



THE QUESTION OF AIDS

Richard Liebmann-Smith

Guidelines on AIDS in Europe

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Richard Liebmann-Smith

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Contents

	Page
Part I	
Introduction	1
Chapter 1—A New Epidemic	3
Chapter 2—AIDS and the Immune System	13
Chapter 3—Clinical Manifestations of AIDS	26
Chapter 4—The Epidemiology of AIDS	42
Chapter 5—The Cause of AIDS	58
Chapter 6—Controlling AIDS	68
Chapter 7—The Social Impact of AIDS	82
 Part II	
Foreword	i
Introduction	1
Magnitude of the AIDS problem	1
Europe	1
Surveillance	4
United States of America	5
Other countries and regions	5
The virus	6
Mode of transmission	6
Infection and major clinical features	7
Mortality and case fatality	8

Laboratory tests	9
Treatment	10
Specific antiviral treatment	10
Treatment of the cellular immune defect	10
Treatment of opportunistic infections and AIDS-associated tumours	10
Blood and blood products	11
Public health importance of AIDS	11
Control measures	12
Preventing the spread of infection in groups with increased risk of infection	13
Preventing the spread of infection from those known to be positive to anti-LAV/HTLV-III	13
Preventing the spread of LAV/HTLV-III in blood and blood products	14
Preventing the spread of infection from identified risk groups to the community by routes other than blood and blood products	14
Preventing the spread of infection to hospital staff and other health care workers	14
Specific prophylaxis	15
Passive immunization	15
Active immunization (vaccination)	15
Chemoprophylaxis	15
References	15
Annex 1. AIDS surveillance in Europe: situation at 30 September 1985	16
Annex 2. The virus	29
Annex 3. ELISA tests for screening anti-LAV/HTLV-III antibodies	33
Annex 4. The case definition of AIDS used by CDC for national reporting	34
Annex 5. Participants in the Consultation on AIDS Policies in Europe - Atlanta, GA, USA, 19 April 1985	40

Introduction

The question of AIDS, the Acquired Immune Deficiency Syndrome, has been before us for over five years. By April of 1985 there were about 10,000 cases of the deadly disease reported in the United States alone, according to the Centers for Disease Control. By April of 1986 that figure is expected to have doubled. What's more, for every reported case that fits the official definition of the syndrome there may be ten more that are not yet officially reportable, but that are, in fact, the same disease. Outside the United States, AIDS has been reported in more than 30 countries.

The epidemic of AIDS is more than a question of numbers. It is the first known instance of a communicable disease that directly attacks the body's defenses, leaving its victims vulnerable to a wide variety of unusual and sometimes untreatable infections and malignancies. In the United States, the victims of AIDS have been mostly young men—sexually active homosexuals—but cases have occurred in other well-defined "risk groups"—intravenous drug abusers, Haitians, and hemophiliacs—and they have also included infants, women, and elderly people.

To medical science, AIDS has posed many questions: What causes it? How does it spread? Where did it come from? How can it be controlled? Some of these questions are now being answered. The primary cause of AIDS is now understood to be a particular virus that is transmitted by

intimate sexual contact or by the exchange of blood or blood products. But even as the answers come they continue to generate further questions: Can a vaccine be made? Can effective treatments or even a cure be developed for those already sick and for those who will become so before a vaccine is available?

And not all the questions of AIDS have been scientific ones. The epidemic has raised serious questions about our entire health care system and its ability to respond to sudden epidemic illness. It has also brought into question our government's funding priorities and raised questions about how we as a nation treat the outcast and the sick.

In the five years since AIDS has been epidemic in the United States we have learned much about the disease and much about ourselves. But the question of AIDS is still not answered. The syndrome continues to be a growing threat to our nation's health and a major challenge to our medical, scientific, and social resources.

Chapter 1

A New Epidemic

Every week a slender, digest-sized newsletter called *The Morbidity and Mortality Weekly Report (MMWR)* is mailed from Atlanta, Georgia to more than one hundred thousand doctors and public health officials across the United States. The *MMWR* is published by the Centers for Disease Control (CDC), a branch of the U.S. Public Health Service. It keeps tabs on the number of deaths in the country from all causes, and on occurrences of “notifiable” diseases—those which doctors are required to report to their local health boards. These include such familiar contagious diseases as measles, mumps, whooping cough, German measles and a variety of venereal diseases. The *MMWR* also alerts its readers to unusual medical problems, outbreaks of illness and environmental health problems. It thus serves as an early warning system and clearing house for information on current trends in the nation’s health.

A rare pneumonia

On June 5, 1981 the *MMWR* carried a report of five cases of *Pneumocystis* pneumonia that had been seen in three Los Angeles hospitals. All five patients with the disease were young men—between 29 and 36—and all were active homosexuals. Two of them had already died.

