The Case of the Florida Dentist

Cutting-edge molecular biology and unpublished scientific papers will feature in a trial to determine whether a dentist tansmitted the AIDS virus to his patient

SOUTHERN FLORIDA IS RAPIDLY GETTING A reputation for sensational court cases. Last month, the West Palm Beach rape trial of William Kennedy Smith captivated the country's attention. In March, the scientific community will want to keep a keen eye on a courthouse just 30 miles away in Stuart, Florida, where a trial is scheduled to start that should produce some fireworks—and perhaps set some precedents in the complex relationship between science and the law.

The case involves Richard Driskill, a 31-year-old citrus worker who was a patient of dentist David Acer. Driskill claims Acer infected him with HIV. So did Kimberly Bergalis, who became a national figure when she testified before Congress last year shortly before she died of AIDS. So does Barbara Webb, who is still alive but has AIDS. The Centers for Disease Control (CDC) in Atlanta says the evidence "strongly suggests" that these three became infected with HIV while receiving dental care from Acer, and all three have received $1 million settlements from Acer's malpractice carrier. Webb and Bergalis received additional settlements from CIGNA Dental Health of Florida, the dental care program that provided Acer's services.

BARRY C. ALLEN

In the middle. *Judge Robert Makemson ordered one research paper turned over to the other side.*

But CIGNA has balked at settling with Driskill, who is asking for $15 million in damages. Why won't CIGNA pony up? Because, say lawyers for the defendant, there is reasonable doubt about whether Driskill got the virus from his dentist. Not only could his lifestyle have made him vulnerable to infection from other sources, they claim, but the CDC has not conclusively established that the virus that infected Acer and Driskill can be distinguished from others in south Florida. So Driskill is taking his claims to a jury.

In a few weeks, if schedules hold, the Florida courtroom will become the scene of a debate more appropriate to the corridors at a scientific meeting than the halls of justice. It is developing into an ever-more-bizarre episode of biology in the public arena—one that touches on such sensitive issues as scientific publication, ethical use of data, and more.

Lawyers for both sides will present a jury with conflicting results from the cutting edge of research on the molecular evolution of viruses to buttress their arguments over the central issue of the case—whether the viruses isolated from Acer and Driskill are the same. Relevant to their case will be two research papers that apparently reach different conclusions on the relatedness of the two viruses. Lawyers in the case have said that both papers have been submitted—coincidentally—to *Science* for publication. And to make things more complicated, even as these papers were undergoing review, the judge in the case, Robert R. Makemson, circuit judge for Martin County, ruled that the paper written by experts for the defense team must be turned over to Driskill's lawyers and to the two scientists whose work they criticize. The judge ordered the paper sealed pending decisions to publish or not to publish by *Science*. And, in yet another twist, one of the papers uses data developed by the authors of the other paper. How did they get it? By using the Freedom of Information Act—a practice that raises the worst fears of government scientists who worry that the FOIA, as it is called, could be used by a competitor to dig out their data before they had had a chance to publish.

One of the lawyers, Driskill attorney David Eaton of Montgomery & Larmoyeux in Florida, puts it very simply: "[This trial] will be a wild one."

The case of dentist David Acer made headlines around the country in the summer of 1990, when the CDC published an article in its publication *Morbidity and Mortality Weekly Report (MMWR)* (27 July 1990, p. 489). It described how a young woman, later identified as Kimberly Bergalis, had become infected with HIV without being sexually active, and with no history of blood transfusions, intravenous drug use, acupuncture, tattoos, or artificial insemination. The only suspicious event in her background was the fact that she had had two molars extracted by Acer, who 3 months earlier had been diagnosed with AIDS.

To determine whether Acer's virus was the same strain of HIV as the one infecting Bergalis, CDC scientists isolated the virus from both and, using the polymerase chain reaction (PCR), amplified portions of the genetic sequence that codes for the outer coat of the virus. They then determined the nucleotide sequences of the isolated regions, and, in collaboration with Gerald Myers at Los Alamos National Laboratory, performed a statistical analysis on the sequences to determine how related they were. Although the viral sequences from Acer and Bergalis could be distinguished from each other, the CDC concluded that they were closer than any two other isolates of HIV ever seen in North America. This striking similarity and the absence of other epidemiological risk factors for Bergalis prompted the CDC to conclude that there was a very real possibility that the dentist had infected his patient.

