality rate is high, at least 50% of patients dying within a year of diagnosis.

2. The number of new cases is rapidly increasing, doubling every 6-12 months.

3. Known therapy is not effective.

4. Chemoprophylactic means are not available.

5. The development of an effective vaccine will probably take several years at least.

6. The long incubation period (up to six years, perhaps more) makes diagnosis difficult at the initial stage of the disease and makes the surveillance of the spread of infection difficult and uncertain.

7. Asymptomatic infection may persist for years.

8. The majority of European countries are as yet insufficiently equipped with reagents for specific serological tests for use in screening.

To formulate a Regional Office policy on AIDS control in the European Region, a Consultation on AIDS Policies in Europe took place in Atlanta, United States, on 19 April 1985, immediately after the International Conference on AIDS (14-17 April) and the WHO Global Consultation on AIDS (18 April). As a result of this meeting, five main activities were suggested.

1. The preparation of Regional Office guidelines on AIDS for public health authorities in Member States. These guidelines are presented herewith.

2. An appeal by the Regional Office to national counterparts for communicable diseases to direct the attention of national health authorities to the seriousness of the AIDS epidemic and to the appropriate control measures. This appeal has been made.

3. Strengthening of AIDS surveillance in the European Region through closer cooperation and collaboration of national institutions with the WHO collaborating centre for AIDS in Paris. Special appeals were made at the thirty-fifth session of the WHO Regional Committee for Europe in September 1985, following a circular letter on 30 May from the collaborating centre to all national counterparts for communicable diseases. A third appeal for all Member States of the European Region to join the surveillance programme has now been made.

4. The designation of new collaborating centres for virology and serology of AIDS in the Region. These would maintain reference reagents for LAV/HTLV-III antibody tests, provide laboratory training of staff to undertake these tests, provide reference facilities for positive sera, and coordinate the evaluation of antibody tests. Such centres have been or are being designated in Belgium, France, the Federal Republic of Germany, Greece, Hungary, Sweden, the USSR and the United Kingdom.

5. The designation of national collaborating institutions and of an individual (or office) responsible for AIDS surveillance and control. The Regional Office has launched appeals to the Member States to this effect.

Although progress in the control of AIDS greatly depends on the further development of basic research on virology, immunology and pharmacology, assertive public health measures are urgently required. It is hoped that these public-health-oriented guidelines will be useful for national health authorities and medically

qualified personnel in their efforts to prevent the further spread of AIDS in the European Region through currently available conventional measures.

J.E. Asvall
WHO Regional Director for Europe

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Introduction

The acquired immune deficiency syndrome (AIDS) is a contagious viral disease with a very high fatality rate. AIDS was first recognized in 1981 in the United States and Europe, since when its incidence has risen rapidly, and cases are seen in many countries of the world. Nearly 18 000 cases have been reported, mostly from the industrialized countries, the highest prevalence being in the United States.

An International Conference on AIDS, sponsored by the United States Department of Health and Human Services and the World Health Organization, was held in Atlanta on 15-17 April 1985. More than 3000 participants from 50 countries attended. This conference was followed by a Global Consultation on AIDS, organized by WHO on 18-19 April, where the participants reviewed the information presented at the conference and assessed its international health implications.[a]

In addition, a Consultation on AIDS Policies in Europe was held on 19 April to consider aspects of specific relevance to the European Region of WHO. This consultation recommended that the WHO Regional Office for Europe should prepare AIDS guidelines for Member States, specially designed for those not yet directly affected by the epidemic. The aim of these guidelines is to give a brief introduction to the AIDS problem and to the public health measures that can be taken to reduce the spread of infection.

Magnitude of the AIDS problem

Europe

Since the beginning of the AIDS epidemic in 1981, prevalence has increased exponentially, with a doubling time of 6-12 months. By September 1985, a total of 1573 cases had been reported to the WHO collaborating centre for AIDS in Paris (see Annex 1). Of these, 92% were in males and 42% were in the age group 30-39 years.

In the first half of 1985, an average of 27 new cases per week were reported to the collaborating centre. The recorded incidence of AIDS varies considerably among countries. The number of cases reported in 21 European countries and estimated rates per million

[a] The worldwide health implications of AIDS, as discussed at the Global Consultation, are described in Bulletin of the World Health Organization, 63: 667-672 (1985).

population are shown in Table 1. The highest rates were in Belgium, Denmark and Switzerland. Some 72% of the Belgian cases and 12% of the Swiss cases were in patients from Equatorial Africa, in contrast to Denmark where no African or Caribbean cases were reported. For comparison, the rate in the United States was 48.4 per million population in June 1985.

