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The Epidemiology of AIDS in Europe

INTRODUCTION

THE ACQUIRED immune deficiency syndrome (AIDS) was first described in the U.S.A. in 1981 [1]. Using the strict clinical criteria adopted by the Centers for Disease Control (CDC), U.S. Public Health Service, over 2500 cases had been diagnosed as of mid-October 1983. More than 1100 of these cases were diagnosed in the first 9 months of 1983 alone [CDC, unpublished data]. Efforts to locate retrospectively diagnosed cases showed that this syndrome, at least in the epidemic form, was new to the U.S.A., with the earliest cases coming to diagnosis in 1979 [2].

The AIDS outbreak in the U.S.A. provoked widespread interest among European clinicians, and soon reports of similar cases began to appear from centers in different parts of Europe. By the present survey, conducted in August and September 1983, 200 cases of AIDS had been diagnosed in Europe (see Table 5 for later update). With the exception of a brief report in the *Weekly Epidemiologic Record* [3], however, there has been no summary of AIDS cases in Europe. The 'AIDS in Europe, Status Quo 1983' meeting, sponsored jointly by the European Regional Office of the World Health Organization and the Danish Cancer Society, 19–20 October, has provided an opportunity to collect and review these cases and to establish guidelines for the collection of further data about AIDS that will be of epidemiologic importance.

METHODS

The AIDS in Europe meeting invited participants who represented both the national health departments, who were responsible for AIDS surveillance, and academic and private researchers engaged in AIDS-related research. All participants were sent questionnaires about AIDS cases in their countries, permitting each to state and use his or her own definition as to what constituted an AIDS case. The use of individual definitions was necessary because no standard definition had previously been agreed upon in Europe, and because it permitted delineation of the definition problem. Questionnaire information sought data about the timing, distribution and place of case occurrence, risk group association and clinical features. Because of duplicated data submitted by investigators from the same areas, we utilized the most authoritative national reporting source as the basic data, with additional reviews of other questionnaires, to obtain the most complete ascertainment of cases possible.

RESULTS

European summary

Two hundred cases of AIDS were reported by participants. Generally, cases were defined according to the clinical criteria established in the CDC definition, but many of the participants also included the necessity of being able to demonstrate an immunologic abnormality, usually of the lymphocyte helper:suppressor ratio at a minimum, as part of their definition.

The distribution over time is presented in Table 1. Eight cases fitting the current AIDS definition occurred prior to 1979 and were found by retrospective searches. The clinical features of these cases have been [4–6] or will be published by individual investigators. The number of cases diagnosed thereafter increased steadily from 2 cases in 1980 to 104 cases in 1983. Cases were predominantly adult males (87.0%). All but 1 of the 21 adult female cases were African (17 of 42 African cases) or Haitian (3 of 8 Haitian cases). Three cases were diagnosed in children.

Because a substantial proportion of the cases in Europe have been diagnosed among non-Europeans who were either resident in or referred to Europe for diagnosis or therapy (26%), the cases among Europeans were analyzed separately (Table 2). Risk groups among the 148 European cases were homosexual or bisexual men (79.7%), homosexual men using illicit intravenous drugs (1.4%), heterosexual users of illicit intravenous drugs (1.4%) and hemophiliacs (4.1%), but cases not fitting in these categories (sometimes because of inadequate information) were a substantial

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Address requests for reprints to: The Institute of Cancer Research, Radiumstationen, DK-8000 Aarhus C, Denmark.

Table 1. Distribution by time and country of diagnosis for all cases of AIDS diagnosed in Europe during August/September 1983

Country	Year of diagnosis						
	Pre-79	79	80	81	82	83	Total
Austria						7	7
Belgium			2	3	7	14	26
Czechoslavkia					1	1	2
Denmark			2	3	5	2	12
F.R.G.	1	1			7	22	31
Finland						2	2
France	6	1	5	3	26	29	70
Greece							0
Italy	1				2		3
Netherlands					3	5	8
Norway					1	1	2
Poland							0
Spain				1	1	5	7
Sweden						3	3
Switzerland			2	2	5	4	13
U.K.				1	4	9	14
U.S.S.R.							0
Total	8	2	11	13	62	104	200

Data contributed by questionnaire were used to develop manuscript and subsequent tables. However, new and revised old data were provided at the conference and are provided in Table 5.

proportion (13.5%). France reported the largest number of cases among Europeans (51) and the F.R.G. was second (30), but almost all areas of Europe reported at least 1 case. Major exceptions were the Eastern European nations, among which only 1 case was diagnosed in a European.