Pneumocystis pneumonia, the report noted, occurs only rarely in the United States, and then almost exclusively among patients whose immunity to disease is already severely weakened—extremely malnourished infants or adults suffering from cancers like leukemia or lymphoma. Most healthy people are extremely resistant to infection by *Pneumocystis carinii*, the protozoan parasite that causes the disease. The appearance of this rare lung parasite in previously healthy young men thus suggested some profound dysfunction in their immune systems, and the fact that all five cases had occurred at about the same time and in the same geographical area suggested that it was the result of something the men had in common.

None of the patients knew one another, however, and none had any known contacts or sexual partners with similar illnesses in common. What they did share, besides their homosexuality, was that all of them had used inhalant drugs called “poppers” (amyl or butyl nitrite) and that all of them showed evidence of infection with cytomegalovirus (CMV). This virus, a member of the herpes family, is a common cause of mononucleosis in young adults. It has been shown to produce temporary disturbances of immunity in otherwise healthy people, specifically in the so-called cell-mediated arm of the immune system. And indeed, laboratory tests of the blood of three of the *Pneumocystis* patients—the other two were not tested—showed severely depressed numbers and activity of the cells involved in this aspect of the immune response. But the results were difficult to interpret, the *MMWR* report concluded, and the role of CMV in the mysterious pneumonia outbreak remained unknown.

A rare cancer

Less than a month later, on July 3, the *MMWR*'s lead article reported further evidence of impaired immunity among homosexual men, and not confined to the Los Angeles area. During the previous 30 months, 26 cases of a rare malignancy called Kaposi's sarcoma (KS) had been diagnosed in homosexual men in the United States. Twenty

cases were reported from New York City, and six from California.

First described more than a century ago by the Hungarian dermatologist Moritz Kohn Kaposi, KS is a cancerous condition in which bluish or purple-brown nodules appear on the skin of the arms and legs, or, less frequently, in the lymph nodes, lungs, gastrointestinal tract or elsewhere in the body. Previous to this new outbreak, KS had been seen in this country only rarely, and then usually in older men of Jewish or Mediterranean ancestry. In these patients the disease is a relatively mild, seldom fatal illness, with which its elderly victims survive an average of 13 years, almost invariably dying of other causes.

There were, however, two known exceptions to the usually "indolent" course of KS: In a belt across equatorial Africa, where it commonly affects adults and children and accounts for up to 9 percent of all cancers, KS is an aggressive, rapidly spreading and often fatal illness. Likewise, among patients receiving immunosuppressive drugs, especially kidney-transplant recipients, the disease can be fast-moving and lethal. And now in the homosexual men who were coming down with it, KS was taking a heavy toll. Eight of the 26 patients described in the *MMWR* had already died, all within 8-24 months of diagnosis.

Meanwhile there were 10 new cases of *Pneumocystis* pneumonia among homosexual men in Los Angeles and the San Francisco Bay area, two of whom also had Kaposi's sarcoma. In all, by the end of August more than 70 cases of KS and/or *Pneumocystis* pneumonia had been verified by the Centers for Disease Control, and the fatality rate was already 40 percent.

Impaired immunity

The presence of these two grave illnesses among previously healthy young men suggested a severe breach in their immune defenses, a view that was further substantiated by the fact that many of these men were also suffering from other so-called opportunistic infections. Such infec-

tions are caused by a variety of viruses, bacteria, fungi, and protozoa that are either not ordinarily harmful or that are easily controlled by an intact immune system. The yeastlike fungus *Candida*, for example, is usually seen clinically only in young infants whose immune systems have not yet fully developed, in whom it is known as thrush. But many of the patients with KS or *Pneumocystis carinii* pneumonia (PCP) also had rampant *Candida* infections affecting their gastrointestinal tracts.

Other KS/PCP patients had a rare form of meningitis caused by another fungus, *Cryptococcus*, while still others had infections of *Mycobacterium avium-intracellulare*, a relative of the common tuberculosis bacterium which sometimes causes pneumonia, but which these men had throughout their bodies. Opportunistic infections with viruses were also common, including severe prolonged infections with herpes simplex, and the almost ubiquitous cytomegalovirus.

By the following spring, as cases of the mysterious new syndrome continued to mount exponentially, the CDC reported further evidence of immune dysfunction in homosexual males around the country. The *MMWR* for May 21, 1982 described 57 men who had unexplained persistent generalized lymphadenopathy—swellings of the lymph nodes in various parts of their bodies. Such swellings often accompany certain infections—the “swollen glands” of infectious mononucleosis are a familiar example—but these patients had no current identifiable illness that could explain their condition. They did, however, have a spectrum of other symptoms such as fatigue, fever, night sweats, involuntary weight loss, and enlarged spleens or livers.