Table 1. Total number of AIDS cases reported in 21 European countries and estimated rates per million population[a]

Country	Number of cases				Rate
	October 1984	March 1984	June 1985	September 1985	
Austria	-	13	18	23	3.1
Belgium	-	81	99	118	11.9
Czechoslovakia	0	0	0	0	-
Denmark	31	41	48	57	11.2
Finland	4	5	6	10	2.0
France	221	307	392	466	8.5
Germany, Federal Republic of	110	162	220	295	4.8
Greece	2	7	9	10	1.0
Hungary	-	-	-	0	-
Iceland	0	0	0	0	-
Italy	10	22	52	92	1.6
Luxembourg	-	-	1	3	7.5
Netherlands	26	52	66	83	5.7
Norway	4	8	11	14	3.3
Poland	0	0	0	0	-
Spain	18	29	38	63	1.6
Sweden	12	22	27	36	4.3
Switzerland	33	51	63	77	11.8
USSR	-	-	-	0	-
United Kingdom	88	140	176	225	4.0
Yugoslavia	-	-	-	1	-
Total	559	940	1226	1573	

[a] Based on 1985 populations.

The distribution by patient risk group is shown in Table 2; 69% of cases were in male homosexuals or bisexuals. Compared to the distribution in the United States, few AIDS cases (6%) were recorded in intravenous drug abusers. Nevertheless, serological surveys have shown that LAV/HTLV-III infection is now spreading among intravenous drug abusers in some European countries. Some 3% of the cases were in haemophiliacs, and for 2% the only risk factor found was blood transfusion. Some of these patients had received transfusion overseas in Haiti and Martinique, the United States and Zaire. Seven per cent of cases were in people with no known risk factors; in this group, the male:female ratio was about 2:1.

Table 2. AIDS cases by patient risk group and geographic origin for 21 European countries,[a] 30 September 1985

Patient risk group	Origin				Total	
	Europe	Caribbean Islands	Africa	Other	Number	%
Male homosexuals or bisexuals	1031	4	11	39	1085	69
Intravenous drug abusers	90				90	6
Haemophiliacs	52			1	53	3
Transfusion recipients (without other risk factors)	30		5		35	2
Both homosexuals/ bisexuals and intravenous drug abusers	21		1	2	24	2
No known risk factor						
males	59	24	81	3	167	11
females	31	10	43		84	5
No information	16	1	16	2	35	2
Total	1330 (85%)	39 (2%)	157 (10%)	47 (3%)	1573	100

[a] Austria, Belgium, Czechoslovakia, Denmark, Finland, France, Federal Republic of Germany, Greece, Hungary, Iceland, Italy, Luxembourg, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, USSR, United Kingdom, Yugoslavia.

Surveillance

During the spring of 1984, a WHO collaborating centre for AIDS was established in Paris.[a] The functions of the centre are:

- to collate and consolidate information on the number of cases of AIDS in Europe and in other areas of the world, based on national reports;

- to present this information by epidemiological characteristics, risk groups and diagnostic categories;

- to ensure rapid exchange of information by publication at regular intervals of an information bulletin (this could also include information on current research or other pertinent data, with the particular purpose of indicating to research workers the types of studies being performed in the different institutions, thus avoiding duplication);

- to provide information about the possibilities of international collaborative studies, provision of reagents, exchange of material, important publications, and meetings on AIDS;

- to advise WHO on all relevant facts and progress on AIDS research.

To ensure simple and uniform reporting, the centre sends standard record forms to cooperating countries each quarter. In October 1985, 21 of the 33 countries in the WHO European Region were reporting to the centre.

At the Consultation on AIDS Policies in Europe, the value of the work of the collaborating centre was acknowledged, and it was recommended that the Regional Office should encourage all countries in the European Region to report to the centre.

In most countries, the reporting of AIDS cases is based on voluntary notification to the national health authorities. In a few countries, notification is compulsory. The consultation further recommended that the Regional Office should encourage the designation of national institutions for AIDS surveillance in all countries.

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United States of America

By 29 July 1985, 12 067 AIDS cases, involving 11 919 adults and 148 children, had been reported to the Centres for Disease Control (CDC) in Atlanta. Some 73% of the cases were in homosexual or bisexual men, 17% in intravenous drug abusers, 1.5% in blood transfusion recipients, 1% in haemophiliacs, 1% in heterosexual contacts of AIDS victims or carriers, and 6.5% in individuals with no known risk factors (1).

