Koch's Postulates and the Search for the AIDS Agent

RICHARD M. KRAUSE, MD

Dr. Krause's paper was presented at the International Congress for Infectious Diseases, held August 24–27, 1983, in Vienna, Austria. It is reprinted from *Reviews of Infectious Diseases*, Vol. 6, No. 2, pages 270–279, March-April 1984.

Tearsheet requests to Richard M. Krause, MD, Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rm. 7A-03 C, Bldg. 31, Bethesda, Md., 20205.

Robert Koch

FOR A BRIEF PERIOD DURING THE ROMANTIC AGE, consumption became a mark of tragic beauty. The English poets Keats and Shelley symbolized the romantic and consumptive youth of the 19th century. Mimi in Puccini's *La Boheme* represented the melancholy ideal, a portrait drawn from an actual young lady who died of tuberculosis.

"Decay and disease are often beautiful, like . . . the hectic glow of consumption." said Thoreau on seeing the first brilliant colors of maple trees in the autumn of New England. And Elizabeth Barrett Browning once remarked, "Is it possible, Robert, that genius is just a matter of phthisis?" Romantics believed that consumption was a trait often associated with gifted and talented people. For it was both professional and popular opinion, during this time prior to the germ theory of disease, that consumption was a constitutional trait. The disease frequently struck young men and women in their prime, condemning many of them to early death. Wrote Keats in the spring of 1819: "Youth grows pale, and spectre thin, and dies."

He could have been describing acquired immune deficiency syndrome (AIDS) in 1984.

Such notions concerning the beauty and genius of the tuberculous patient were swept away in 1882 when Koch discovered that tuberculosis was an infectious and contagious disease. Suddenly patients with consumption were shunned like the plague. The Romantic Age for consumption was over. With a turn of the screw, tuberculous youth, once thought tragically beautiful and artistic, were now abandoned by their friends and society. Dubos eloquently portrays these changing social attitudes regarding tuberculosis in his book *The White Plague* (*1*).

While the comparison should not be strained, there is a resemblance between this changing attitude toward tuberculosis patients in the 19th century and recent public alarm about AIDS in the homosexual population. For several decades, homosexuals have been moving into many areas of public life. Often gifted, talented, and artistic, they have been accepted, if not interwoven, into the social fabric of our age. In this respect, at least, there is a parallel between the emergence of homosexuality as an optional lifestyle in the 1980s for those with this sexual orientation and the socially popular consumptive of the Romantic Age. But now there is a growing fear that homosexual patients with AIDS—and even healthy homosexuals—might harbor a deadly virus that could be transmitted through ordinary social contact. Table 1 shows the sexual orientation of AIDS patients who have been interviewed in the United States. Approximately 65 percent are homosexual and 10 percent bisexual.

Many of the heterosexual patients with AIDS are known to be drug addicts, another group in which AIDS frequently occurs. It is suspected that the disease is spread by the use of contaminated needles for intravenous drug injection. Indeed, in certain establishments called "shooting galleries," the same needle will be used by 50–100 different drug addicts during the course of one day. Secretary Margaret Heckler and Assistant Secretary Edward Brandt of the U.S. Department of Health and Human Services have identified AIDS as the number

Table 1. Sexual orientation of patients with AIDS

Sexual orientation	*Percent of total*
Males, homosexual	64.5
Males, bisexual	9.4
Males, heterosexual	16.2
Males, sexual orientation unknown	4.3
Females[1]	5.6

[1] Refers primarily to women who are consorts of bisexual and heterosexual men.

'While the comparison should not be strained, there is a resemblance between this changing attitude toward tuberculosis patients in the 19th century and recent public alarm about AIDS in the homosexual population.'

one health priority of the U.S. Public Health Service. Some of you have asked at this congress, and with good reason, if this is not overreaction to a health problem that is, in reality, dwarfed by the heavy burden of morbidity and mortality caused by the common infectious diseases in the world. The Director-General of the World Health Organization has said, for example, that in 1983 1 million children will die of malaria in Africa alone.

There are several reasons why we have given AIDS such high priority. First, the cause is unknown. Second, the disease is fatal. Third, the number of cases continues to increase and the disease is now occurring in other countries. Figure 1, with a plot of the number of cases diagnosed in the United States in 3-month intervals, shows this dramatic increase. Where will it end? Why are the international consequences of this disease currently focused largely in the United States? Already there is epidemiologic evidence that cases in other countries can be traced to contacts in the United States.

