AIDS: the researchers behind the disease

By JOHN BARBOUR
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There was a twitching in the network, a signal something was out there, something wiggling in the web of recognition, as discomfiting as an unaccountable blip on a radar screen or footsteps on a dark staircase.

No one knew in those early days of 1981, but an awesome virus was insinuating itself into the human race, threatening its procreation and its survival against disease.

In the years that followed, disbelief pursued researcher and public alike. Homosexuals were adamant that not enough effort was made because at first acquired immune deficiency syndrome (AIDS) was considered a homosexual disease. Yet...

"The first cases of heterosexual transmission were reported in late 1982," says Dr. James Curran, head of the Sexually Transmitted Diseases section of the Centers for Disease Control in Atlanta. "It was very difficult to get people in the United States to believe it. And now people want to know why you didn't tell them."

From day one, whoever the victims, for many of the physicians and researchers at the bedsides and in the laboratories, the disease was a grim, unacceptable reality. It would re-orient careers, obsess creative minds, sublimate egos to a single goal, disrupt family life, squeeze two work weeks into one, year after year, and engrave the visage of death deep into the common consciousness.

Now, six years later, the virus has been identified and is being dissected, one drug with some effect and some side effects has been rushed into use, new drugs are on the horizon but a vaccine is likely still years away and there is still no cure.

The lights still burn late into the night in the same laboratories, children still content themselves with absent parents, men and women home late from the labs still awaken at 3 a.m. and go to their notebooks. In research centers from Boston to Bethesda, Md., when snow paralyzes traffic and government workers are given the day off, scientists trudge through the drifts to attend their flasks and beakers.

Patients die in greater numbers. The terror enlarges. There is no relief in the war, and indeed researchers use phrases like "the people in the trenches," meaning those at the bedsides of the ill and dying. But of the hundreds in the vanguard of AIDS research, thousands now work the ramparts from here to Zaire. The research atmosphere remains electric.

Besides epidemiologists, the AIDS effort inherited a group of doctors on the front line of virology and its links to cancer. Throughout their training they faced the inevitability of strange deaths. Some coped, some did not. Dr. William Blattner of the National Cancer Institute remembers two of his cohorts who committed suicide, and weekly one-on-one psychiatric sessions to help doctors face their dying AIDS patients.

Dr. Sam Broder of NCI will never forget the patient in Ward 3B: "This one patient was almost a complete distillation of AIDS. It was almost an incarnation of everyone. He was a young man. He was gay. He had visited Haiti. He had experimented with intravenous drugs. He had pneumocystis. He had all sorts of viral infections that were active. He developed a lymphoma. He had a total destruction of his immune system. And he died."

"And I can remember very distinctly our turning to each other... It was recognized that there was something going on, but in that era there was just no way of grasping it. We didn't know."

In the beginning, no one knew; not enough to describe it, name it. The health network was drawn around a new and complicated virus. Into the net were drawn hundreds of researchers as much captives of the illness as were the unlucky patients.

Skepticism and serendipity met on the plains of the new disease.

Dr. Jim Goedert was a young physician at the National Cancer Institute in 1981. His sister-in-law in Connecticut had a friend whose brother uncovered more cases.

It was Jim Goedert's systematically gathered cases which provided the early sentinel estimates of how devastating AIDS would become. The doubting Goedert ended up convincing others. Only some 50 cases then, the
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— Dr. James Curran, Centers for Disease Control in Atlanta

The patients who volunteered for either the Phase I trial that we conducted, or Phase II tests,” he says. Human tolerance of the drug was unknown. No one knew what to expect.

Phase I was for toxicity. Patients submitted to gradually increased doses until they showed toxic effects.

Next came Phase II, a double blind placebo trial involving 280 critically ill patients, half of whom would not know that they were getting sugar-coated pills.

The test was prematurely decoded in September 1986, seven months after the first doses were given, because “there was an unequivocal improvement in survival, a strong difference in death rate,” Broder says.

In fact, there were 16 deaths among the 137 patients given the sugar pills, one death among the 145 receiving AZT. Also the AZT patients showed clear clinical improvement.

By January 1987, an advisory body of the Food and Drug Administration recommended that AZT be prescribed under certain conditions.

“I don’t think you’re going to find another drug that’s been developed that fast,” Broder says. So fast that researchers are using it before they know everything about it.

There is a strong positive attitude at NCI and among AIDS researchers in general, Broder says. When he was given an assignment in drug development, there were no guidelines. He asked his chief what his instructions were. ‘Basically your instructions are

SEE AIDS, 18A

Dr. William Haseltine in his Boston office with a collection of vials and bottles which mark advances his lab has made in AIDS research

enough so it can be farmed out to labs elsewhere. We think that a few years from now, the chemical candidates range from sea slug extract to film developer.

Meanwhile, he says, “modern biology is exploding all over the place.”

Before long there will be technology that could make available over-the-counter tests for the AIDS virus, using body fluids, perhaps saliva. Vaccines might be 10 years off, and because of the long latency period between infection and overt disease, it may take another five years to test for effectiveness.

