Recent Setbacks Stirring Doubts About Search for AIDS Vaccine

By GINA KOLATA

Bleak results from recent experiments indicate that the quest for a vaccine against AIDS will be even more difficult than many experts had imagined. The results also raise the possibility that current lines of vaccine research may be fruitless.

A year ago, the search for a vaccine seemed off to a good start as a French scientist injected himself with an experimental vaccine and also began testing the vaccine on volunteers in Africa. Shortly afterward, the Food and Drug Administration approved the first human tests in this country of vaccine candidates that had shown some promise in animal tests.

Recent Major Setbacks

But the effort has suffered major setbacks in recent weeks, scientists say, as two important animal studies indicated that the main current approach to a vaccine might not work. Chimpanzees given doses of a type of antibody that blocks the AIDS virus in laboratory dishes were not protected against AIDS infections. And monkeys, immunized with an inactivated virus that causes a disease similar to AIDS, had an excellent antibody response but were completely unprotected against the monkey version of AIDS.

A successful vaccine would protect a person from becoming infected with the AIDS virus by bolstering the body's defenses. Scientists are also working to develop drugs that defeat the virus once a person is already infected, or reduce the severity of the disease it causes.

AIDS: Confronting The Epidemic

Third of four articles.

While no one has entirely abandoned hope, the recent findings have sorely disappointed the large cadre of scientists who have mobilized to search for a vaccine that could curb the global epidemic of the fatal disease. "They are real setbacks and they raise serious concerns about the viability of the vaccine program," said Dr. Jerome Groopman of New England Deaconess

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AIDS Vaccine Search: Setbacks

Raise Doubts on Approach

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Hospital in Boston.

Dr. Malcolm Martin, a molecular biologist at the National Institute of Allergy and Infectious Diseases in Bethesda, Md., said, "I think the field has come around in general to have a much more pessimistic outlook on vaccines." Dr. Martin played a major role in developing an experimental vaccine that is now being tested in volunteers.

"There are no easy fixes," Dr. Martin added. "I'm not saying we will ever have a vaccine."

The theory, or at least the hope, behind current efforts is to find a vaccine that will stimulate the body's immune system to ward off invasion by the AIDS virus. Researchers are seeking an agent that elicits production of "neutralizing antibodies," a type that defeats the virus in the laboratory, and also provokes "cell-mediated immunity," in which "killer" cells of the body's defensive system attack cells infected with the virus.

Some Doubts On Vaccines

From the beginning scientists have been unsure whether a vaccine for acquired immune deficiency syndrome would be possible. Both neutralizing antibodies and killer cell responses occur in people who are infected with the AIDS virus, but they do not halt the virus's deadly progress. The hope, though, is that the virus might be stopped if the immune defenses had already been in place when the virus first enters the body.

But the new animal results have caused experts to ask whether their basic assumptions hold true. The AIDS virus seems to be breaking the normal rules of immunization.

"I don't know of anything like this," said Dr. Maurice Hilleman, a vaccine researcher with 45 years of experience who is director of the Merck Institute of Therapeutics in West Point, Pa. "This is the first time in vaccine development that neutralizing antibodies don't seem to amount to much."

Discouraged scientists note that their slow progress is a far cry from the ebullient statement made in 1984 by the Secretary of Health and Human Services, Margaret Heckler, who announced that the AIDS virus had been isolated and proudly proclaimed that a vaccine would be available within two years.

Still, scientists say that it is too soon to judge whether the new results are temporary setbacks or foreshadowings of failure.

"Is a vaccine possible?" said Dr. Robert Gallo of the National Cancer Institute. "Anyone who gives you an answer to that is talking preposterously. There is still too much uncertainty."

Dr. Malcolm Gefter, an immunologist at the Massachusetts Institute of Technology in Cambridge, Mass. agreed. "I wouldn't say the outlook is gloomy," he said. "It's just that it hasn't been bright." The recent studies have simply shown that the "quick and dirty" approach in which scientists "clone a viral protein, inject it and get protection against the AIDS virus" will not work, Dr. Gefter said. He added that these first attempts were only the beginning. "There are all sorts of things that could be tried and haven't been tried yet," Dr. Gefter said.

Approaches In the Search

Vaccine studies are proceeding in several directions. Daniel Zagury of the Pierre-et-Marie Curie University in Paris has injected himself and volunteers in Zaire with a vaccine consisting of a synthetically made protein from the AIDS virus, GP-160, that is delivered by the vaccinia virus, the virus used to inoculate against smallpox.

In the United States, the Federal Government and six medical research institutions are recruiting volunteers for vaccine studies that also use synthetic GP-160, in this case injected directly rather than delivered in a virus. The vaccine is made by MicroGeneSys Inc. of West Haven, Conn. In addition, Oncogen, a biotechnology company in Seattle that is a subsidiary of Bristol Meyers, is recruiting volunteers to test a vaccine consisting of a different AIDS protein, GP-120, attached to a vaccinia virus.

At the same time, scientists are testing a variety of other potential vaccines in small laboratory animals such as guinea pigs and in chimpanzees and macaques. Although the chimpanzee is closest to humans and is the only animal that can be chronically infected with the AIDS virus, antibody responses can be stimulated in other species.

