
THE FIRST MYSTERY

DURING TWO HARROWING YEARS OF INVESTIGATION, JAMES CURRAN (M.D. 1970) LED THE TEAM OF EPIDEMIOLOGISTS WHO DEFINED THE SCOURGE THAT CAME TO BE CALLED AIDS.

BY JAMES TOBIN



In the last days of May 1981, James Curran, director of research on sexually transmitted diseases at the Centers for Disease Control (CDC), was startled by one note in the endless stream of articles, directives and data that passed under his eyes each month. It came from a colleague, Mary Guinan, M.D., Ph.D., who had just seen data slated for the next *Morbidity and Mortality Weekly Report (MMWR)*, the CDC publication that alerts doctors and hospitals to outbreaks of disease.

Curran was in San Diego for a national conference on STDs. He had been studying hepatitis B in gay urban enclaves, so he knew more than most straight people about sexual practices among gay men, and how they made the men vulnerable to infection. When he saw Guinan's note, he thought immediately of the disease pattern he had seen with hepatitis B — a blood-borne virus passed from person to person through sexual contact.

is it? Not what causes it — the question of etiology has to wait. First, epidemiologists must detect the clinical nature and extent of the disease. That means answering these questions: What symptoms and signs define the problem? Is it actually new? Who has it? Who doesn't? Where are they? In what groups? Starting when? Is it increasing?

Curran scribbled a note back to Guinan: "Hot Stuff ..."

While still in San Diego, he spoke with physicians who worked with gay patients. They told him of similar cases in California and New York. Curran then learned that some young men with the rare *pneumocystis* pneumonia, or PCP, also were suffering from a skin cancer, usually lethal, called Kaposi's sarcoma. It was not only very rare, but it normally struck only elderly men in Mediterranean countries.

A fatal lung disease and a fatal cancer. At first glance they seemed to have nothing in common. Except that both were associated with compromised immune systems.

IF THE EVIDENCE POINTED TO SEXUAL TRANSMISSION, THEN CURRAN, AS HEAD OF STD EPIDEMIOLOGY, WOULD HAVE TO TACKLE THE BASIC QUESTION THAT MUST FIRST BE ANSWERED IN ANY OUTBREAK OF UNKNOWN ORIGIN: WHAT IS IT?

The draft reported a rare pneumonia found in five young homosexual men in three Los Angeles hospitals. The cause of illness was a microbial parasite called *pneumocystis carinii*. All five men also had a fungus of the mouth and throat known as thrush, and a herpes virus called cytomegalovirus.

As Curran knew, these three microbes were quite common in human populations and normally not life-threatening. They caused serious illness only in people with weakened immune systems, usually transplant recipients who took immunosuppressive drugs to keep their bodies from rejecting new organs.