Laboratory studies of the blood of some of these men also revealed abnormalities similar to those observed in the blood of the KS and PCP patients already reported. The ratios of two populations of white cells—the so-called helper and suppressor T lymphocytes—were nearly the reverse of normal values in many of these patients, but the relationship between such findings in the KS/PCP patients and those with lymphadenopathy remained to be determined, the report concluded. It was possible, though, that the lymph-

adenopathy patients represented an early stage of the same syndrome that had led to serious illness in the others. Indeed, one of the patients in the lymphadenopathy group had gone on to develop Kaposi's sarcoma during the course of the study.

A transmissible agent?

Just as the natural course of the new syndrome remained mysterious, so too did its cause. Although it seemed that the risk of contracting the illness was higher among those homosexual men who had larger numbers of sexual partners, there was little evidence that whatever was causing the epidemic could be transmitted directly from one person to another.

Then, on June 18, 1982, the *MMWR* carried a report of a cluster of KS and PCP cases among homosexual males in Los Angeles and Orange Counties in California. The group consisted of 13 patients, eight with KS and five with PCP, and the medical detectives of the CDC had been able to confirm that in the five years prior to the onset of their symptoms nine of the patients had had sexual contact with other men who later developed KS or PCP. These patients were also part of a wider interconnected series of cases that included as many as 15 patients from eight other cities. One KS patient, not from California, in addition to having had sexual contact with two KS patients in Orange County, said he had also had sexual contact with one KS patient and one PCP patient from New York City and two or three PCP patients from Los Angeles County. Could such suspicious links occur by chance?

Using Kinsey report data, the CDC estimated that there were between 185,000 and 415,000 homosexual males living in the Los Angeles County area. The probability that seven of the 11 patients with KS or PCP would have sexual contact with any one of the other 16 reported patients in the area seemed "remote." And the probability that two patients living in different parts of Orange County would have sexual contact with the same non-Californian with KS

appeared to be even lower. The clear implication of such a statistically unlikely cluster of cases was that something causing the syndrome had to be either shared or transmitted among the men involved.

So although the existence of the "L.A. cluster" lent increasing weight to the idea that an infectious agent such as a virus was at the root of the epidemic, other factors could not be ruled out definitively, among them the possibility that certain drugs, such as amyl and butyl nitrite, might either be directly inducing immune suppression or carrying some unusual impurity that did. Indeed, one study in New York had drawn a statistical correlation between the use of such drugs and the risk of contracting KS, and among the patients in the L.A. cluster exposure to inhalant sexual stimulants and a variety of other "street" drugs was common.

Drugs and blood

Illicit drug use became an even more important factor in the widening epidemic as additional cases of what appeared to be the same syndrome broke out in a new population. Among the cases reported in the *MMWR* for June 2, 1982 were a number in people who were apparently neither homosexual nor users of inhalant sexual stimulants. The principal risk factor in this new group of patients was the use of intravenous (IV) drugs, principally heroin, cocaine and amphetamines.

The young men and women in this new group who were getting sick were not necessarily hard-core addicts. More often they were occasional drug users who frequented "shooting galleries"—illicit operations set up in storefronts or abandoned buildings in poor neighborhoods. In such settings recreational drug abusers can purchase their drugs by the shot, with sometimes as many as 50 people receiving injections from the same unsterilized syringe.

Further evidence that whatever was causing this epidemic of immune deficiency could be transmitted through blood came with the appearance of the syndrome in yet

another group—hemophiliacs. The *MMWR* for July 16, 1982 reported three cases of PCP among patients with hemophilia, all of whom were heterosexual and none of whom had a history of intravenous drug use.

These patients suffered from Hemophilia A—an inherited deficiency of a protein known as Factor VIII, which is necessary for normal blood clotting. Without Factor VIII these hemophiliacs are at risk of severe bleeding, especially into the joints, as a result of, for example, falls or bumps. The CDC estimates that there are as many as 20,000 such people in the United States, most of whom receive treatment for their Factor VIII deficiency by regular injection of Factor VIII from healthy donors. This material can be prepared either from the fresh frozen blood plasma of a single donor, or as a concentrate manufactured commercially from pooled plasma collected from thousands of donors.

The hemophiliacs who came down with PCP had all received their Factor VIII in the form of the concentrate, and none of them had received it from the same lots.

The Haitian connection

In the same month as its report on hemophiliacs, the *MMWR* contained a report on still another population that was coming down with the mysterious immune deficiency syndrome. From five states came reports of 34 cases of Kaposi's sarcoma and opportunistic infections among Haitians living in the United States, most of them recent immigrants from that Caribbean island country. None of the 23 Haitian males who were questioned reported any homosexual activity, and only one gave a history of IV drug use.