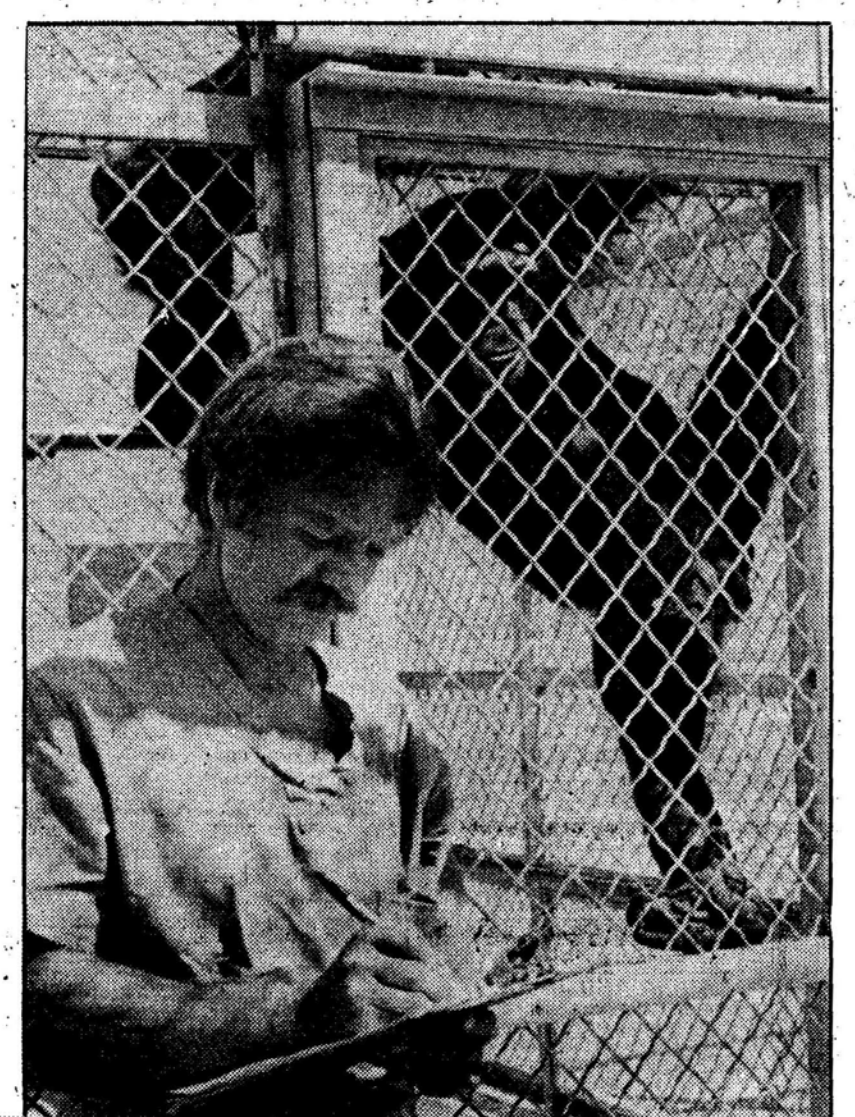
Both GP-160 and GP-120 are proteins from the viral envelope, which forms the surface of the AIDS virus. Scientists reasoned that the surface proteins are what the immune system encounters when a person is first infected with the virus. "Classically, with envelope viruses, envelope proteins provide immunity," said Dr. Anthony Fauci, who as director of the National Institute of Allergy and Infectious Diseases is in charge of Federal vaccine research.

But investigators also want to try vaccinating with proteins from the core of the AIDS virus. Researchers have noticed that people infected with the AIDS virus make antibodies to the interior core proteins and speculate that these proteins might induce a protective immune response. "Probably, in the near future, there will be a vaccine candidate made up of a core protein," Dr. Fauci said. "That hasn't been done yet, but since this is an unprecedented infection causing an unprecedented disease, we have to cover all bases."

Another idea is to try a killed virus vaccine, a proposal championed by Dr. Jonas Salk who used this approach in his polio vaccine. He reasons that killed AIDS viruses would help induce cell-mediated immunity and also might induce a better antibody response. But some experts wonder whether they can be certain that injecting even a killed AIDS virus will be safe.



National Institute of Allergy and Infectious Diseases



Above: Dr. Malcom A. Martin, a Federal scientist, discusses an X-ray film used in AIDS vaccine research with Rosamond Rutledge, a colleague. Left: Dr. Jorg Eichberg, a researcher in Texas, carried out vaccine experiment in chimpanzees with disappointing results.

Obstacles To Research

Fundamental stumbling blocks stand in the way of all these vaccine ideas, experts say. One problem is that the human AIDS virus does not make any animal, including chimpanzees, ill with AIDS, making the relevance to humans of any animal experiment uncertain.

"We are limited and bottlenecked by the lack of an animal model," Dr. Gallo said. "We have to do our tests in man. But how do you know which vaccine is the better candidate? You really don't."

In addition, scientists still do not know why the body's normal immune response to an AIDS virus infection is unable to defeat it.