Recently, CDC published estimates of AIDS prevalence in certain high-risk groups, showing rates of 175-205 per 100 000 single men living in Manhattan, New York and San Francisco, and rates of between 200 and 270 among intravenous drug abusers in New York City and New Jersey. Prevalence among patients with severe haemophilia is estimated at 300 per 100 000 (2).

Other countries and regions

In Canada, 248 cases had been reported by 14 June 1985. The distribution by sex, age and risk group is similar to that reported from the United States.

In the Caribbean area, most cases are registered in Haiti, 340 having been reported by 31 December 1984. AIDS prevalence in Haiti is 60 per million population, which is the highest rate reported anywhere in the world. Compared to Europe and the United States, cases in females account for a significantly higher proportion, and heterosexual activity may be an important factor in the transmission of AIDS in Haiti.

In South America, 226 cases have been registered in 10 countries, including 182 cases reported from Brazil.

In Africa, cases of AIDS have been reported from several countries in the central part of the continent. Congo and Zaire have recently been identified as having a high incidence of AIDS. Contrary to both Europe and the United States, the male:female ratio is nearly 1:1, and the virus is widely spread in the community. Heterosexual activity seems to play an important role in the transmission of the virus. According to recent epidemiological data, the use of contaminated needles and syringes in health care facilities may also be a major factor in transmission.

No information is available from most countries in Asia, although six cases have been reported from Japan.

In Australia, 67 cases had been reported by March 1985. The distribution of cases by risk group resembles that reported from the United States.

The virus (see also Annex 2)

The etiological agent of AIDS is a retrovirus described in the scientific literature as lymphadenopathy-associated virus (LAV), human T leukaemia virus or human T lymphotropic virus type III (HTLV-III) or AIDS-related virus (ARV). The definitive name will be a matter for approval by the International Committee on Taxonomy of Viruses, in accordance with the rules governing virus nomenclature. In this text, it will be referred to as LAV/HTLV-III, which combines the two most widely used names.

The virus has a specific tendency to infect a subset (OK T4+) of the T lymphocytes and has been shown to be present in brain tissue. The virus replicates in actively dividing T4 lymphocytes and, like other retroviruses, can remain in lymphoid cells in a latent, unexpressed state that can be activated. The virus is prone to mutation, and in particular the protein antigens of the envelope keep changing, which may create problems for the development of an effective vaccine.

LAV/HTLV-III is heat-sensitive. The virus is readily inactivated by ether, acetone, ethanol (20%), sodium hypochlorite (0.2%), beta-propiolactone (1:400 dilution), sodium hydroxide (40 mmol/l) and glutaraldehyde (1%), but is relatively resistant to ionizing radiation and ultraviolet light. The inactivation procedures used in preparing hepatitis B vaccine from human plasma have been shown to inactivate LAV/HTLV-III.

Mode of transmission

LAV/HTLV-III has been isolated from human blood, saliva and semen. Epidemiological data indicate that LAV/HTLV-III infection in humans is transmitted during intimate sexual contact and by blood and blood products. The infection may be transmitted from infected pregnant women to their children.

In the United States, cases of AIDS in individuals with no known risk factors have constituted a small and rather constant proportion of the total number of cases throughout the years, indicating a slight spread of AIDS from the risk groups to the general population. This also seems to be the case in Europe, where the proportion of indigenous AIDS cases in individuals with no known risk factors has been consistently low. Nevertheless, the spread of

LAV/HTLV-III infection outside risk groups has begun in both Europe and the United States.

In Africa, epidemiological information obtained recently suggests that exposure to contaminated needles and syringes in health care facilities may play a role in the transmission of LAV/HTLV-III infection. This may also apply to Haiti.

There is no evidence of LAV/HTLV-III transmission by casual social contact or by sneezing, coughing or the sharing of meals.

There is concern over the occupational risk for health care workers taking care of AIDS patients or handling specimens from them, but the additional risk is low (3). The virus can be transmitted by accidental needlestick injury (4). As at 26 September 1985, only one confirmed and two possible cases of transmission to health care personnel had been observed worldwide; these were caused by needlestick injury with contaminated needles (5). A few cases have been reported in health care workers with no known risk factor for acquiring AIDS, but there is no evidence that these were caused by exposure to AIDS patients.

Infection and major clinical features

The natural history of LAV/HTLV-III infection is still unknown. It is assumed that the infection in many cases will remain subclinical. Some infected individuals will develop transient or intermittent symptoms, and others will develop chronic lymphadenopathy with or without other symptoms, such as weight loss, diarrhoea and fever. It is estimated that 100 000 individuals in Europe and 0.5-1 million in the United States are infected with LAV/HTLV-III. How many of these will develop AIDS is unknown, but rates of between 5% and 20% have been reported.