"It is not clear," the report stated, "whether this outbreak is related to similar outbreaks among homosexual males, IV drug abusers, and others, but the clinical and immunologic pictures appear quite similar." As in the other cases, laboratory analysis of blood samples from the stricken Haitians showed severe dysfunction of the T lymphocytes, with a marked decrease in the absolute number of "helper"

T cells and an inversion of the normal ratio of those cells to the T-suppressor cells. The Haitians showed a slightly different pattern of opportunistic infections than the other groups, but the same high mortality rate—nearly 50 per cent.

Just what it was that put Haitians at special risk for developing the deadly syndrome was far from clear, but the CDC did note that 11 cases of Kaposi's sarcoma had been diagnosed in Port au Prince, the capital of Haiti, over the past two and a half years. It was possible then that the syndrome may have existed not only among Haitian immigrants to the U.S., but also in Haiti itself.

A name for the plague: AIDS

By September of 1982, the CDC had received reports of almost 600 cases of the lethal immune disorder, which now received the name Acquired Immune Deficiency Syndrome. The incidence of AIDS was roughly doubling every six months from 1979, with an average of one or two new cases now being reported every day.

But although the syndrome had a name, AIDS, there was no specific diagnostic test for it. The CDC developed a working definition of the syndrome for the purpose of conducting its own surveillance of the epidemic. AIDS, according to this definition, was the appearance of some disease at least moderately predictive of a defect in cell-mediated immunity occurring in a person with no known cause for diminished resistance to that disease. Such diseases included the by now all-too-familiar *Pneumocystis* pneumonia, Kaposi's sarcoma and a short list of specific opportunistic infections.

The CDC acknowledged that this definition might not catch the full spectrum of AIDS manifestations, which could range from an absence of any symptoms at all despite laboratory evidence of impaired immunity, to such nonspecific symptoms as fever, weight loss and persistent generalized lymphadenopathy, to a number of diseases that, while serious, were not in themselves sufficiently indicative of a

profound immune deficiency. Thus, as James Curran, head of the CDC Task Force on AIDS, has estimated, for every certified case of CDC-defined AIDS there might be as many as 10 others that, although not quite fulfilling the CDC definition, were nonetheless actually the same syndrome or early stages of it. And, the CDC report noted, while the current mortality rate from AIDS was 41 percent, the eventual mortality rate after a number of years threatened to be far higher.

Infants with AIDS

Meanwhile the epidemic continued its relentless spread to encompass a new group of victims—babies. The *MMWR* for December 17, 1982 carried a report of four cases of unexplained immune deficiency in infants under two years of age. In addition, six other children had died of opportunistic infections with unusual immunodeficiencies, and 12 more were reported to have unusual immunodeficiencies, but without life-threatening opportunistic infections.

Although cautious about characterizing these cases as AIDS, the CDC pointed out that the mother of one of the four children had subsequently died of PCP, probably as a result of AIDS, and that the mothers of the other three were either Haitian or intravenous drug users and therefore at increased risk for AIDS. Furthermore, the immunological profiles of the infants resembled those seen in adults with AIDS while not fitting other explanations of immune deficiencies in children.

If the children did in fact have AIDS, the report concluded, then exposure to whatever was causing the syndrome had to have occurred very early in their lives—either while the infant was still in the womb or very shortly after birth.

Other victims

As the cases among infants suggest, not everyone who has come down with AIDS has been a member of the prin-

cial groups presumed to be at risk—homosexual men, intravenous drug abusers, Haitians and hemophiliacs. The CDC has reported cases of the syndrome in the female partners of exclusively heterosexual AIDS patients, as well as in people with no known risk factors who have developed AIDS after receiving transfusions of blood from donors later identified as having AIDS. There have also been a small but disturbing number of cases that cannot be assigned to any of the recognized risk groups, including the transfusion group, who nonetheless have contracted the disease. Such cases may simply be the result of insufficient or incorrect information, or they may represent cases transmitted by other routes.

Since it was first recognized AIDS has been found far beyond the three large U.S. coastal cities from which it was originally reported. Practically every state in the union has now seen it and the disease has been reported in more than 30 foreign countries. In Europe, most of the cases among homosexual men have been traceable to sexual contact with American homosexuals at risk for AIDS, but other cases on the continent appear to have their origins in Africa. Of more than 40 cases recently reported in Belgium, virtually all have some direct connection with central Africa, and it now appears that there may be an epidemic of the same disease in Africa itself.

The AIDS epidemic has thus become of world-wide concern, and everyone has a stake in finding answers to the questions: What causes it? How is it spread? How does it cripple immunity? And how can it be controlled, treated, and ultimately prevented?