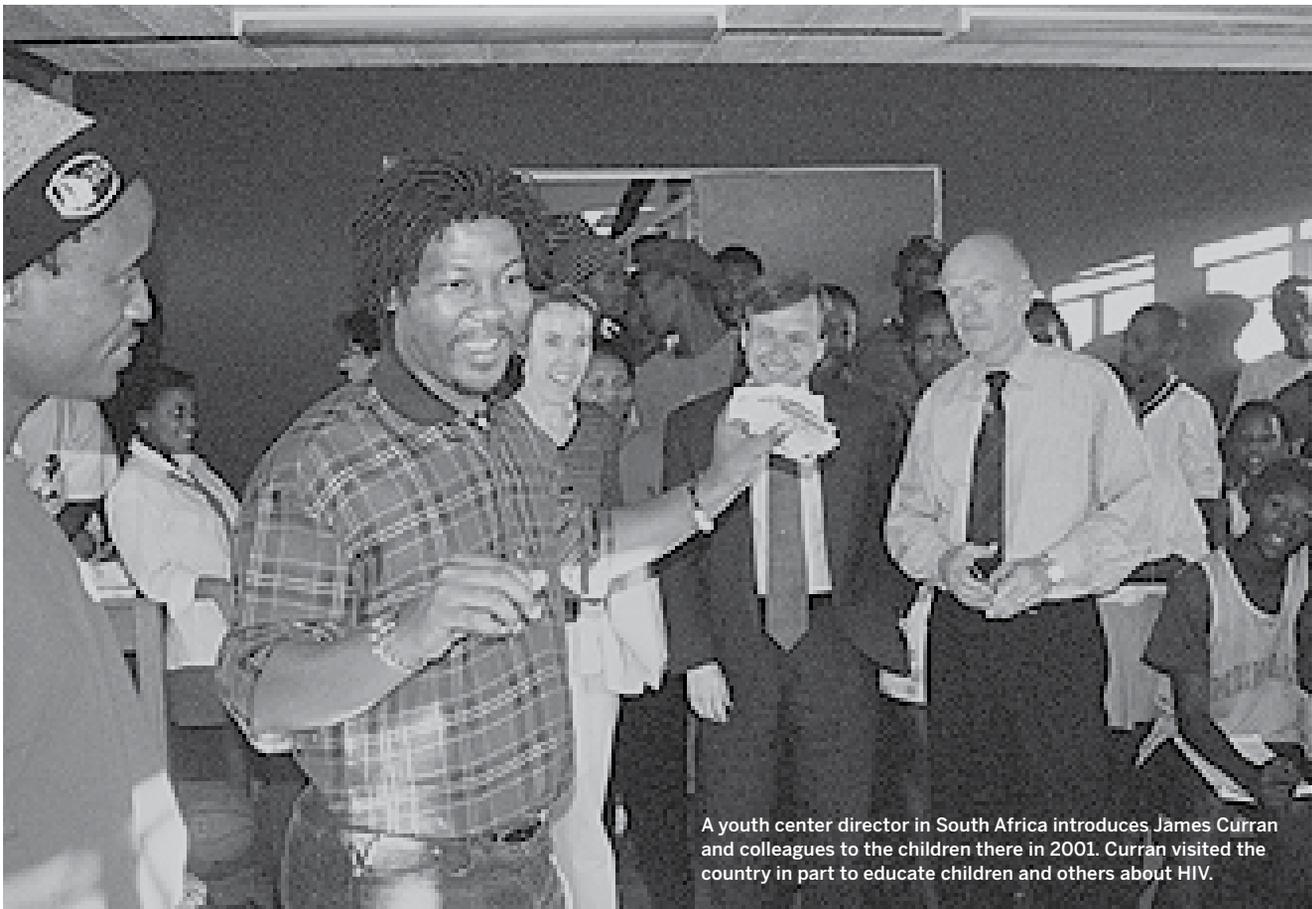
None of the five men in Los Angeles was a transplant recipient. None was known to have had immune deficiencies before. Now two of them had died. This was exceedingly unusual. It was the sort of thing that makes epidemiologists like Curran fear that a new disease is at large.

If so, and if the evidence pointed to sexual transmission, then Curran, as head of sexually transmitted disease epidemiology, would have to tackle the basic question that must first be answered in any outbreak of unknown origin: What

Days later, back at CDC headquarters in Atlanta, Curran's boss asked him to chair an inter-specialty task force to investigate. The appointment was to last for three months. Curran led the task force for the next 15 years.

Curran's interest in epidemics had started some 20 years earlier. As a student of Jesuit teachers at University of Detroit High School, he had developed a desire to fight disease far away. After earning a Bachelor of Science at Notre Dame, he went to medical school at Michigan, graduating in 1970. To fulfill his military obligation, he became a commissioned officer in the CDC's Public Health Service. He was assigned to the University of Tennessee, where he studied complications of gonorrhea and other infections in women.

That research led him to a master's degree in public health at Harvard, a residency in preventive medicine, and a permanent post at the CDC, where he rose to lead STD



A youth center director in South Africa introduces James Curran and colleagues to the children there in 2001. Curran visited the country in part to educate children and others about HIV.

research. In the late 1970s and early '80s, the STD branch was involved in trials of a hepatitis B vaccine. They had met often with physicians who treated gay men. So Curran had the knowledge and contacts to hit the ground running on a new problem that might be associated with what the *MMWR* termed “a homosexual lifestyle.”

Curran quickly called a meeting of the new team: doctors from other CDC divisions, including cancer, viral diseases, and parasitic diseases, plus colleagues from his own STD branch. There were also recruits from CDC's Epidemic Intelligence Service (EIS) — the cadre of young, post-grad M.D.s sometimes called the “medical FBI,” who serve two years tracking disease outbreaks in the field.

They discussed what was known — not much beyond the *MMWR* report. They needed more information as quickly as possible.