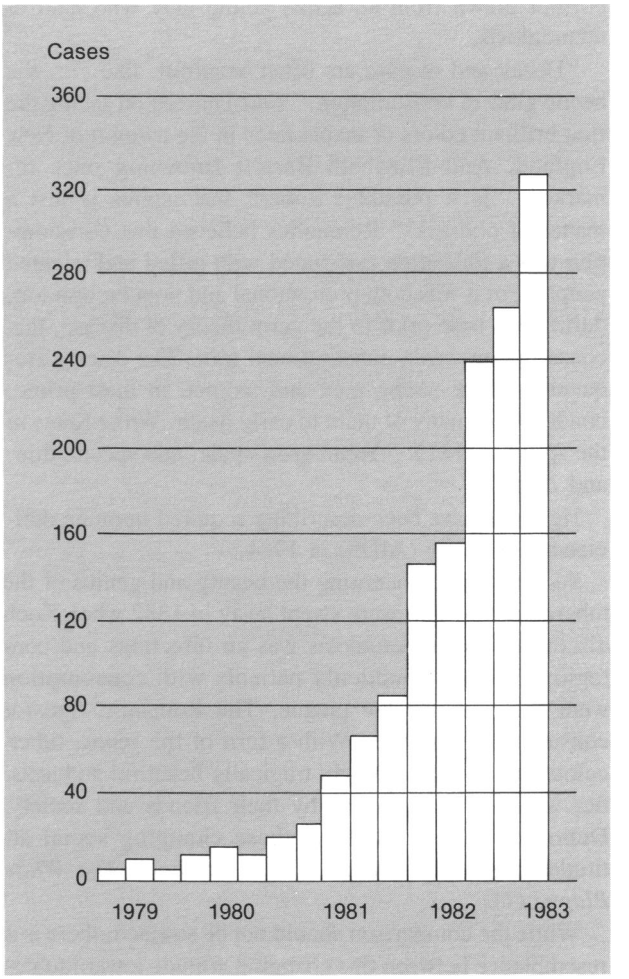
The fourth reason that AIDS has been given high priority concerns the social and economic factors associated with this problem. There is understandable fear and alarm among the so-called high-risk groups; there is also the danger of growing public reaction, rising from the concern that even casual contact with homosexuals and others in these groups may be dangerous. Such public reaction has already led to consequences that impinge on the rights of these people, who are citizens or residents of the United States. Knowledge about the cause, diagnosis, treatment, and prevention of AIDS is the only remedy to counter this new lethal disease and its associated social consequences.

There is one important difference between tuberculosis and AIDS. Tuberculosis was and can be, even today, contagious among the general population, whereas in the United States, transmission of AIDS by casual contact is unlikely. No nurse or physician or medical investigator who has attended to these patients, or who has worked with blood and other specimens from these patients, has acquired the disease. There is no reason for the general public to alter ordinary patterns of social interaction with homosexual individuals.

As I reflected about the history of tuberculosis and the parallels between the troublesome societal issues of that disease in the 19th century, after Koch's discoveries, and AIDS now, it occurred to me that other lessons can be applied to the current AIDS epidemic. There are two major points to be made: first, I shall consider Koch's postulates and the discovery of the tubercle bacillus, relating this discovery to the current search for the causative agent of AIDS; and second, going beyond the search for the agent itself, I shall discuss certain aspects of the epidemiology of tuberculosis. In 1910 Koch recognized that facts of practical importance concerning the treatment and prevention of tuberculosis were learned from such studies, and I believe they are relevant to the occurrence of AIDS today.

I was prompted to consider this theme after reviewing three of Koch's papers: the original paper in which he identified the tubercle bacillus as the cause of tuberculosis; a paper written 8 years later in which he set forth Koch's postulates; and his last paper, called "Epi-

Figure 1. The number of cases of AIDS in the United States reported to the Centers for Disease Control. Cases have been tabulated quarterly



Note: 5 cases diagnosed before 1979.

demiologie der Tuberkulose," written in 1910 just months before his death. From these three papers emerged the link between tuberculosis and AIDS.

At the time Koch wrote his last paper, 28 years had passed since his discovery of the tubercle bacillus, and yet there was still no vaccine to prevent, or drug to treat, tuberculosis. Was Koch disappointed in the lack of achievements of three decades? If so, any pessimism is obscured by his optimism in his last paper as he recounts the epidemiologic evidence that documents the progress to combat the disease. During those decades much had been learned about general medical measures for the successful management of tuberculosis. For example, epidemiologic studies showed that the occurrence of the disease in a population was determined by factors other than exposure to the etiologic agent, and it was possible to influence these adverse factors and decrease the incidence of the disease. But Koch's last paper was not only concerned with such epidemiologic matters. It was also a call for action, urging the medical community and general public to develop programs, both social and medical, that would decrease the mortality caused by tuberculosis.

Let us remember, then, as we search for the causative agent of AIDS with the principles of Koch's postulates, that we have a parallel responsibility to examine the epidemiologic and social aspects of AIDS. Every possible option for control and prevention must be employed until vaccines and specific drugs are available.

Koch's Postulates

Koch's discovery of the tubercle bacillus as the cause of tuberculosis was first reported at the usual monthly meeting of the Physiological Society of Berlin on the evening of March 24, 1882. Koch's paper was entitled simply "Ueber Tuberculose" (*2*). Paul Ehrlich later recalled the evening as the "greatest scientific event" of his life. Ehrlich was not usually given to overstatement or hyperbole. Let me suggest that those who are currently searching for the AIDS agent read Koch's paper. Might I even suggest that editors of journals do the same? If authors and editors of AIDS papers adhered to the rigors of Koch's analysis of the facts, we would not be annoyed by premature claims concerning the etiology of AIDS.