Dr. Bernard Moss of the National Institute of Allergy and Infectious Diseases has found that all patients infected with the AIDS virus do produce killer cells that attack other body cells infected with the AIDS virus. But, Dr. Moss says, "since these people go on to develop AIDS, these cells obviously are not eradicating the virus."

Likewise, people infected with AIDS make large amounts of several kinds of antibodies. But nearly all the antibodies they make have no effect against the AIDS virus. Neutralizing antibodies, the type that should deter the virus, are usually mysteriously missing early in infection and when they do appear a year or two later, they do not seem to affect the course of the disease.

Vaccine experts are puzzled. In infections with other viruses, anyone who makes neutralizing antibodies is protected against the disease. In AIDS infections, the role of neutralizing antibodies is unclear.

"There is no correlation between neutralizing antibodies and whether a person is healthy or sick," Dr. Martin said. "I don't know what neutralizing antibodies mean."

Dr. Hilleman said that the way researchers ordinarily go about developing vaccines is to inoculate people with viruses or virus particles that induce them to make neutralizing antibodies. Anyone who makes these antibodies is protected against the disease. "For ordinary viral infections, that's it," Dr. Hilleman said. "That's the name of the game."

The Race In Testing

Despite their uncertainties, scientists felt they had no time to lose in starting to test vaccines. "Since this is an unprecedented infection causing an unprecedented disease, we felt we had to cover all bases," Dr. Fauci said. Last August, Federal scientists began preliminary tests of a vaccine candidate consisting of GP-160. Since then, the Food and Drug Administration has approved the expansion of this test and also the testing another vaccine, made of viral coat protein GP120 attached to a vaccinia virus.

The GP-160 protein was chosen because it easily elicited neutralizing antibodies in guinea pigs, rabbits and chimpanzees, according to Dr. Fauci.

At the National Institutes of Health, homosexual men who are not infected with AIDS are being recruited to test the GP-160 vaccine. A total of 81 volunteers are needed, but only about 35 have been enrolled so far. This study "started off slow, for a variety of reasons," according to Dr. Fauci. He added that it has been difficult to recruit volunteers, in part because the volunteers are afraid of the "stigma" of having antibodies to AIDS, even though they will not have the disease.

The Federal study is a test only of the vaccine's side effects and its ability to elicit neutralizing antibodies. The investigators are not planning to determine if the vounteers are protected against AIDS and they counsel the volunteers to assume that they are not protected.

Volunteers for Study

The 35 volunteers who have participated in the study so far received one of two relatively low doses of the vaccine. They failed to make any neutralizing antibodies to the vaccine, Dr. Fauci reports. "They had no antibody response," he said. There are no data yet on whether cell-mediated immune responses occurred. Dr. Fauci said he was not surprised by the lack of neutralizing antibodies because the vaccine doses were so low. Higher doses are to be tried.

Dr. Gefter cautioned that the negative initial result was not definitive because it sometimes took fairly large doses or several booster shots before people made neutralizing antibodies to vaccines. The hepatitis B vaccine, he said, elicits neutralizing antibodies only after six months and three vaccine shots.

The GP-160 vaccine study is continuing at the National Institutes of Health, where volunteers are sought for two higher vaccine doses and it is also being expanded to include women and heterosexuals, Dr. Fauci said. The expanded study will be conducted at six medical research centers.

The study of GP-120 attached to vaccinia viruses is now at the stage of recruiting volunteers, who are to be homosexual men not infected with AIDS. Dr. Lawrence Corey of the University of Washington in Seattle, who is directing this study, said 60 volunteers were needed and that "things

are going O.K." He added that "we're busting our rear ends to do this as quickly as possible."

Dr. Zagury in Paris has reported that the GP-160 vaccine that he is testing on himself and some Africans elicited both neutralizing antibodies and cell-mediated immunity but he has not reported any evidence that the vaccine protects people against the virus.

Critics of Studies

All the human vaccine studies have their critics who point out that none of the vaccine candidates have protected chimpanzees against AIDS virus infections. Although chimpanzees do not become ill with AIDS, the virus multiplies in their cells.

"To my knowledge, no one has shown that they can protect one chimp from infection," Dr. Gallo said. "That's our problem."

Others have argued that if chimpanzees had a large enough amount of neutralizing antibodies in their blood before they were infected with the AIDS virus, the antibodies might block the AIDS infection in its tracks. The recent studies are leading experts to question even that assumption, however.

Dr. Alfred Prince of the New York Blood Center devised a test to see whether neutralizing antibodies would make a difference in chimpanzees. He decided to give the animals antibody injections to insure that they had plenty of neutralizing antibodies before they were injected with the AIDS virus.

Dr. Prince pooled antibody-containing blood serum from patients who made relatively large amounts of neutralizing antibodies and his colleague, Dr. Jorg Eichberg of the Southwest Research Foundation in San Antonio, Tex., injected the serum directly into chimpanzees.

In the first experiment, Dr. Eichberg gave the chimpanzees a standard dose of neutralizing antibodies. It was a dose that, were it any other disease than AIDS, would have easily protected the animals, Dr. Prince said. The antibodies did nothing.