Telephoned queries went out across the country to state health services, hospitals, physicians who treated gay men in appreciable numbers: Had anyone seen cases like the cluster of five in Los Angeles?

Then members of the task force boarded planes. Curran believed in “shoe-leather epidemiology,” especially early in an investigation — looking for clues in patients' everyday lives, tracing patterns that might help the investigators construct formal surveys to follow.

They were striving for enough data to create what epidemiologists call a case definition, a bland term for a crucial set of understandings. To know what they were studying, they had to establish standard clinical criteria — a common set of symptoms and signs. They had to be sure that similar-appearing cases in different places at different times were in fact the same thing — apples and apples.

Curran wanted a highly specific definition. That meant the investigators might miss hard-to-diagnose cases. But the point right now was to identify epidemiologic patterns, and that demanded a case definition with hard edges.

Within three days of the *MMWR*'s release, Curran was in New York, where colleagues at New York University introduced him to a man his own age. Like Curran, he had graduated from a Catholic high school in the Detroit area.

When Curran had left home for Notre Dame, this man had left for Yale, where he trained to become an actor. Now he lay in a bed with *pneumocystis* pneumonia, his body speckled with purple swellings. No one in the CDC team had seen a case of Kaposi's sarcoma before.

"That was the first time that I really felt that these two conditions must be related," Curran said later. "That gave us, I think, one of the most important fundamental clues that this was a single epidemic with an underlying problem."

Over the next year, Curran visited the sick man many more times.

"He was treated with chemotherapy and things that probably did not help him, and I eventually watched him die," he said. "I realized that there was a certain unfairness to this, because our paths in life were not separated by much, but he died while I lived."

By July, Curran and the CDC team had gathered enough intelligence for a case definition. The new disease

— and it was indeed new, they were now sure — consisted of: 1) life-threatening opportunistic infections, and/or 2) Kaposi's sarcoma in patients under 60; and 3) no known underlying illness or history of immunosuppressive therapy. The infections and the rare skin cancer were the results of some agent that undermined the body's ability to fight fatal infections.

At NIH, there were early skeptics. How could these dissimilar symptoms share a single etiology? Curran persisted in making the case, in part by naming his team the Task Force on Kaposi's Sarcoma and Opportunistic Infections.

"We were committed to that concept," he recalled. "We would present our data by the number of cases of Kaposi's sarcoma, the number of cases of opportunistic infections, and the number of cases of both. In every instance, they paralleled each other. They were all going up; they were all in the same age groups; they were all in the same places. So this was really one epidemic."



In 1984, Curran (seventh from left) was a collaborator on Project SIDA (Swedish International Development Agency) in Zaire. The research team's study first demonstrated the global extent of AIDS.

ONE KEY LEAD WAS A RARE DRUG CALLED PENTAMADINE, TYPICALLY PRESCRIBED FOR PNEUMOCYSTIS PNEUMONIA. THEY TRACED EVERY RECENT USE TO THE PRESCRIBING DOCTOR, THEN TO THE PATIENT. MANY WERE FOUND TO HAVE THE NEW SYNDROME.

That summer of 1981, the shoe-leather epidemiologists aimed at the next questions: Who, exactly, had the disease, and what could the population of patients tell them about the cause?

With their new case definition in hand, Curran's team set out to find every known case in the U.S., living or dead. EIS officers went to the 18 largest cities, combing through the last five years of pathology files at the biggest hospitals. One key lead was a rare drug called pentamidine, typically prescribed for *pneumocystis* pneumonia. They traced every recent use of pentamidine to the prescribing doctor, then to the patient. Many were found to have the new syndrome.

The epidemiologists went to see the patients. They put them through detailed interviews — some 30 pages of questions about every aspect of their lives.

In New York, where Curran himself headed the team, many interviews were held at the Barbazon, a famous old hotel that had been converted into a residence for elderly ladies. Every evening, the ladies would look on as young women doctors would greet gay men in the lobby, board the elevator, disappear upstairs for a time, then reemerge from the elevator and say goodbye. What the ladies thought was going on, Curran never discovered.

The answers began to yield a coherent picture of two groups of patients.

The first — and by far the largest — consisted of gay men with an average age of 35. They were heavily concentrated in a few big cities — New York, Los Angeles, San Francisco — where there were large, strong gay enclaves. The men were openly gay, not closeted. They frequented gay social clubs, many had sex with multiple partners, and many used isobutyl nitrite or amyl nitrite, commonly called “poppers” — chemical stimulants to enhance the sexual experience.