Non-European cases (Table 3) included 1 citizen from the U.S.A. and 1 from Nicaragua, both of whom were homosexual or bisexual men. The remaining 50 cases were from Africa (42) and Haiti (8). All the cases reported from Belgium (26) have been Africans, and additional cases among Africans have been diagnosed in France (11), Switzerland (4) and Czechoslovakia (1). All the Haitian cases have been diagnosed in France. Details about these African and Haitian cases have been published [7–9] or are presently in press.

The disease features among European cases (Table 4) will be discussed in detail in companion articles. Opportunistic infections were most common (73.6%), including those who also had Kaposi's sarcoma (15.5%). Kaposi's sarcoma as the sole manifestation of AIDS, occurring in 23.0%. Diseases diagnosed as AIDS without either an opportunistic infection or Kaposi's sarcoma were reported in 3.4% of cases, but this reflected a lack of information in some cases. Kaposi's sarcoma was notably more common among homosexual and bisexual men. Fifty (87.7%) of 57 European cases with Kaposi's sarcoma occurred among homosexual men. No cases of Kaposi's sarcoma occurred among the 6 hemophiliac AIDS cases.

Among the African cases 31 (73.8%) had opportunistic infections, including 2 who also had Kaposi's sarcoma. Five (11.9%) had Kaposi's sarcoma as the sole manifestation and the remainder (14.3%) either had other manifestations or had inadequate information to categorize them. The Haitian cases all had opportunistic infections, but 2 cases also had Kaposi's sarcoma.

DISCUSSION

The principal clinical manifestations of this syndrome both in the U.S.A. and Europe have been opportunistic infections and Kaposi's sarcoma [8, 10–14]. In summary, most of these illnesses appear to be secondary to a profound depression of cellular immunity, and it has been appreciated that nearly all of the cases in whom tests were conducted had a demonstrable immunologic abnormality. While a variety of abnormalities involving both B and T lymphocytes of the helper and suppressor types have been described, the most consistent finding appears to be a low or inverted T cell helper:suppressor ratio [15, 16]. The European investigators who used an immunologic abnormality as part of the diagnostic criteria for AIDS most often mentioned this test. However, it is not required in the definition described by the CDC.

The CDC definition (Appendix) is purely

Table 2. Distribution of all cases among European citizens (classified according to risk group) that were diagnosed in Europe during August/September 1983

	Year of diagnosis																														
	Pre-79					79					80					81					82					83					Total
	Homosex.	Both*	Drug†	Hemophil.	Other	Homosex.	Both	Drug	Hemophil.	Other	Homosex.	Both	Drug	Hemophil.	Other	Homosex.	Both	Drug	Hemophil.	Other	Homosex.	Both	Drug	Hemophil.	Other	Homosex.	Both	Drug	Hemophil.	Other	
Austria																										4	1	1	1		7
Belgium																															
Czechoslovakia																										1					1
Denmark											2					3					4				1	2					12
Fed. Rep. Germany	1									1											2			1	3	22					30
Finland																										2					2
France	4				2	1					1				4	2				1	14				2	19			1		51
Greece																															0
Italy					1																2										3
Netherlands																					2				1	4					7
Norway																					1					1					2
Poland																															0
Spain																1					1					2		1	2		7
Sweden																										3					3
Switzerland											1				1	2					2				2	1					9
United Kingdom																1					4					6	1		1	1	14
U.S.S.R.																															0
Total	5				3	1				1	4				5	9				1	32			1	9	67	2	2	5	1	
	8					2					9					10					42					77					148

*Both refers to both homosexual and drug using.
†Drug refers to users of illicit intravenous drugs.