Koch's postulates are the principles that establish a relationship between a microbe and a disease, but in that first paper, they were not set forth in a formal fashion as we know them today. They first appeared in the familiar form 7 years later in a paper entitled "Ueber Bakteriologische Forschung" ("On Bacteriologic Research") which he gave at an International Medical Congress in Berlin in 1890. Although the elements of the postulates can be detected in the initial paper, Koch clearly needed time to formalize them as general principles that could be applied to the evidence linking any particular microbe to a specific disease. The following is a translation of Koch's postulates from the original German of that 1890 paper (*3*).

'It is conceivable that the agent then emerged from "hibernation" under the influence of changing sexual practices and circumstances. If this is what happened, the agent followed the familiar path of other microbes that have exploited troubled situations: the plague in the 14th century; tuberculosis during the industrial revolution; and malaria in Europe during World War I, when it spread north of the Arctic Circle for the first time in recorded history.'

If one can now, however, prove: first, that the parasite in each individual case of the disease in question can be found and indeed under conditions which correspond to the pathologic changes and the clinical course of the disease; second, that it does not occur in any other disease as a chance and non-pathogenic parasite; and third, that it is capable of being isolated . . . from the body and in pure cultures sufficiently often transformed in order to cause the disease anew; then it can no longer be a random accident of the disease, but between the parasite and the disease can be conceived except that the parasite is the cause of the disease.

Today we recognize additional criteria that establish a causal relationship between a microorganism and a disease. One of the most valuable is the occurrence of large amounts of specific antibody following an infection. Another is a high degree of specific immunity to the infectious agent following a recent recovery.

It is obvious that many technical difficulties impede the fulfillment of all of Koch's postulates for every infectious disease, and certainly this will also be the case with AIDS. What a perplexing matter AIDS is today! We have yet to see clearly the dimensions of the enigma. Do repeated infections with viral agents such as hepatitis B, cytomegalovirus, and Epstein-Barr virus—all known to induce partial immunosuppression—set the stage for attack by the unknown AIDS agent? Does ingestion of semen augment immunosuppression, resulting in a susceptibility to an etiologic agent that under other circumstances might be relatively harmless? Or has a new microbe arisen like a phoenix from the cauldron of

evolution and flourished here and now because of the special social and sexual circumstances of the times? All of these questions remain unanswered. In truth, much will remain unknown about the natural history of AIDS, even when we have discovered the etiologic agent. As Koch would warn us, discovery of the etiologic agent is only the first step, albeit an optimistic one, on a long and weary road before fundamental discoveries are translated into practical advances.

There are those who believe that the AIDS agent will be an entirely new microbe, and this may indeed be so. Such a view is consistent with classical and neo-Darwinian concepts. On the other hand, it seems to me equally possible that the AIDS agent has been around for quite some time, long dormant, but there nonetheless. Initially lethargic, the unknown microbe was perhaps first transmitted sluggishly and in a sporadic fashion. During this indolent period, the agent struck infrequently because that special set of ecologic conditions favoring rapid transmission did not exist. It escaped recognition because no cluster of cases occurred to attract attention. It is even possible that during this period there were sporadic cases of AIDS, but they did not necessarily occur in the same high-risk groups recognized today. It is conceivable that the agent then emerged from "hibernation" under the influence of changing sexual practices and social circumstances. If this is what happened, the agent followed the familiar path of other microbes that have exploited troubled situations: the plague in the 14th century; tuberculosis during the industrial revolution; and malaria in Europe during World War I, when it spread north of the Arctic Circle for the first time in recorded history.

Once it was recognized that tuberculosis was infectious, three important medical steps were taken: (*a*) early detection of cases, (*b*) development of the sanatorium method of treatment, and (*c*) public health measures for prevention. Early detection was the key to successful prevention and treatment of tuberculosis.

One tubercular physician recalls his experience in the sanatorium, the only "cure" before the days of antimicrobial therapy. He was lucky; his disease was detected early by the clinical and laboratory tests then available. However, the cure, it should be stressed, was nonspecific. There was no medication to combat the tubercle bacillus directly. The cure was accomplished by the special routine of the sanatorium: fresh air; plenty of rest; regular exercise; a simple and hearty diet; a regular regimen—rest after lunch, a walk after supper; and, most important, companionship. After 9 months, this young physician was sufficiently recovered and was in fact, asked to stay on as a physician at the sanatorium. His elation is understandable; for him, his rehabilitation was complete.

Until we know the cause of AIDS and have specific treatment, I believe that we must make every effort to detect early cases or identify those individuals who may be afflicted with a predisposing or related condition that may be an early stage of the disease. If we can do that, perhaps the medical and nursing skills we already possess could abort the case, prevent progression, or even bring about a cure. These notions may seem farfetched, but part of the problem in our current thinking about AIDS is that we *begin* with the definition of the *terminal* stage of the disease. It is a definition that boxes us into a corner, creating an impossible checkmate.