The basic abnormality caused by LAV/HTLV-III infection is an impairment of the cellular immune response followed by a decrease of resistance to various infections, many of which are opportunistic, and/or the development of certain types of cancer.

According to the CDC surveillance definition (6), which has been adopted internationally, AIDS is:

- histologically verified Kaposi's sarcoma in individuals under the age of 60 years; or

- life-threatening or fatal opportunistic infections indicating cellular immune defect in individuals where no underlying cause of immune defect can be established.

CDC has recently adopted a revised case definition of AIDS for reporting purposes (Annex 4). The most important amendment to the definition is the introduction of laboratory testing for LAV/HTLV-III infection and for reduced cellular immunity, so that negative results on testing will lead to the exclusion of such patients suffering from AIDS. In the absence of test results, patients satisfying the above-mentioned clinical criteria will continue to be included. The clinical features of AIDS in Europe and the United States are similar.

In countries where appropriate diagnostic techniques are available, the surveillance definition for AIDS given by the Centers for Disease Control and published by WHO (7) was endorsed by participants at a recent meeting of the WHO collaborating centres on AIDS on 24-26 September 1985. Surveillance definitions are now being developed for use in countries where access to diagnostic techniques is limited.

Based on a report from the WHO collaborating centre in Paris (Annex 1), 65% of the recorded AIDS patients in Europe suffered from opportunistic infections alone, 20% from Kaposi's sarcoma and 13% from both.

A number of other symptoms have been considered as prodromal stages of AIDS. These include more or less chronic lymphadenopathy, excessive weight loss, fever and diarrhoea. These various clinical conditions have been termed lymphadenopathy syndrome (LAS) or AIDS-related complex (ARC). Some patients with LAS/ARC subsequently develop AIDS, but the exact proportion is unknown.

In infants, the clinical manifestations of LAV/HTLV-III infection resemble those seen in adults, although diarrhoea may be a more prominent symptom. Suspicion of AIDS in infants should be raised when one of the parents belongs to a risk group for AIDS, and either the mother or the infant has serological evidence of LAV/HTLV-III infection.

Mortality and case fatality

The case fatality rate in AIDS is very high. Over 50% of AIDS patients die within a year after diagnosis has been confirmed, and a further 30% within the next 2-3 years. The fatality rate is related to the symptoms: 56% in those with opportunistic infection, 25% in those with Kaposi's sarcoma, and 59% in those with both. In certain high-risk groups in the United States, the risk of dying from AIDS is estimated as similar to that from heart disease or cancer (2).

Laboratory tests

Demonstration of a reduced T-cell immune response is important to the diagnosis, since the majority of AIDS patients have a low number of T-helper cells. A decreased ratio of T-helper to T-suppressor cells may be an indirect indicator of reduced cellular immunity.

Tests for antibody against LAV/HTLV-III have recently been made commercially available. Demonstration of LAV/HTLV-III antibody gives strong support to the establishment of the diagnosis, since most AIDS patients and nearly all with LAS/ARC are antibody-positive.

Demonstration of antibody against LAV/HTLV-III is considered a specific and sensitive test for infectivity, since LAV/HTLV-III has been isolated from most of the antibody-positive individuals studied. Nevertheless, the correlation between infectivity and presence of antibody is not absolute. There is a low frequency of both false positive and false negative test results, and LAV/HTLV-III has been isolated from antibody-negative persons. A test for viral antigen, which might be more valuable than a test for infectivity, is being developed; it is unknown whether such tests will be more specific or sensitive than the currently available tests for antibody against LAV/HTLV-III.

A variety of assays are available for detecting anti-LAV/HTLV-III. These include enzyme-linked immunosorbent assay (ELISA), solid-phase radioimmunoassay, immunofluorescence (IF), radioimmunoprecipitation and Western blot assays. The tests most widely used for screening purposes are ELISA and IF. Both can be performed in most diagnostic laboratories, require relatively simple equipment, and can be carried out in two working days. Serum that is repeatedly positive by ELISA or IF should be tested by an additional method before the final diagnosis is made. The additional method might comprise:

- a repeat of the same type of assay (ELISA or IF) but with reagents obtained from a different manufacturer;

- demonstration that serum is positive with the test antigen but not with a control antigen prepared from uninfected cells;

- the use of techniques that detect antibody against one or more structural components of the virus, e.g. radioimmuno-precipitation that detects antibody to the p-24 protein, or Western blot assays that detect antibody against one or more of the core or structural proteins.