'We Were Really Shocked'

Then Dr. Eichberg gave the chimpanzees 10 times as many neutralizing antibodies. "It was a really huge dose," Dr. Prince said. But, he added: "once again, there was no protection whatsoever. We were really shocked."

Dr. Prince said he is "now trying to figure out what this means." It could be that the dose of AIDS virus he used to test the chimpanzees was so high that it overwhelmed the ability of the antibodies to protect, he said. But over all, the finding has disturbed experts.

In the second recent study, Dr. Ronald Desrosiers of the New England Regional Primate Research Center in Southborough, Mass., tried to immunize macaques against a monkey virus, called SIV for Simian Immunodeficiency Virus, that causes a disease closely related to human AIDS.

He tested both killed viruses and viruses that he had taken apart and reassembled with a substance called Quill A that is derived from from a South American bush. This sort of reconstitution has been shown by others to greatly enhance the effectiveness of viral vaccines. "It's state-of-the-art," Dr. Desrosiers said.

Both vaccines appeared at first to be effective. The macaques made plenty of antibodies to the monkey virus, Dr. Desrosiers said, including neutralizing antibodies. But then, when Dr. Desrosiers inoculated the vaccinated monkeys with live SIV, "they all became persistently infected," he said. "The vaccinated animals did no better clinically than those that were not vaccinated," Dr. Desrosiers said.

"We learned a lot," Dr. Desrosiers added. He and his colleagues are now reasoning that the AIDS virus may be evading the vaccines and neutralizing antibodies because it can persist for a long time in the body, hiding in the genetic material of cells and giving no sign to the immune system that it is there. That means, Dr. Desrosiers said, that if any AIDS virus slips through the barrier of neutralizing antibodies, a person could become infected. "Most vaccines don't protect absolutely," he said. "But once the AIDS virus gets its foot in the door, it's there for life."

Tantalizing Problem

Dr. Prince also asks whether the AIDS virus might escape neutralizing antibodies by constantly changing the makeup of its outer coating. "The virus might be so variable that there are always a few that escape," he said. If so, a vaccine may be impossible.

For now, however, scientists say they are having to regroup and consider again how to defeat the AIDS virus with a vaccine.

"We're early in the game," Dr. Prince said. "The AIDS virus is obviously a harder nut to crack than most." In fact, he added, "it is the most difficult virus I ever saw to immunize against."

"As of now, it looks like finding an AIDS vaccine is going to be a very long and very difficult problem," Dr. Hilleman said. "But those of us who have been working with vaccines for many years are never optimistic about any vaccine," he added. "You are never optimistic until you have your license to market the vaccine in your hand."

Infected Boy Shows Signs of AIDS

TAMPA, Fla., Feb. 15 (AP) — One of three brothers who were banned from school because they were infected with the AIDS virus has developed AIDS-related complex, but his doctor says he can remain active.

Ricky Ray, who is 11 years old, does not have a severe or life-threatening illness stemming from acquired immune deficiency syndrome, said Dr. Jerry Barbosa, a specialist in pediatric hematology and oncology at All Children's Hospital in St. Petersburg.

"Ricky's ARC is stable and he is showing no signs of progession," Dr. Barbosa said. "He never posed a threat in the past, and he doesn't pose a threat to anyone in the present. If anything, Ricky is feeling better. He's full of energy."

Ricky's brothers, Robert, 10, Randy, 8, remain in good health, Dr. Barbosa said. All three are hemophiliacs who were infected by contaminated clotting factor before the spring of 1985, when screening of blood donations for the virus began.

Treatment With AZT

The symptoms of AIDS-related complex may include weight loss, loss of appetite, fever, night sweats, skin rashes, diarrhea, tiredness, lack of resistance to infection or swollen lymph nodes. As their immune systems deteriorate, most ARC patients eventually develop full-fledged AIDS, characterized by life-threatening infections and cancers.

Information about Ricky's condition came seven weeks after it first was reported that he was taking AZT, azidothymidine, a drug approved for the treatment of AIDS. Some doctors prescribe it to AIDS virus carriers whose immune systems are declining even before they are diagnosed with AIDS.

The boys' medical records are on public file as part of a lawsuit filed against the DeSoto County School Board by their parents, Louise and Clifford Ray. Dr. Barbosa filed the latest test results in court Friday.

The Ray brothers were banned from regular classes in DeSoto County in August 1986 after they tested positive for AIDS virus antibodies. A Federal judge ordered their return to the classroom.

Less than a week after they started school last fall, a fire destroyed the Rays' home. The authorities ruled the fire arson but no arrests have been made.

The Rays moved to Sarasota, where the boys now attend school.

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U.S. Confronting AIDS With Sense of Realism

By BRUCE LAMBERT

America is confronting AIDS in 1988 with a new sense of realism and a surge of activity by a broad range of public and private groups, according to health policy experts who only a year ago were lamenting the nation's complacency.

Although the experts see the intensified national response as a hopeful development, they say that the nation's efforts to stem the fatal disease are still belated, disjointed and sometimes misguided.

"Within the last year, the awareness has changed dramatically," said Dr. Mathilde Krim, founding chairman of the American Foundation for AIDS Research. "It happened almost palpably, and suddenly everybody would like to do something."