By now the definition of AIDS is commonplace. I repeat it here to emphasize that it is an end-stage diagnosis, useful for epidemiologic and surveillance purposes, but one that must be modified if we are to examine new possibilities of prevention and therapy.

Acquired immune deficiency syndrome (Centers for Disease Control surveillance definition):

(1) Presence of reliably diagnosed disease at least moderately indicative of cellular immune deficiency (e.g., Kaposi's sarcoma in a patient less than 60 years of age; pneumocystis pneumonia).

(2) Absence of known causes of underlying immune deficiency and of any other reduced resistance reported to be associated with the disease (e.g., immunosuppressive therapy, lymphoreticular malignancy).

Life-threatening opportunistic infections seen in AIDS:

(1) Viral: disseminated cytomegalovirus, progressive herpes simplex virus, progressive multifocal leukoencephalopathy.

(2) Bacterial: disseminated *Mycobacterium avium/Mycobacterium intracellulare* complex, disseminated *Mycobacterium tuberculosis*.

(3) Fungal: esophageal candidiasis, cryptococcal meningitis, aspergillus pneumonia.

(4) Protozoal: *Pneumocystis carinii* pneumonia, *Toxoplasma gondii* encephalitis, cryptosporidium enteritis, chronic isospora infection.

A patient that meets this case definition is already in an advanced, terminal stage of the disease, when opportunistic infections are fatal because of complete and irreversible immunologic paralysis. Diagnosing AIDS at this stage is similar to diagnosing tuberculosis when there is open cavitation and the sputum is flooded with the hemorrhage of arterial blood. Even Keats and Shelley knew that coughing up bright red blood was the kiss of death.

In order to detect cases early in the course of the disease, we must learn much more about its natural history. One fertile area of investigation concerns the prodromal period of AIDS. Most patients give a history of nonspecific complaints lasting from 2 to 8 months: fever of unexplained origin; night sweats and chills;

lymphadenopathy; diarrhea; weight loss; dysphagia; fatigue, apathy, and depression; diminished libido, and impotency. Observations over many months on high-risk groups indicate that there are certain individuals who have immunologic abnormalities in the prodromal period. Dr. Thomas Quinn of the National Institute of Allergy and Infectious Diseases has suggested that a search be made in prodromal patients for a unique constellation of signs, symptoms, and laboratory abnormalities that would be highly predictive of subsequent AIDS. He has proposed the term "AIDS-related complex" as describing such individuals. His scheme, shown in table 2, proposes that the diagnosis of AIDS-related complex be based on the occurrence of a combination of clinical findings and laboratory abnormalities. In this connection it bears a resemblance to the Jones' criteria for the diagnosis of acute rheumatic fever. It should be remembered that the clinical usefulness of the Jones' criteria was preceded by long-term studies on the natural history of rheumatic fever. The particular grouping of clinical findings and laboratory abnormalities indicative of early AIDS will require similar studies on natural history.

In the absence of knowledge of the specific etiology of AIDS, we will not have a specific serologic test. But this lack of knowledge need not frighten us. Recall, for example, the bizarre serology of syphilis, the Wassermann reaction, which despite its obscure nature, played a major role in the prevention and control of syphilis. I would be delighted with a test similar to the Wassermann reaction, despite all its imperfections, for detection of early cases of AIDS. Let us remember that the Wassermann reaction does not detect antibodies to syphilis but "a special change in syphilitic blood." Until we know the cause of AIDS and can develop more precise diagnostic procedures, let's get on with the job of devising a test that detects a "special change" in AIDS blood.

In drawing certain parallels between tuberculosis and AIDS, I am not for a moment suggesting sanatorium-like treatment for patients with AIDS or AIDS-related complex. Rather, what we need to remember is that we are often successful in developing treatments that "manage"

Table 2. Diagnosis of AIDS-related complex

Two clinical findings	plus	*Two laboratory abnormalities*
Fever > 3 months		↓T-helper cells
Weight loss > 10 percent BWT[1]		↓T-helper/T-suppressor ratio
Lymphadenopathy, 3 months		↑Serum globulins
Diarrhea		↓Blastogenesis
Fatigue		Anergy
Night sweats		

[1] BWT = body weight total.

'Who is a clinical epidemiologist? He is a triple-threat person: a good clinician; a skillful, original laboratory investigator; and a creative epidemiologist. A clinical epidemiologist retains those three skills in some appropriate mix and applies all three in research on disease. Such medical scientists were pathfinders in the past, but where are they today?'