Table 3. Distribution of all cases among non-European citizens that were diagnosed in Europe during August/September 1983

Country where diagnosed	Citizen of:	Year of diagnosis Pre-79	79	80	81	82	83	Total
Belgium	Africa			2	3	7	14	26
Czechoslovakia	Africa					1		1
F.R.G.	U.S.A.					1		1
France	Africa					4	7	11
	Haiti					6	2	8
Netherlands	Nicaragua						1	1
Switzerland	Africa					1	3	4
Total				2	3	20	27	52

See Table 5 for update.

Table 4. Distribution of illness type for persons classified by risk group or country of origin—all cases diagnosed in Europe during August/September 1983

	Type of AIDS-related illness OI	OI+KS	KS	other or unknown	Total
European					
Homosexual	65	21	29	3	118
Both	1	1			2
Drug		1	1		2
Hemophiliac	5			1	6
Other	15		4	1	20
Total	86	23	34	5	148
American					
Homosexual	2				2
Total	2				2
Other					
African	29	2	5	6	42
Haitian	6	2			8
Total	35	4	5	6	50
Total	123	27	39	11	200

OI = opportunistic infections; KS = Kaposi's sarcoma.

clinical in scope. Originally restricted to certain diseases, namely *Pneumocystis carinii* pneumonia and Kaposi's sarcoma, it has subsequently expanded to include other conditions common among immunosuppressed persons. It also specifies that the person must have no other recognized cause for an immune abnormality and, in the case of Kaposi's sarcoma only, that the case be <60 yr old. This definition, while imperfect, is routinely used in the U.S.A. The participants of this meeting agreed that this definition will be used at least for the purpose of epidemiologic surveillance by all AIDS investigators in Europe. Only by adopting a common standard will European cases be comparable to those in the U.S.A. Should the need arise to change this definition, such changes should then be made by the CDC and the European investigators jointly, under the auspices of the World Health Organization. At the moment, use of the CDC criteria will eliminate few of the cases diagnosed in Europe included in this report. However, without adherence to a necessity of finding an immunologic abnormality as part of the diagnosis, it is possible that a number of additional cases, heretofore rejected by some authorities because of inadequate immunologic documentation, may become apparent.

In the development of the epidemic in the U.S.A., certain groups became obvious as being at a high risk for AIDS. These included, initially, homosexual men and users of illegal intravenous drugs, but later investigators saw similar cases among hemophiliac patients and probably

recipients of other blood products [17]. Homosexual men constitute the largest group of AIDS cases in the U.S.A. (71%) and a similar proportion of European cases in this report (80%). Not surprisingly, the distribution of AIDS in the U.S.A. has resembled the distribution of members of these risk groups, particularly homosexual men. Large urban centers, especially New York City, have had a disproportionately large number of cases, but as time has passed more and smaller communities have reported cases [18]. In Europe the pattern has been similar, but the very widespread occurrence of cases is notable. Most are still occurring among the principal cities of Europe, however. Since the distribution of AIDS cases in Europe is also dominated by cases among homosexual men, this probably reflects the distribution of members of this risk group.

Many of the homosexual cases from the smaller U.S.A. communities have reported sexual contact with men from the epicenters of AIDS. Promiscuity and travel are typical lifestyle habits in this risk group, and members report a large number of anonymous sexual contacts [19,20]. It has therefore been difficult to state authoritatively that AIDS can be passed from person to person through homosexual contact. However, such transmission seems likely since several small clusters of cases have occurred among men who were sexually in contact with each other [20], and may also have occurred through heterosexual contact [21]. Furthermore, the similarity in AIDS risk groups to those at high risk of developing hepatitis also suggests transmission by a similar manner [22]. The cases among European homosexual men have also reported homosexual contact with U.S. men, either in the U.S.A. or in Europe, or with another AIDS case [11], adding further substance to the concept of transmissibility.