In other words, the risk was not in being gay, per se. It was in the fast-lane lifestyle of the major gay communities. That was too fine a distinction for public perception, perhaps, but epidemiologically it was crucial.

The suspicion that sexual behavior played a key role grew stronger with a close study of the 13 known cases in greater Los Angeles. Of these, nine were found to be linked by sexual contact, and were linked to 90 others around the country — some 40 percent of the first 220 known cases of the syndrome.

The second group of patients, much smaller, consisted of injecting drug users. Most of these victims already were dead, but the CDC's investigations showed that they were not predominantly gay.

Theories abounded. Some medical experts suspected a toxic supply of poppers was the source. That, in fact, would have been a relief to Curran's team.

“Had it been something like isobutyl nitrite, it would not have taken us very long to get rid of that as a risk,” he said. “That would have been a much more pleasant outcome than a persistent, lifelong, transmissible virus. But from the very beginning, since we came from an STD background and had been studying hepatitis B, this really looked like a hepatitis B viral pattern. Our top hypothesis was always that an infection was causing this.”

Grim support came in the summer and fall of 1982. A baby boy died of the familiar symptoms after receiving blood transfusions. Then Bruce Evatt, M.D., head of CDC's hematology group, reported that an elderly Florida man had just died of *pneumocystis* pneumonia. The man was not gay; he was not an injecting drug user. But he had hemophilia.

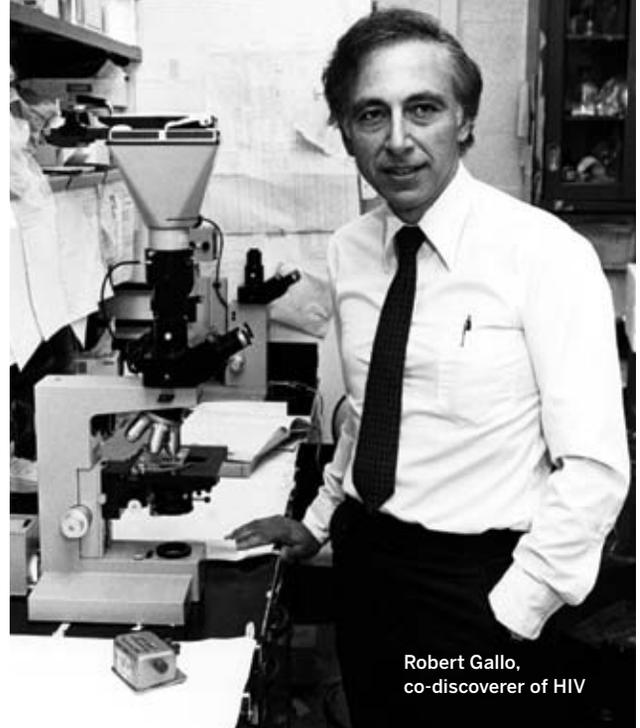
Curran recalled the startled realization that shot through the room.

“We were all thinking ‘blood,’” he said. “It was going to be in the blood supply.”

That was because hemophiliacs receive regular doses of a clotting factor produced from blood given by multiple donors.

Within days, another fatal case of PCP was reported in a hemophiliac in Colorado. Then came a third report — a hemophiliac boy who never had left Ohio.

“When the cases started occurring in persons with hemophilia,” Curran remembered, “and it was the same disease pattern as the cases in gay men, everyone became convinced — almost everyone — that this was caused, probably, by some blood-borne virus that could be sexually transmitted. ... The hemophilia cases were kind of the canary in the coal mine.”



Robert Gallo,
co-discoverer of HIV

Not long after, Curran spoke at a meeting at the National Cancer Institute. Also scheduled to speak that day was Robert Gallo, M.D., of the NIH, whose lab had recently discovered the first cancer-causing retrovirus in humans.

Curran spoke directly to Gallo. He explained that the number of cases seen to date probably represented the tip of a vast iceberg. The time had come for virologists such as Gallo to begin an urgent search for an unknown virus.

“I recall ... that he [Curran] provoked me, in a way,” Gallo told NIH interviewers later. “I was not angry, but it was a little disturbing to be challenged as to ‘How come there are no virologists involved? Where are the virologists?’ and so

tied up with previous research commitments to undertake new ones.”