No epidemic in the nation's history has elicited such a broad and complex response.

Despite the welcome shift to activism, experts warn that the nation desperately needs an even greater effort to halt the spread of AIDS and to prepare for the inevitable flood of patients.

"We're still running behind the virus," said New York City's Health Commissioner, Dr. Stephen C. Joseph. The University of Michigan's dean of public health, June E. Osborn, said, "Things we're doing now should have been done two years ago."

Acquired immune deficiency syndrome is posing troubling issues throughout society. Theologians debate about condoms, courtroom officers demand rubber gloves, television producers mull safe-sex themes, dating services offer to match singles who have passed the antibody test and officials clash over giving clean needles to drug addicts.

In the perceived absence of strong Federal leadership, other forces are filling the vacuum: state and local governments, hospitals, physicians, private groups and businesses. The ad hoc result is a peculiarly American response to AIDS: an emerging patchwork of laws, regulations, health care and educational measures and efforts by governments at every level as well as by voluntary and self-help groups.

The most glaring weakness in the response, experts say, is the

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lack of effective action to curb the spread of AIDS among drug addicts, their sex partners and babies.

Still, as the epidemic enters its eighth year and the caseload has surpassed the 50,000 mark, health authorities, advocates for AIDS victims and public officials see signs of a nation finally mobilizing.

Nearly 600 AIDS-related laws have been proposed across the country, 90 of them enacted last year. Some political leaders are taking a harder line on issues like mandatory testing and tracing of sexual and needle-sharing contacts of those found infected, measures that many health experts fear will be counterproductive. But voluntary measures favored by health professionals, such as AIDS education, are also growing rapidly.

With some exceptions, fears that the threat of AIDS would lead to severe, repressive measures have not materialized, at least so far. Polls suggest that the public is increasingly compassionate toward AIDS patients.

Although many critics have decried what they see as President Reagan's lack of leadership on AIDS, he has established a commission that, after initial stumbling, has gained new respect as it confronts some of the most urgent concerns. This week, for example, the commission will hold hearings in New York on the slow progress in finding new treatments and other issues. But with the nation embarked on a Presidential campaign season, clear direction from Washington may not come until after a new administration takes office next year.

A Surge In Actions

The past year saw a dramatic rise in anti-AIDS actions around the country. Before 1987, for example, no state required its local schools to teach about AIDS, but by the end of the year 18 had done so. More are expected to follow, spurred by grants and a model curriculum from the Federal Centers for Disease Control.

Longtime centers of the epidemic such as New York stepped up their efforts. Criticized for lacking a master plan, the city is now drafting one. The city also distributed a million free condoms, sponsored blunt television commercials ("Don't go out without your rubbers") and distributed a video to high schools. The state expanded treatment programs to reduce long waiting lists for addicts,and the city prepared to experiment with distribution of clean needles to addicts. The state authorized a 500-bed hospital expansion to help care for AIDS patients.

The accelerating political pace on AIDS has brought some results that are helpful and others that, in the view of public health experts, are wasteful or counterproductive. But extreme proposals such as for the quarantining of AIDS patients have made little headway.

This sampling from the last few weeks illustrates the trends:

¶Los Angeles's Board of Supervisors voted to crack down on unsafe sex in bathhouses. Virginia's Governor authorized physicians to report infected people to health officials so their sex partners could be notified.

¶Louisiana and Illinois became the first states to require testing of marriage applicants for infection with the AIDS virus. The Newark City Council overrode a mayoral veto to force testing of convicted prostitutes.

¶Florida's Governor said he was considering a plan for detention facilities for recalcitrants who continue to infect others despite warnings. On Long Island, the Suffolk County Legislature overrode a veto to require that spouses of infected persons be notified.

"Quick-fix solutions like premarital testing, which run counter to what public health authorities would like, are in the forefront," said Karen S. Walker, who is the senior editor of AIDS Policy and Law, a newsletter.

Health experts question the value of many of these initiatives. Illinois hospitals were overwhelmed with requests when the premarital testing law took effect Jan. 1, forcing some couples into other states or wedding postponements. Health experts say scarce funds for AIDS prevention would be better spent on high-risk groups.

More extreme proposals are pending, including one to authorize Missouri courts to order testing based on anonymous telephone tips, and another to test every resident of Virginia over the age of 5.

Most such proposals have not been adopted, according to monitors at George Washington University's Intergovernmental Health Policy Project. But the project director, Richard E. Merritt, mused, "One wonders whether the forces of moderation will continue to prevail."

Dispute On U.S. Role

While many experts believe Federal medical institutions have done a good job of tracking the epidemic and mounting scientific research, many also say the Government has neglected issues of prevention, civil rights and care of patients. This has inevitably shifted responsibility to state and local governments and led to a diversity of responses, a situation that some condemn but others say has its merits.

"A centerpiece of the AIDS problem has been the lack of a coherent, cohesive and well-thought-out national policy," said Dr. Lonnie R. Bristow, a trustee of the American Medical Association.