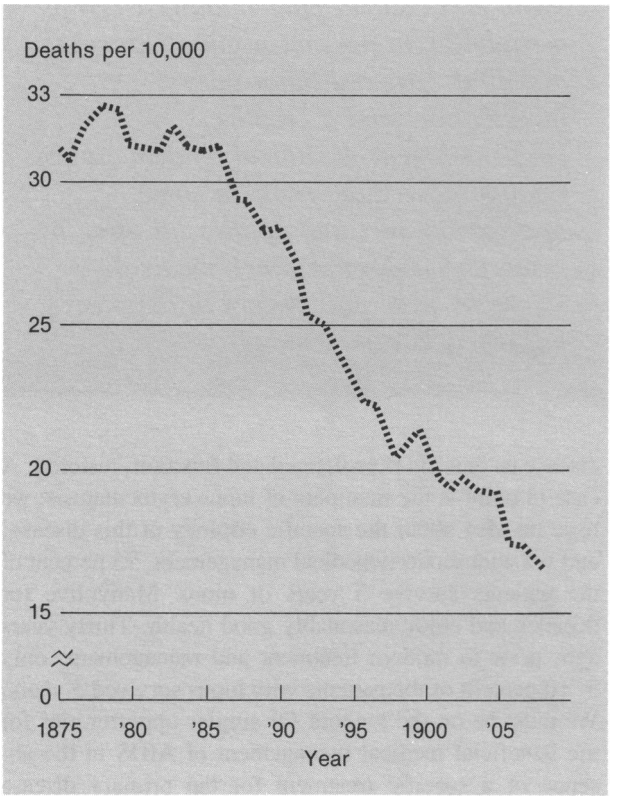
disease so that life is prolonged and function, restored. A case in point is the treatment of lupus erythematosis; we have no idea about the specific etiology of this disease, and yet with modern medical management, 95 percent of the patients survive 5 years or more. Many live for decades and enjoy reasonably good health. Thirty years ago, prior to modern treatment and management, only 5–10 percent of the patients with lupus survived 5 years. We must be on the lookout for similar opportunities for the beneficial medical management of AIDS in the absence of a specific treatment for the primary disease process.

Epidemiology of Tuberculosis

Let me turn now to Koch's last paper, "Epidemiologie der Tuberkulose" ("Epidemiology of Tuberculosis"), which reveals, as he puts it, "some interesting and practical facts." These considerations, I believe, are relevant to the occurrence of AIDS. In this paper he looked back over the 28 years since his discovery of the causative organism and examined the changing incidence of tuberculosis. Remember that in this 28 years no specific antibiotic treatment had been discovered. Nevertheless, by 1910, there was a general impression throughout much of the world that the disease was on the decline. Koch asked the critical questions, Is this true? If so, why?

Koch began his historical review of the preceding 30 years by examining the mortality due to tuberculosis in Prussia (fig. 2 shows the decline in the mortality rate for tuberculosis in Prussia per 10,000 people from 1875 to 1908). He correctly reasoned (and I translate from the German), "We therefore have every reason to find out the cause of this decline of tuberculosis in order to see whether it is accessible to our influence and whether it would be possible, if the decline should cease, to remove the obstacles and, if possible, accelerate its present

Figure 2. The decline in the mortality rate for tuberculosis in Prussia for every 10,000 people from 1875 to 1908



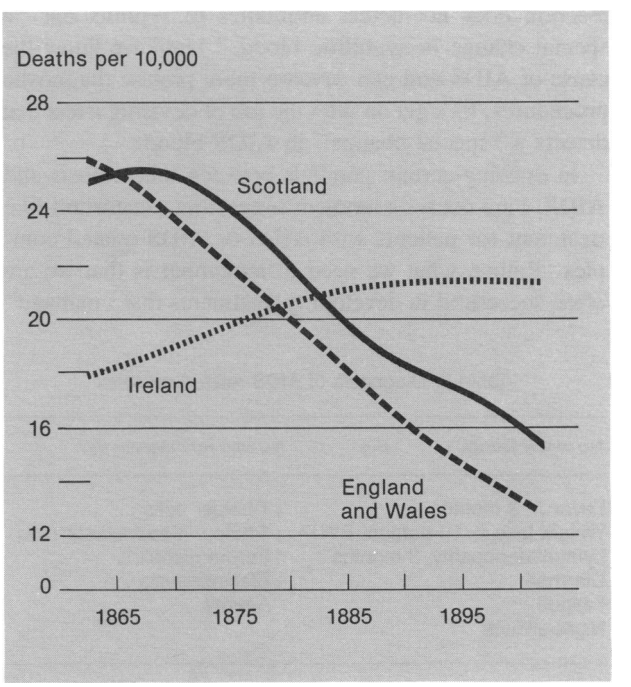
SOURCE: reference 4.

course" (*4*). With reasonable modesty he stated at the beginning of his paper that the decline in tuberculosis was, in part, linked to the discovery of the organism. However, from an analysis of the epidemiologic data, he concluded that in Germany, social legislation, especially health insurance, was one of the important reasons for the decline in mortality.