The phone rings and Dr. Haseltine tells a colleague in Europe that has learned of the supporto evidence in a particular project. Urgent, certainly, but shortcuts cannot be tolerated.

If the sheer force of man-hours can do it, progress must be forthcoming. Take AZT, for instance, the one drug that has shown effectiveness against the AIDS virus.

It can track the virus down even to the central nervous system where it is known to reside. It has serious side effects, decreasing the body’s ability to manufacture red and white blood cells, a condition reversible when the dosage is withdrawn or modified.

What is unknown is how long it is effective, but AZT is the best bet yet and it was simply plucked off the shelf.

Broder of NIH helped shepherd AZT from test tube to treatment in record time, less than two years.

“The public has to be realistic,” he cautions. “We do not have a cure.”

We think we have drugs that can fool the virus and prevent it from replicating by causing it to accept a false building block. That’s what we think AZT does. When the virus accepts the false building block, it has no mechanism available to repair its mistake.”

AZT had been kept in stock by Burroughs Wellcome, a pharmaceutical firm, because of the drug’s activity against a mouse retrovirus and possible uses in veterinary medicine. Since AIDS was a retrovirus, it seemed worth a try.

Broder’s team showed it worked against the AIDS virus in the test tube in February 1985. The first human got the drug five months later.

“The real heroes of the AZT story are
AIDS
CONTINUED FROM 17A

to cure it," he was told.
The cross-pollination of ideas continues. Dr. Robert Gallo's NCI lab is a virtual United Nations. Researchers from 17 countries have contributed to work with him. He is now on the road almost constantly, sharing his research insights into retroviruses with other scientists.

Retroviruses, as a human threat, have turned biology upside down. Most human viruses are based on RNA, which precedes DNA, the genetic material that is the same genetic material as the human cell. But retroviruses are based on RNA, which precedes DNA, and this is what causes human leukemia. They are cousins to HTLV-3, the AIDS virus.

Carran first saw Gallo a few years back in 1981, when the puzzle was fresh. He and Gallo were the featured speakers at a session trying to bring loose ends of the mystery together. The program ran late and Carran, out of town, was invited to speak first.

He remembers directing his talk to Gallo and saying, "There's another virus out there. Why don't you get to work on this?"

Gallo remembers that as he listened to Carran's outline of what was then known about AIDS, its behavior in the population, "I was already in agreement with him on the infection and propagation and growth of the AIDS virus. HTLV-3. In 1984. Now he wonders if other yet-unknown viruses have been found in the brains of some cancer patients. The circumstance of AIDS may unlock new doors, new understanding of cancer and that to me was exciting.

Looking back, Gallo and other researchers wipe their collective brow and imagine what might have been. If AIDS had struck in the 1960s before the basic information on retroviruses was known. 'We'd have been helpless,' he says.

Some wonder if a helpless society, reacting to fear, would have built vast quarantine camps in the wilderness to contain the disease.

The fear was palpable. Gallo remembers the "unresting fear" and "people putting their hands in AIDS materials every day." One technician on his staff was cut in the lab as a result of his pregnancy, although he urged her to quit. He was not ungrateful. "We needed her.

Today there is a hand-penned sign on his computer that reads "Danger" and he keeps a sign there by his secretaries: "No gloves at all in this office," a reminder to researchers to remove lab coats and take "on safe protective lab gloves in the lab or in the halls."

Absent-minded perhaps, preoccupied certainly. "The thing that's different about AIDS is the continued intensity," says Carran.

In the past six years, parts of personal lives were swept away. Carran, 36 in 1981, with a new baby girl, became a commuter to New York. In the first year and a half of her life he made 46 trips to New York, he can't remember where he was that first Christmas.

Sam Broder has a wife and two teenage daughters. He is rarely home before 8 p.m. He finds the travel to remote parts of the world as difficult as the long hours. "At least if I'm home, something happened, I could go home. If I'm away, I'm away."

Time lost from the family is truly lost. "The last five years of my life have been gratifying at one level. But there is no question about the number of things that have been taken away that can't be retrieved." That's one thing I advise people just getting into research, to consciously recognize in advance, they can't have it both ways. They can never redeem something they've given up.

Bob Gallo has tried to dissuade friends from scheduling a tribute to him on his 50th birthday, three weeks hence.

A research technician at Abbott Laboratories inspects a batch of biochemically treated beads used in the test to screen blood for AIDS.

The virus is like a Stealth bomber. It has learned to elude the radar of the immunological process. We are trying to find chinks in its armor. We are making a systematic study of the whole virus, looking for clutches in its surface.

— Dr. William Haseltine, Drug Discovery Group for NIH

There is too much yet to do, he says. Try me at 79.

When Bill Haseltine takes time out at his lab, it's because something good has happened, a discovery of some sort. They uncork a bottle of inexpensive California champagne and drink a toast, the half-dozzen of them. Then they dutifully date the bottle and note down the day and put the bottle on the top shelf in Haseltine's office where some 45 bottles already reside. Then they go back to work.

Bob Gallo smiles at this ritual, but it's not for him. "Champagne gives me headache," he says.