The cases among users of illegal intravenous drugs in Europe constitute a smaller proportion of all European cases than is observed in the U.S.A. Perhaps there are fewer drug abusers among Europeans, but even in the U.S.A. the distribution of drug-related AIDS cases is heavily weighted towards certain areas, specifically New York City, New Jersey and Miami [CDC, unpublished data]: for example, until this summer no cases of drug-related AIDS had been recognized in San Francisco. One possible explanation is that among drug-using persons in Europe there has not been a long enough period of contact with AIDS for disease to appear.

Hemophiliacs constitute a small but recognizable subset of European cases, just as they do in the U.S.A. Although some European countries manufacture their own factor VIII for distribution to their hemophiliac population, most rely on commercial sources. Commercially manufactured factor VIII is either imported from the U.S.A. or made commercially in Europe from blood products that are at least in part obtained from the U.S.A. There is therefore no assurance that the use of European-manufactured factor VIII products will provide any protection against the development of AIDS.

The non-European cases of AIDS are a subset of particular interest because they suggest an additional risk group based on geography. In this regard 42 cases were diagnosed among Africans evaluated in Belgium, France, Switzerland and Czechoslovakia. This distribution may reflect the distribution of Africans from Central Africa that are resident in, or coming for evaluation to, Europe. The U.K., with a large number of Africans of East, West and Southern African origin, has had no cases among this population, suggesting that the risk within Africa is so far limited to certain regions. (See Table 5 for up-to-date information.) More than one-third of African cases were female, in contrast with the very high proportion of males among European cases. Most of these cases had opportunistic infections, but the occurrence of Kaposi's sarcoma, either alone or with opportunistic infection, was more common than it was among the non-homosexual AIDS cases among European or U.S. citizens.

The relationship between these African cases and AIDS in Europe is not well established. Kaposi's sarcoma is endemic to parts of Central Africa [23], and thus African patients with this disease as their only manifestation of illness will have to be regarded as AIDS cases with suspicion. Investigations to document the immune abnormality in this situation will be of great interest. But in Africa endemic Kaposi's sarcoma is typically not associated with opportunistic infections [24], such as were more common in the African AIDS-type cases reported in Europe. The spectrum of opportunistic infections in these patients has been reported elsewhere [7–9, 25], as well as in the companion article on AIDS symptoms and signs [26]. While some cases may be questionable, many fit the criteria for AIDS as provided by the CDC definition. Some investigators have proposed that AIDS might be occurring endemically in the setting of Central Africa but has only recently spread to Europe and the U.S.A. [7]. It is curious that the frequency of AIDS diagnosed among Africans has increased in the past 4 yr in a manner similar to the epidemic curve of all cases. While this may reflect only referral bias and improved recognition skill, it does raise questions as to how much of the epidemic curve in non-Africans is due to the same phenomenon. Alternatively, AIDS could be new

Table 5. Update of AIDS information provided at the 'AIDS in Europe, Status Quo 1983' conference, Aarhus, Denmark, 19–20 October 1983

Country	Year of diagnosis						
	Pre-79	79	80	81	82	83	Total
Austria						7	7
Belgium			2	4	8	24	38
Czechoslovakia					1	1	2
Denmark			1	2	4	6	13
F.R.G.	1	1			7	33	42
Finland						2	2
France	6	1	5	5	30	47	94
G.D.R.							0
Greece							0
Hungary							0
Ireland						2	2
Italy	1				2		3
Luxembourg							0
Netherlands					3	9	12
Norway						2	2
Poland							0
Spain				1	1	4	6
Sweden					1	3	4
Switzerland			2	3	5	7	17
U.K.				2	5	17	24
U.S.S.R.							0
Yugoslavia							0
Total	8	2	10	17	67	164	268*

Data provided by participants as newly reported cases or as revisions of case status according to new clinical information or better understanding of the AIDS definition. These most recent counts were not used to modify the content of this manuscript or the tables because information was not collected in a standardized format. However, the distribution of the additional cases appeared to follow a similar pattern as in earlier cases.