Koch recognized also that the treatment of tuberculosis had made great progress because of changes in hygiene, diet, and, most especially, because of the tuberculosis sanatoria. He took note of the epidemiologic data from Great Britain, which clearly indicated the importance of the new sanatorium method for treating tuberculosis, effecting, in turn, the decrease in mortality. He came to this conclusion by observing that death rates for tuberculosis in England, Scotland, and Ireland had behaved differently. Figure 3 shows the decrease in mortality in England and Scotland and an increase in mortality in Ireland. Koch notes the observations of the English epidemiologist Newsholme on this matter. After examining all factors—living quarters, nutrition, salary, medical care, and emigration habits—Newsholme concluded that the decisive factor in determining the mortality for the three sectors of the United Kingdom was the type and manner of medical care. In England and Scotland, the tuberculosis patients covered by the welfare program were referred directly to private sanatoria. In Ireland, they received a subsidy without being obliged to enter a sanatorium. Most chose, therefore, to remain in their living quarters; under these circumstances they received neither proper medical care nor the benefits of sanatorium treatment.

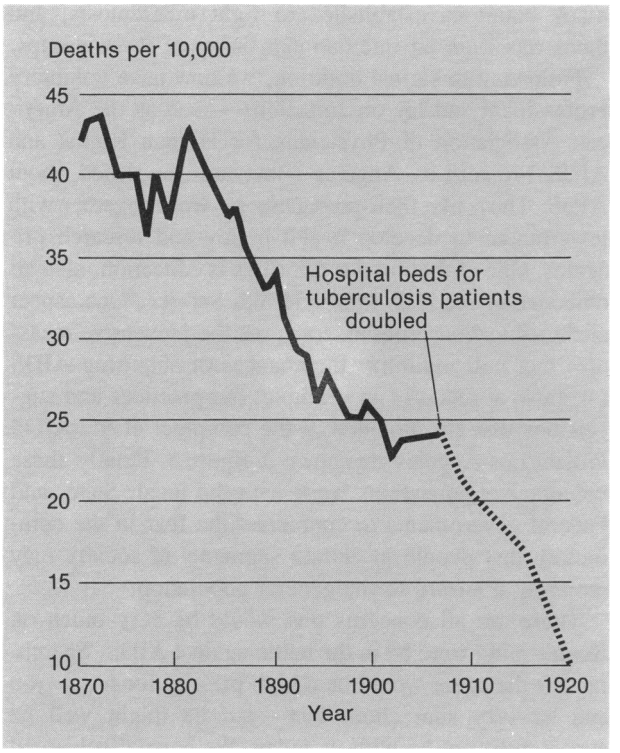
To reinforce his view that the sanatorium was important in the decline in the death rate of tuberculosis, Koch turned to data from America. Plotted in figure 4 is the mortality rate for pulmonary tuberculosis per 10,000 inhabitants in Manhattan and the Bronx from 1869 to 1907. Beginning in 1888, the mortality rate declined from about 43 deaths per 10,000 inhabitants per year to about 23 deaths per 10,000 in 1902. Then the rate did not decrease for the next 5 years. Clearly, here he found a city in which a block had occurred. The major theme of Koch's paper, as I mentioned earlier, was to determine if there were impediments to a continuous drop in mortality. When officials in New York perceived that the mortality curve had begun to flatten, efforts were intensified, and the number of beds in sanatoria were increased from 2,500 to 5,000. Koch was delighted to learn of this direct attack on "this impediment" to the decline in mortality. He did not live to see what influence this new effort would have. However, I have plotted in figure 4 the subsequent decrease in the mortality rate following this intensified effort. Between 1905 and

Figure 3. Mortality rates for tuberculosis in England, Scotland, and Ireland



SOURCE: reference 4.

Figure 4. Mortality rates for tuberculosis in New York City



SOURCE: modified from reference 4.

1920, the number of deaths was decreased by more than one-half, dropping from 25 to 10 per 10,000 per annum.

There were, of course, two reasons why the sanatorium method of treatment reduced the death rate due to tuberculosis. Koch stressed the influence of sanatorium treatment on the cure of patients and, thus, on mortality. A side effect of such treatment was the prevention of secondary spread from primary cases to family and social contacts. This, of course, also had a beneficial influence on the death rate.

It is instructive to speculate on the progress in Koch's thinking about tuberculosis during the 28 years from the original discovery of the tubercle bacillus to the last paper on the epidemiology of the disease. As an older man, he had developed a maturity of judgment and a breadth of vision that is lacking in the brilliant and crisp analysis of the scientific facts in the description of the initial discovery. He now recognizes the need for epidemiologic research to learn about the natural history of the disease and to evaluate methods of treatment and prevention.

A Commentary on AIDS

Koch's conclusions are just as relevant to the current epidemic of AIDS as they were to tuberculosis in 1910. From such knowledge we can plan strategies for prevention, diagnosis, and treatment, such as those I have suggested concerning the detection and treatment of early cases. Furthermore, knowledge of the natural history and epidemiology of AIDS will be needed in the future to employ wisely the vaccines, specific therapy, and public health practices that are sure to follow, once we have identified the infectious agent of AIDS.