Several European countries, with much smaller caseloads than in the United States, already have sent mailings on AIDS to every resident. That has yet to be done here. Federal officials plan the first such mailing later this year, but are still undecided on its content. In the meantime, Alaska and Massachusetts are spending state money to send their residents the AIDS report by the Surgeon General of the United States.

"States and localities are left to fend for themselves," acknowledged Dr. Bernard J. Turock, the Illinois public health director. Yet he and some others value state autonomy on public health in tailoring AIDS policies to local needs and tastes. But Dr. Osborn of the University of Michigan asked, "Must we waste precious time and lives, relearning the lessons of this epidemic in every new city and town, reinventing the wheel?"

In Chicago, Paul Varnell of the Illinois Gay and Lesbian Task Force said, "The city keeps waiting for the state to do it, the state keeps waiting for the Federal Government to do it — and the Federal Government says it should be up to the state and local governments."

Chaotic Mix Of Policies

Fragmented responsibility for AIDS has resulted in a chaotic mix of policies, replete with contradictions, duplication, gaps and disparities.

What is required teaching in one school may be banned in a neighboring community. Condoms are distributed free to homosexual men in New York City jails, but are contraband in New York State prisons.

San Francisco, where gay groups have political influence and the city had surplus funds, formed a model health system for AIDS patients. But in more conservative Texas, burdened by both the nation's fourth-highest AIDS caseload and a shattered oil economy, advocates say that funds to fight the disease are scarce.

Some 22 states have passed laws governing the testing of applicants for health or life insurance for infection with the AIDS virus. Connecticut requires applicants to be tested, while adjacent New York forbids it. Massachusetts also prohibited testing until Gov. Michael S. Dukakis recently overruled his insurance commissioner, who quit in protest.

Privacy rules conflict. New York refuses to record AIDS antibody test results by name, while Colorado requires confidential reporting of names to health officials so that sexual and needle-sharing partners of infected people can be reached if necessary. (In practice, half the names given turn out to be pseudonyms.) Which approach works best to combat the spread of the disease is not yet clear.

The extent of discrimination and legal action to prevent it varies by location. In California, a Federal court reinstated an AIDS-infected teacher to his job and a state agency ruled that the Raytheon Corporation could not bar an infected employee. But prehiring testing is so common in Dallas, said the president of the Gay Alliance, William Waybourn, that "the testing issue is one I think we've lost."

Hospitals Jammed

Fighting the epidemic at the front lines is the nation's health care industry. Individual efforts are often valiant, but in some major cities the system is already under stress — with an onslaught of patients yet to come.

New York City's public and private hospitals have been overwhelmed largely because of mistaken AIDS projections by state planners. Ambulances divert patients from one hospital to another. Even heart attack and stroke victims sometimes linger in emergency rooms up to three days waiting for a bed in the intensive care ward.

Greater Miami was likewise unprepared for the 1,397 cases it has had so far. Health Network, a local group, says its referral list has only five physicians accepting private patients. Indigents are served at Dade County's Jackson Memorial Hospital. There they face a three-month appointment backlog to see an AIDS specialist, and an even longer wait for treatment.

Often working heroically under the workload, doctors, nurses and orderlies have put in long hours, sometimes to the point of burnout. There have been notable lapses: food trays left outside patients' doorways, a New York City dentist fined for turning away an AIDS patient and some surgeons refusing to operate. But most health workers have put aside any personal qualms.

Trying to mold national policy, the American Medical Association last June promulgated guidelines on testing that were incorporated into legislative bills, and in December it proclaimed the ethical duty of physicians to treat AIDS patients.

New Sense Of Realism

A new sense of realism is motivating and shaping the nation's response to AIDS, if for no other reason than that events require it. Nan D. Hunter, who handles AIDS issues for the American Civil Liberties Union, said, "City and states are being forced to confront this disease — they don't have any choice."

Geography no longer offers sanctuary from the virus. AIDS, once viewed as an exotic New York-San Francisco disease, then as an urban disease, is now everywhere to some degree.

"We hear of the smallest hospitals in the smallest rural towns seeing AIDS cases," said Mary Lou Johnson, administrator of Colorado's state task force on AIDS, one of 40 such panels sprouting around the country. New York's State Health Commissioner, Dr. David Axelrod, said, "The rest of the country is unfortunately catching up with us."

An aide to the United States Conference of Mayors, Richard D. Johnson, said that concern intensified "just about a year ago, in the aftermath of the Surgeon General's report," adding: "That's what made people sit up and take notice, that's when we started getting lots of calls. Government has a tendency not to deal with something until it has to."

Gov. George Sinner of North Dakota said, "We are in a position to learn from the tragedies of New York and California." With only seven cases, his state issued a 131-page "Plan for Action" of education, confidentiality, nondiscrimination and testing of prisoners, prostitutes and marriage applicants.

Adding to the sense of urgency is "the fading hope for a magic bullet" for a cure or vaccine, said Kristine M. Gebbie, Oregon's health commissioner, who is a member of President Reagan's panel.

The Public Is Concerned

Public opinion is also changing. Surveys indicate Americans are better informed and their mood is shifting from fright to concern. A recent Gallup poll found 87 percent of the respondents expressing compassion.