It was the first time the CDC had determined that a health care worker appeared to have infected a patient with HIV, and there is still no good explanation for how the transmission took place. But there was more to come.

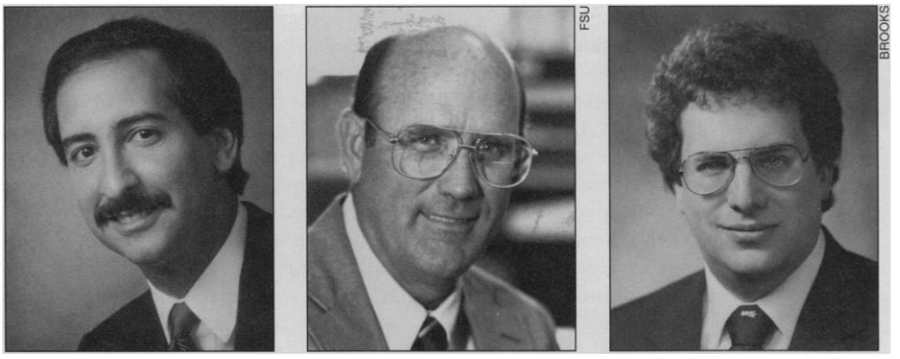
At the end of August 1990, just days before he died, Acer wrote to all the patients in his practice, informing them he had AIDS. Nearly 600 came forward to be tested for HIV, and two tested positive. One was an elderly woman named Barbara Webb, who, like Bergalis, had no risk factors for AIDS. The second was a male who reported "multiple heterosexual partners and a history of

non-IV drug use, including one hospitalization for toxicity" according to a second *MMWR* report (18 January 1991, p. 21). He was subsequently identified as Richard Driskill. In a third *MMWR* article (14 June 1991, p. 377), the CDC modified its description of Driskill, saying his additional risk factors were unproven.

The CDC, with the help of Myers, performed a molecular analysis of the viruses isolated from Acer and his infected patients. This time, the CDC included eight control viruses, isolated from other HIV-positive individuals in the area around Acer's practice who had not been patients of Acer. In the third *MMWR* report, the number of control viruses rose to 31. The viruses infecting Bergalis, Webb, Driskill, and Acer were all very similar to one another, and quite different from the control viruses.

After the second *MMWR* report came out, the lawsuits began flying. Although CIGNA settled with Webb and Bergalis, the company argued that Driskill's alleged sexual habits and history of drug use opened the possibility that he had contracted the virus from someone other than his dentist.

There seems to be plenty of scope for legal wrangling around the scientific data (see box). Even James Curran, head of the HIV/AIDS program at the CDC points out that it cannot be proved definitively that Acer transmitted the virus to his patients. "Our conclusion is that [the viruses] are the same," says Curran, but the CDC isn't saying with certainty who transmitted what to whom. "The only common denominator is that they all



Defense experts. *Lionel Resnick, Lawrence Abele, and Stanley Weiss* (left to right) *challenged the CDC's analysis of the scientific evidence.*

Trying to Pin Down an Ever-Changing Virus

A key question in the court battle between Richard Driskill and CIGNA Dental Health of Florida is whether the virus that infected dentist David Acer is the same as the one that infected Driskill. While they obviously belong to the same class of virus, HIV, the issue of "sameness" is not all that clear cut.

The reason is that HIV has a tendency to change slightly each time it replicates. So even if you were able to compare the entire genetic sequence of a virus isolated at two different times from the same infected individual, the two sequences would not be identical even though the viruses were clearly the same. For example, it took years to be certain that the first two AIDS isolates that were sequenced—HTLV-III and LAV—were really the same virus even after the sequences were published.

As a practical matter, it's not an easy job to do a complete sequence on all 9500 base pairs that make up HIV, so in doing comparisons, researchers such as Gerald Myers of Los Alamos National Laboratory have focused on small segments of the viral genome that they amplify using the polymerase chain reaction technique. In particular, researchers have focused on a viral gene called *env*, especially a region of the *env* gene known as V3 that is highly susceptible to mutations. The variability of V3 is part of the reason that HIV is so hard for the immune system to defeat: V3 is a crucially important region for immune recognition.