In the spring of 1983, long before the virus was identified, Curran’s task force had issued recommendations for preventing the spread of the contagion — to avoid sexual contact with people at risk of being infected and to take steps to protect the blood supply. Many lives doubtless were saved as a result. Curran’s task force still faced years of work, but the CDC’s progress to the point of being able to urge lab scientists and the public to take specific actions

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on. Curran was certainly thinking of a viral disease as early as anybody in the world, I would say.”

By 1984, Gallo’s lab had co-discovered (with a French team) the human immunodeficiency virus (HIV). They then proved that HIV caused the new disease, now called acquired immune deficiency syndrome, or AIDS. This led to a blood test for HIV, which in turn made it possible to safeguard the world’s blood supplies.

Later, Gallo cited the importance of the contribution of Curran and his colleagues at the CDC. “I shudder to think what might have occurred,” he wrote, “had they and others not forced what turned out to be an eleventh-hour warning on a research community that sometimes sees itself as too

was, he believes, a signal achievement. Gallo agrees.

“I think he [Curran] has been somewhat forgotten,” Gallo said. “But I would say that he was the prime mover in the entire government ... to get people thinking about the disease and doing something.” **[M]** [MORE ON THE WEB](#) ✦

This article is based principally on interviews that James Curran gave to Medicine at Michigan, the National Institutes of Health, and the PBS documentary program “Frontline.” Other sources included Robert Gallo’s oral history with the NIH; Elizabeth W. Eberidge, Sentinel for Health: A History of the Centers for Disease Control (1992); Robert C. Gallo, Virus Hunting: AIDS, Cancer, and the Human Retrovirus (1993); and Lucianne Bailey, et al, Introduction to Epidemiology (2005).

JAMES CURRAN COMMENTS ON AN UNCERTAIN FUTURE

JAMES CURRAN, DEAN OF THE ROLLINS SCHOOL OF PUBLIC HEALTH AT EMORY UNIVERSITY IN ATLANTA, GEORGIA, AND DIRECTOR OF THE EMORY CENTER FOR AIDS RESEARCH, ASSESSES THE CURRENT STATE OF THE EPIDEMIC, NEARLY 30 YEARS AFTER HIS TEAM AT THE CDC TRACED THE DISEASE'S FIRST STEPS IN THE U.S.

“The recent information on the Thai HIV vaccine trial provides slight encouragement because of the significant but modest protective effect researchers noted. The bad news is that there are now tens of millions of carriers of the virus and 4 or 5 million getting infected each year. Especially in the hardest hit developing countries, tuberculosis and HIV have become dual epidemics. Both of these chronic infectious killers tend to affect the same populations. HIV suppresses the immune system leading to activation of tuberculosis and increased spread of the *bacillus*, while TB becomes the leading cause of death among HIV-infected persons in many countries in Africa. The bacterial synergy also greatly facilitates the emergence and spread of multiple drug resistance in TB and of other drug resistance, rendering the treatment of dually infected persons nearly impossible. Clearly, the approach to HIV and TB must be integrated in many countries and communities.

“On a global basis, we can be encouraged that science has helped us in a lot

of ways — discovery of the virus and of the blood test, the way to prevent transmission of the virus from mothers to newborns, and particularly the therapies now available. The problem is that the therapy is extremely expensive, and the treatment will have a very hard time keeping up with the epidemic. It’s hard to imagine having the medical resources available to treat 30, 40, 50, 60 million people with HIV for the rest of their lives, given resistance patterns and the inadequacy of the medical system in many countries that are hard hit. What’s needed most is a safe and effective vaccine; that has to remain the highest basic science priority.

“Scientists also are revisiting the concept that there might be some way to cure people with HIV, to relieve them of the need for lifelong therapy and reduce the number of carriers. Both of those are very high priorities. HIV remains a highly stigmatizing disease, mostly because it’s typically transmitted by sexual contact and also by drug abuse. Countries have to get beyond the stigma and deal with HIV as it affects their own population. And

because it’s in every country, this has to be accomplished over and over and over, in every community.

“[In the United States,] I think there needs to be more public attention to the problem, because the youth of today are not as motivated or concerned as the youth of 15 years ago. And they’re not as bad off as the youth of 30 years ago. But particularly gay youth are not as concerned about AIDS. So you end up with people getting infected before they become smart.”