Singles night at the Village Presbyterian Church in a suburb of Kansas City, Mo., devoted its Tuesday night program throughout January to AIDS presentations, attracting rapt crowds of hundreds. The speaker, Virginia E. Allen, heads a local AIDS agency, the Good Samaritan Project.

"My first speech on AIDS, in 1985, was in an auditorium set up for 200 people, and only six showed up," she said. But now the program is in hot demand, with 669 presentations last year and 1,500 expected this year. Audiences have grown to as large as 1,700, often overflowing. Good Samaritan has extended to surrounding states. Ms. Allen recalls a trip to a rural town with a population of about 400 and drawing 300 to her talk.

"The majority are very responsive," she said. "They want to find out how to protect themselves, and how to help others." Among its programs, Good Samaritan organized a network of teenage AIDS advisers in nearly 100 schools and a toll-free telephone hot line.

Kansas City's experience is not unique. In Montgomery County, Md., 300 government, business and civic leaders gathered last month to discuss the impact of AIDS on hospitals, social services and employers. In Providence, R.I., 80 business officials convened to talk about AIDS issues. In remote Canton, N.Y., near Canada, an AIDS forum packed an auditorium and lasted into the night.

While the nation was preoccupied with the report of a family of AIDS-infected hemophiliac boys burned out of its home in Arcadia, Fla., a less publicized drama was playing out in Arcadia, Ind. There the residents welcomed Ryan White, an infected youngster. Gov. Robert D. Orr, a conservative Republican, shook his hand and bestowed an award.

Irrational panic still occurs. Swimmers deserted the Williamson, W.Va., pool when an AIDS patient showed up. Some immigration employees wore plastic gloves for Haitian applicants. The Radford, Va., schools barred a theater group because it once performed with AIDS patients onstage. A Simsbury, Conn., school canceled a basketball game this month on the rumor than an opposing player might have AIDS.

Leadership can help allay such fears, asserts Dr. Woodrow A. Myers, Indiana's health commissioner. He believes Mr. Reagan should use the power of the Presidency and his skills as the great communicator to calm the public. A fireside chat or an AIDS baby in the President's lap could do wonders, Dr. Myers said.

Business, Volunteers

Beyond government and the health care industry, other segments of society are beginning to confront AIDS.

Business, for example, is beginning to grapple with issues of job discrimination, sick leave, health insurance and the worries of co-workers.

"Within the last 12 months there been a radical expansion of corporate awareness," said B. J. Stiles of the National Leadership Coalition on AIDS, which promotes business involvement on AIDS.

A Fortune magazine survey of executives ranked AIDS among their top three concerns. The International Business Machines Corporation sent brochures to all 240,000 domestic employees. The Public Service Electric and Gas Company of New Jersey has provided speakers, pamphlets and videotapes for its 13,000 employees.

Some private groups are finding AIDS a thorny issue. The United States Catholic Conference released a policy statement on AIDS in December, only to have its reference to condoms denounced by two Cardinals, John J. O'Connor of New York and Bernard Law of Boston.

Self-help efforts are growing. Groups like the Gay Men's Health Crisis, formed near the beginning of the epidemic in New York to help patients and lobby for better policies, have grown into major professional organizations. A host of smaller groups, local and national, have sprung up to help patients or push for desired laws. Frustrated by the slow pace of drug development, a group of New York AIDS patients and physicians formed Community Research Initiative to organize their own drug experiments.

Fund-raising efforts have drawn volunteers from celebrities like Elizabeth Taylor, to unknowns like Brent Earle, who last year ran 10,000 miles to publicize the cause.