A few words should be said about the natural history of infectious diseases. What do we mean by this term? Theobold Smith defined it many years ago when The Rockefeller Institute for Medical Research was founded. Our first priority, he said, is to "study infectious diseases from *all points of view*" [italics added]. I can think of no better definition than that. Unfortunately, research on natural history is not a popular subject these days. It is often described, in a pejorative way, as a "fishing expedition." Of course that is exactly what it is. There is no way to discover the latent period of AIDS, for example, without long-term observations on all aspects of the disease, including the epidemiologic circumstances.

Research on natural history is the domain of clinical epidemiologists, but unfortunately they are in short supply. Who is a clinical epidemiologist? He is a triple-threat person: a good clinician; a skillful, original laboratory investigator; and a creative epidemiologist. A clinical epidemiologist retains those three skills in some appropriate mix and applies all three in research on disease. Such medical scientists were pathfinders in the past, but where are they today? It is my belief that clinical epidemiologists of infectious diseases are an endangered species. There are several reasons for this. Many clinical epidemiologists migrated to research on cancer and chronic diseases; the rest drifted into matters of practical importance, such as surveillance of disease outbreaks. This neglect must change if we are to conquer AIDS and many other infections with the same success that we achieved for poliomyelitis, rubella, and rheumatic fever.

Of course, this diversion into the natural history of AIDS must not detract from the search for its causative agent. Yet, clues as to the identity of the agent may come from research on natural history, from answers to questions such as whether the agent is an old microbe in new garments, or whether it is a new agent rising out of the cauldron of evolution. We must ask why AIDS is occurring now, in the 1980s, just as Koch asked why tuberculosis was occurring in 1880. I believe the microbe that causes AIDS, either a new one or a previously unrecognized pathogen, has taken advantage of recent undercurrents of opportunity just as tuberculosis took advantage of the particular climate of the industrial revolution. Uncovering these undercurrents may provide important clues about the etiology of AIDS.

Although there must be many as-yet-unknown influences that have favored the occurrence of AIDS, one likely influence deserves comment. The AIDS epidemic has exploited the same undercurrents of opportunity that now propel the epidemic of other sexually transmitted diseases (STD). In short, AIDS is riding the crest of STD. The reasons for the recent epidemic of STD, and now of AIDS, are multifactorial, complex, and beyond the scope of these remarks. There are surely biologic factors concerning microbes that propel the STD epidemic, as well as AIDS. However, I believe that, in addition to the biology of microbes, social forces arising from changing patterns in human behavior are also important. Therefore, there is a parallel between the societal and behavioral forces that influenced the occurrence of tuberculosis in the 19th century and those that now influence the occurrence of AIDS in 1984.

The varied patterns of sexual preference common today are nothing new. Vivid descriptions of such patterns are portrayed in the Old Testament and in the early Greek literature. What is new in our age and what has fueled the current epidemic of STD are the special circumstances of our current lifestyle. Mobility and frequent travel, of course, enhance the number of potential sexual contacts, but there are other important factors including an increase in family dissociation, contraception practices, the availability of abortion, and the influence of television and other mass media on behavior. It is probably also fair to say that a broad-based economic prosperity in the United States and Western Europe has enhanced the patterns of behavior that spread STD. So very much has changed in our lifestyle since World War II, and these social changes have influenced the sexual practices of both heterosexual and homosexual people. As physicians we must recognize the medical consequences of these changes, and we must plan research strategies to combat those diseases that exploit troubled situations.

These matters concerning social practices bring me to my final reference to Koch's last paper and his strategy to control tuberculosis. Koch said this: "Popular works on tuberculosis are destined to play an important part in the enlightenment of the people." Education, he recognized, would be an important aspect in the control and prevention of tuberculosis. When no spectacular cure, such as antibiotics, was forthcoming in the early years of tuberculosis research, physicians and laymen joined together and formed voluntary organizations to battle the disease. Through education they dispelled the fear of tuberculosis. In the United States, a national tuberculosis association was founded in 1904. Its goal was to prove that something could be done. Its members worked hard for the sanatorium method of treatment. They educated legislators to enact laws requiring that tuberculosis be fought as a public health problem with public funds. In the early years, there were national organizations in many countries established to fight tuberculosis, and there was even an international union of these groups.

Following this great tradition, we now have voluntary professional and lay organizations—such as the American Association of Physicians for Human Rights and AIDS Project/Los Angeles—that are concerned about AIDS. They, like their predecessors, work together with government to develop health policy and research priorities. One of their major priorities is education, also an objective of the U.S. Public Health Service. One aspect of the education program concerns the preventive measures that will minimize the chances of acquiring AIDS for those at risk. As an example, the practices and suggestions that are provided in the pamphlet of the AIDS Project/Los Angeles are shown in figure 5. Finally, these voluntary organizations work with the local, State, and Federal governments to counteract the fear in the community that people in certain segments of society may represent a hazard to the general population.