*Includes 59 African cases from: Zaire (45), Congo (5), Mali (2), Gabon (2), Rwanda (2), Brundi (1), Chad (1) and Cameroons (1), as well as citizens of Haiti (8), U.S.A. (1) and Nicaragua (1).

to Africa, but if so, it would have started there approximately the same time as it did in Europe and the U.S.A.

The very early cases of AIDS-like illness that have been reported among Europeans [4–6] are also interesting. Some are indistinguishable from typical AIDS cases by the CDC criteria and even either share risk group similarity (i.e. homosexuality) or have travel histories that exposed them to Africa. These cases lack detailed immunologic evaluation, but this should not restrict them from being considered as possible cases. One possibility is that they represent AIDS that was restricted in distribution because lifestyle factors, particularly promiscuity among homosexuals, were less extreme than they later became. Another possibility is that they represent unrelated 'background' cases that are now reported because they share a risk group similarity to the current problem. It is peculiar that very early cases have not been reported among U.S. citizens. In the absence of a definitive marker that can be detected on material that might still be available from such cases, it is unlikely that the relationship of these cases to the later outbreak will be resolved.

The need for markers is obvious. From an epidemiologic standpoint, the issue of origin and spread will remain confused until such a marker is available. Certainly the marker will have immediate and widespread application to screening and assessing risk. So far, none of the proposed markers have been sensitive or specific enough to serve in this capacity, but refinements of these assays are still underway. Short of defining the 'AIDS-agent' if such exists, as we feel it does, no surrogate markers are likely to be fully sufficient, although such markers may still help to predict risk. Identifying this agent remains, therefore, of paramount importance to understanding this disease.

These problems emphasize the need for animal models. Recent outbreaks of transmissible illnesses that have some resemblance to AIDS have occurred in primate colonies in the U.S.A., sometimes with devastating results [27]. However, there is no evidence that these outbreaks are identical to each other or are related to AIDS in

humans [28]. So far no personnel associated with these colonies have been diagnosed as having AIDS.

While the cause of AIDS and measures to reduce or eliminate this disease remain elusive, almost all of the cases indigenous to Europe and North America have been in defined populations, such as sexually active homosexual men, intravenous drug users and recipients of certain blood products. Clearly, the evidence suggests that AIDS cannot be acquired by causal contact with members of the risk groups or even with AIDS patients themselves. Even medical personnel dealing with AIDS patients, who might theoretically be expected to be at risk, have had no cases of AIDS. This epidemic is, therefore, likely to remain rather limited to the subgroups that are already known, and to some other groups which are at high risk of hepatitis B that have not yet been investigated. In this regard, the patients from Africa and Haiti are under active investigation.

Nevertheless, AIDS is a major public health problem for the membership of the high risk groups and of widespread concern to the general public. It is also a condition that, once understood, promises to provide new scientific insight into the interrelationship between immunology, opportunistic diseases and neoplasia. We therefore feel that AIDS deserves extensive support for clinical and ethiologically related research in Europe.

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APPENDIX

CDC definition for the diagnosis of AIDS

For the limited purposes of epidemiologic surveillance (in Europe and the U.S.A.), a case of 'the acquired immune deficiency syndrome', also known as AIDS, will consist of a person who has had:

I. a reliably diagnosed disease that is at least moderately indicative of an underlying deficiency in cellular immunity,

but who, in addition, has had:

II. no known underlying cause of cellular immune deficiency nor any other cause of reduced resistance reported to be associated with his or her disease.

Not to be considered in diagnosing a case are either the presence or absence of a laboratory documented immune abnormality or the association of a possible case with recognized risk groups.

Also notably absent in the definition are symptoms and signs such as lymphadenopathy, fever, weight loss, night sweats and persistent diarrhea. Although these sometimes occur in patients who concomitantly or later develop CDC-defined AIDS, by themselves they are not specific for AIDS and require further evaluation and observation to verify the diagnosis.

A complete list of conditions and exclusions for the diagnosis of AIDS according to the CDC definition is available from:

AIDS Task Force,
CDC,
Atlanta,
GA 30333, U.S.A.