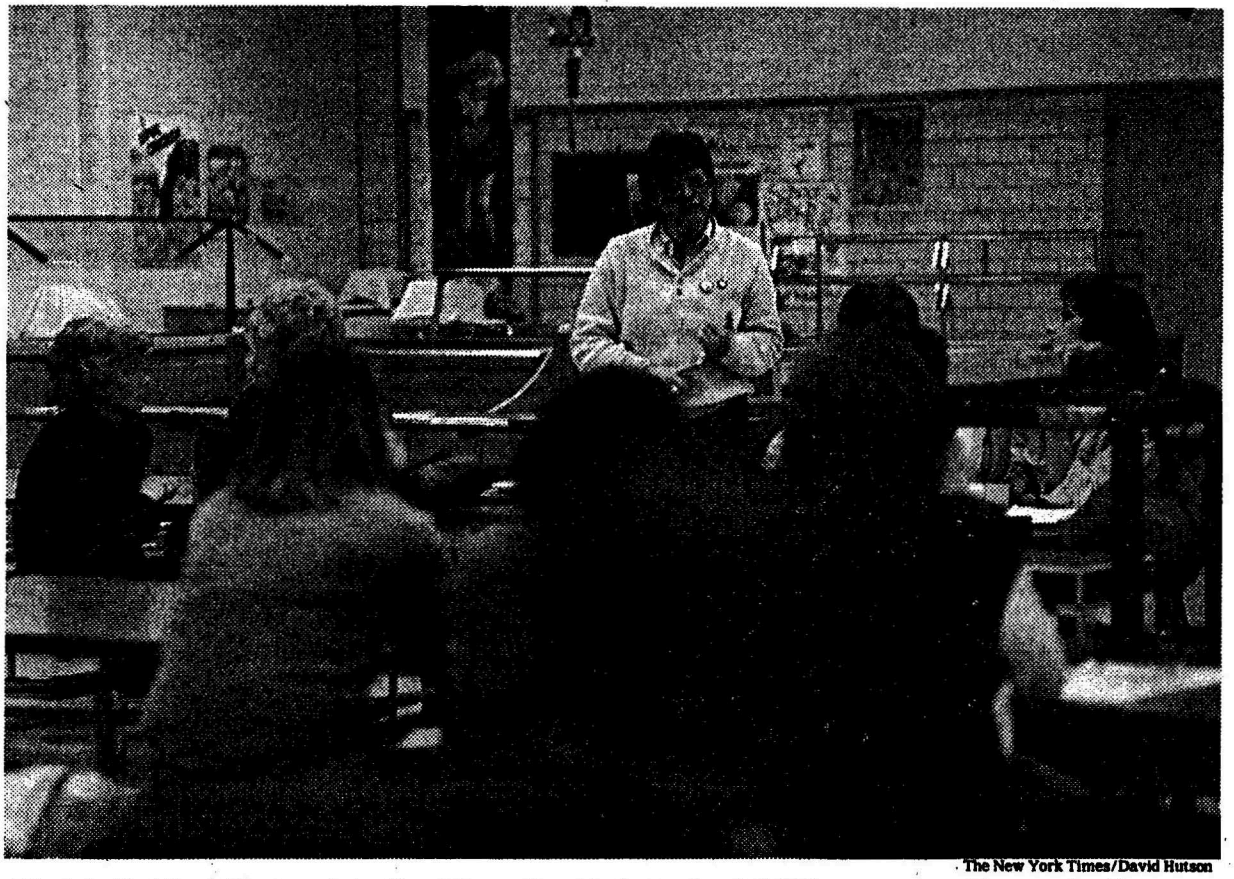
"As a country, we have denied that AIDS will sooner or later affect almost every one of us in some way until now, there is an almost universal realization that it does," said Mr. Stiles.

And Dr. Joseph of New York City said, "The way mankind responds to crisis is first disbelief, then denial, then the third stage is mobilization, and we're at the horizon of that now."



The Indianapolis Star/Jeff Atteberry

Ryan White talking with classmates at Hamilton Heights High School in Arcadia, Ind., where his infection with the AIDS virus has been accepted.



The New York Times/David Hutson

Virginia E. Allen, director of the Good Samaritan Project, a local AIDS agency, speaking on the disease to parents at at Park Hill Junior High School in suburban Kansas City, Mo.

Wider Use of Experimental Drug For AIDS Ailment Is Approved

By PHILIP M. BOFFEY
Special to The New York Times

WASHINGTON, Feb. 16 — Federal health officials today announced approval for wider use of an experimental drug to treat AIDS patients who suffer from a life-threatening form of pneumonia.

Dr. Frank E. Young, the Commissioner of Food and Drugs, said that the experimental drug, trimetrexate, had been approved for expanded distribution to treat AIDS patients who have pneumocystis carinii pneumonia and cannot take the two standard medications for it because of severe adverse reactions.

The deadly pneumonia strikes most victims of acquired immune deficiency syndrome and is the most common cause of death in AIDS patients.

Dr. Young said that trimetrexate was the first AIDS-related drug to be granted approval an investigational new drug under revised regulations that allow a promising drug to be used in certain life-threatening or serious circumstances, even though the drug has not yet completed all the clinical tests normally required to prove safety and efficacy.

Move Is Praised

The Government's action was praised as potentially "very significant" by William Bahlman, a spokesman for the AIDS Coalition to Unleash Power, a New York-based advocacy organization for AIDS patients. Mr. Bahlman said the action would constitute "a breakthrough" if it encouraged similar broad distribution of a wide range of other drugs for AIDS patients.

However, Dr. Young said that no other AIDS-related drugs currently under review at the the Federal agency have progressed far enough through testing to warrant consideration for wider distribution.

The announcement today was made at the start of a two-day meeting sponsored by the agency and the American Medical Association on the implications of the new regulations, which went into effect last June.

Drug's Toxicity Counteracted

Trimetrexate was first developed by the Warner-Lambert Company, of Morris Plains, N.J., as an anti-cancer drug. It has been tested in humans as a treatment for the AIDS-related pneumonia by scientists at the National Cancer Institute since 1985.

Dr. Young estimated that 25 percent of the AIDS patients infected with the pneumonia are unable to tolerate the standard drugs, trimethoprim/ sulfamethoxazole and injectable pentamidine.

Trimetrexate itself is so toxic and potentially lethal at the doses needed to treat the pneumonia that it must be administered with leucovorin, an approved drug that protects the patient's cells from injury by trimetrexate.

The National Insitute of Allergy and Infectious Diseases will distributue both drugs free to patients who qualify. Physicians seeking information can call 1-800-426-7527 from 8 a.m. to 8 P.M. Eastern Standard Time Monday through Friday, except in Michigan, where the number is 1-800-833-0014.

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