These are all concerns that would be very much on Koch's mind were he in the battle against AIDS. Searching for the agent would be a high priority for him—you can be very sure about that—and he might well be successful were he with us today. We have also learned that he would ask penetrating questions concerning the epidemiology of the disease and be alert to commonsense methods of treatment and prevention in the absence of antibiotics and vaccines.

Successful prevention, control, and treatment of AIDS will require hard work as well as good luck. Discovering the agent will be the beginning, not the end. It is for that reason that I have discussed both Koch's early paper on his postulates and his final paper on epidemiology, written 28 years later. Even when we know the cause and

Figure 5. Preventive measures, taken from a public education pamphlet for persons at risk for AIDS

AIDS: What Preventive Measures Can I Take?

- Exercise regularly
- Eat a nutritionally balanced diet
- Get plenty of rest
- Reduce emotional stress
- Reduce your number of sexual partners
- Avoid oral ingestion of fecal matter, semen, or urine
- Use condoms whenever possible
- Refrain from inserting foreign objects into the rectum
- Avoid a shared source of lubrication or shared douching equipment
- Curtail use of drugs

Modified from AIDS Project/Los Angeles pamphlet

possess the means to treat and prevent AIDS, success in its eradication will require the wise application of new knowledge that is consistent with the epidemiology and etiologic determinants of the disease. In 1952 René Dubos wrote in *The White Plague:* "We know from the experience of the last 10 years since drugs have been available for the treatment of tuberculosis, that they alone will not eliminate the disease from endemic areas. Social action and political action and education of the people are essential ingredients for the successful eradication of tuberculosis. The control of tuberculosis requires the integration of biological wisdom into social technology and the management of everyday life." From Koch's last paper we learn that he was as aware of these issues in 1910 as was Dubos in 1952 when he wrote *The White Plague*.

Conclusion

If we abide by the scientific guidance of Koch's postulates, we are sure to discover the cause of AIDS. Furthermore, if we adhere to his wisdom on the epidemiology of tuberculosis, which revealed practical facts concerning treatment and prevention, we cannot fail in curtailing the AIDS epidemic.

I believe that I am the last plenary speaker of this congress, and I do not recall that Dr. Ignaz Semmelweis has been mentioned, either the man or his work. He should not go unnoticed at this First International Congress on Infectious Diseases, because his famous work on the prevention of childbed fever was done here in Vienna.

Three years ago I attended a play about Semmelweis by Harold Sackler, an American playwright. The play closed after 2 weeks, clearly something less than a popular success, and as such it mirrors the personal life of Semmelweis. But Semmelweis the man deserves our attention. Through the eyes of Sackler, poet and playwright, the significance of Semmelweis' discovery is endowed with a special humanity.

Through careful observations of many childbirths, Semmelweis concluded that the hands of the physicians, unlike those of the midwives, were contaminated with germs from autopsy material. When, in some cases, Semmelweis convinced his colleagues to disinfect their hands before they moved from autopsy room to maternity ward, their patients were spared the lethal infection. But these convincing observations were greeted with doubt and skepticism. Semmelweis' advice was not accepted by the medical establishment, those "grave-diggers with forceps," as Samuel Beckett calls us in "Waiting for Godot." Semmelweis was discredited. While doing laboratory research on childbed fever, he died of the same infection that caused this illness. The tragedy of young Dr. Semmelweis is humanity's tragedy. And so, the play is not a success story but a morality play.

In writing about his play, Sackler said this: " . . . we stand in the face of suffering and death, ultimately helpless. Yet the measure of man is the degree to which he refuses to live by this commonplace. Somehow to intervene, even briefly, between our fellow creatures and their suffering or death, is our most authentic answer to the questions of our humanity."

Dr. Mahler, the Director-General of the World Health Organization, opened this congress by quoting Kipling. Mahler predicts that "n'er the twain shall meet" if the rich nations do not make a major moral and financial commitment to the health and welfare of the world's poor. It may be that all of us disappoint the Director-General because we have not yet closed the gap between East and West and North and South, as he so dramatically contrasts the health of the rich and poor nations. Perhaps we have failed in our efforts to do all we can about that; but let us remember that for one brief moment, here in Vienna, more than 100 years ago, young Dr. Semmelweis intervened, for all of us, between our fellow creatures and their suffering and death.

References

1. Dubos, R., and Dubos, J.: The white plague: tuberculosis, man and society. Little, Brown and Company, Boston, 1952.
2. Koch, R.: Ueber tuberculose. Berliner klinische Wochenschrift 15: 1–15 (1882).
3. Koch, R.: Ueber Bakteriologische Forschung; vortrag in der Allgemeinen Sitzung des X. Internationalen Medicinischen Congresses, Aug 4, 1890. Verlag von August Hirschwald, Berlin, 1890.
4. Koch, R.: Epidemiologie der Tuberkulose. Zeitschrift fur Hygiene und Infektionskrankheiten 67: 1–18, Oct. 28, 1910.