When Myers assisted the Centers for Disease Control (CDC) in analyzing the virus obtained from Acer and his patients, he focused on a 300-base pair region spanning V3, and another 350-base pair stretch that encompasses two other variable regions called V4 and V5 and a constant region, C3. In the 18 January 1991 issue of *Morbidity and Mortality Weekly Report (MMWR)*, Myers and the CDC concluded that the sequences in the V3 region were closely related, with an average difference of only 3.4%. In the V4-C3-V5 region, the viruses differed by only 1.8%. In both cases these regions were more closely related to each other than they were to other viral strains that Myers has stored in an extensive sequence database at Los Alamos.

But Jay Levy, a virologist at the University of California at San Francisco, says there are potential problems with this type of analysis. "If there's great similarity [in the variable regions], then you would assume that the viruses are related," he says. But, he adds, "you're assuming that since it is a variable region, that variations will automatically occur there. That may be incorrect. Some people would say you'd do better looking at a stable region because, if there's a difference, you know they're *not* related." (Because he has a paper under review, Myers declined to be interviewed.) Steve O'Brien, an evolutionary biologist at the National Cancer Institute, agrees with Levy that there are some unproven assumptions in making predictions about how similar two viruses are. "There is no accepted criterion to make those kinds of decisions," he says. Instead, the best scientists can do at the moment is increase the likelihood that they are making a correct prediction of "sameness." Scientists will have more confidence in their predictions only when they have a better understanding of the frequency and type of mutations that are passed on from one viral generation to the next—the type of question that researchers in molecular evolution have been trying to answer for the past 25 years. O'Brien adds that it's not a matter of showing that Acer's virus has unique features that are shared by viruses infecting some of his patients. "You also need to demonstrate the absence of those sequences in the geographic locale," he says. "I'm not sure that we can unless you are extremely vigorous" in collecting samples of HIV from the surrounding population.

Ultimately, O'Brien believes it will be important for AIDS researchers to gain a better understanding of HIV variation. Not only will that information help resolve the legal dilemmas like the one in the dentist's case, but it should also say something about how and when a latent HIV infection becomes pathogenic and causes AIDS. "These questions can be solved using the principles of molecular evolution and phylogenetic evolution," he says. "I'm convinced of it. The dentist is a very exciting case from an intellectual point of view, and it is going to tell us a lot." ■ **J.P.**

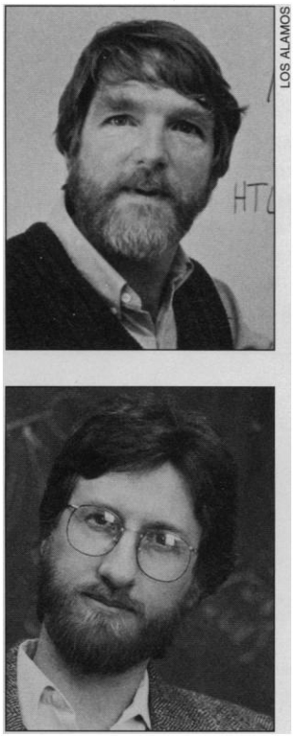
went to the same dentist," says Curran.

CIGNA's lawyers, in addition to checking out Driskill's sexual habits, hired scientists who could help them poke holes in the CDC's analysis of the case. One of these scientists was Stanley H. Weiss, director of the Division of Infectious Disease Epidemiology at the New Jersey Medical School. Weiss, who has written extensively on acquiring the virus in a medical setting, argues that the CDC was not absolutely thorough in collecting physical evidence—such as a gynecological exam to assess the possibility of sexually transmitted diseases—in its initial analysis of the Bergalis infection, and that it did not perform enough control comparisons to be sure that the viruses found in Acer and his patients weren't otherwise found in south Florida. "The CDC is using a new, innovative research technique, and its practical application requires an enormous amount of control data to know...the proper way to apply it," says Weiss.

Weiss gets some support on this from an independent source, Steve O'Brien, who studies molecular evolution at the National Cancer Institute. O'Brien agrees that researchers have a lot of work to do before they can resolve all the scientific issues in determining how closely two viruses are related. "I'm not saying it's beyond resolution, I'm just saying it's likely to be controversial, and there's likely to be some differences of opinions," he says.

Weiss adds that from what's been published so far, it's not really possible to evaluate just how the CDC reached its conclusions. "The amount of data that has been provided publicly by the CDC in the *MMWR* reports is very limited. So if someone wanted to interpret that information for themselves, I think they'd want access to much more information."

That, apparently, is how Lionel Resnick felt. Resnick, chief of retrovirology laboratories at Mount Sinai Hospital in Miami, was also hired by CIGNA to challenge the CDC's molecular analysis. He recruited Lawrence G. Abele, dean of arts and sciences at Florida State University, whose research focuses on molecular evolution, to help him with the project. (Abele is not a paid consultant to CIGNA.) Using data from the CDC and Myers, obtained through the FOIA, they prepared their own molecular analysis. Both Resnick and Abele declined to be interviewed for this article, but Driskill's lawyer, Eaton, says Resnick stated in pretrial depositions that he and Abele used the data obtained from the CDC to prepare a paper criticizing the procedures the CDC used in drawing its conclusions. They then submitted the paper to *Science* for publication. At nearly the same time, the CDC, along with Myers and James Mullins of Stanford University, also submitted an article to *Science*, expanding and elaborating on the work presented in the earlier *MMWR* reports, which relied on the data obtained by Resnick and Abele.* (No author from either paper would agree to be interviewed for this story.)



A match? *Gerald Myers* (top) *and James Mullins found striking similarities in the viruses.*

Eaton, Driskill's lawyer, complains that while it may have been legal for the researchers to use the FOIA to obtain the CDC's data, they behaved unethically. "If you take someone else's work, and you don't ask permission to use it, that's wrong." However, Barbara Mishkin, an attorney for the Washington firm of Hogan and Hartson and an expert on scientific ethics—who is not involved with this case—says that data gathered by government scientists is fair game, "especially when it forms the basis for public policy."

Now, even before the normal process of reviewing can be carried out, these papers have become objects of intense interest in the court case. On 9 January, Judge Makemson ordered Resnick to hand over to Driskill's lawyers copies of the paper criticizing the CDC's work. But he also took the unusual step of sealing the document—ordering that it not be released to the public at large—because CIGNA's lawyers argued that it would interfere with *Science*'s normal publication procedures. CIGNA would obviously like to have *Science*'s stamp of approval on the article before the case goes to trial, but John Hamilton of the Miami law firm of Wicker, Smith *et al.*, who is representing the company, says it's not essential. "The fact that something is accepted by a scientific publication is not evidence," he says. "The opinion of the expert is what is accepted by the court, not the article."

But Eaton looks at it very differently. "I would like the [Resnick and Abele] paper to be published because it would be so severely criticized," he claims. The court has not yet ordered the CDC to hand over its paper to CIGNA's lawyers. In fact, Driskill's lawyers claim they haven't even seen the CDC paper, since neither the CDC scientists nor Myers or Mullins are working for Driskill's legal team. But Eaton says he is anxious to get his hands on the paper, and intends to subpoena the CDC, *Science*, and anyone else he can think of to get hold of a copy. He adds that it is "critical" to get the CDC paper into the open scientific literature because it will be an important factor in arguing his case.

These scientific details will dominate the trial, but there's another explosive issue that will be hovering in the background: whether this case suggests that health care workers should be tested for infection with HIV. Driskill's complaint alleges that Acer, knowing he had AIDS and could transmit it to his patients, nevertheless decided to "gamble that he could continue the practice of dentistry for profit." On the basis of past experience, however, it was not a big gamble: While there have been several documented cases in which HIV has been transmitted from patients to health care workers—for example, through needle sticks—until this episode came to light, there had been no known cases of transmission in the other direction. Despite impassioned pleas from Acer's patients, especially Kimberly Bergalis in a moving appearance before a House committee last fall, the CDC has declined to recommend mandatory testing for health care workers.

As of now, the trial is set to start on 30 March, and both sides expect to be busy arguing over the admissibility of evidence between now and then. With $15 million at stake, the debate over the fine points of molecular evolution takes on added importance. Then there are the complications created by potential unprecedented uses of the scientific publishing process. And finally, a jury of nonscientists will be confronted with complex molecular arguments, and a judge will have to reconcile reasonable access to scientific data with the integrity of the publication process. All in the setting of one of the most emotional of current public debates: whether there is sufficient reason to take dramatic steps to protect the public against health practitioners with AIDS. Fireworks are likely. Says lawyer Eaton: it will be "Sex, lies and videotape." But that's only the beginning. ■ JOSEPH PALCA

*Monte Basgall, a spokesman for *Science*, has acknowledged in press interviews that a paper on which Resnick is a co-author has been sent out for review. He would not comment on the CDC paper. *Science*'s News Department has not seen either paper.