they were promising. Like several other experimental AIDS vaccines, the Chiron vaccine is based on a recombinant version of the HIV envelope protein. The envelope protein is combined with an emulsifying oil and an adjuvant, a system Chiron researchers believe can greatly increase the immune-stimulating capacity of the vaccine.

"Alarm bells started going off. . . . I was worried about reporting research that hadn't gone through peer review."

—Bruce Little

This combination has been injected into 25 healthy volunteers at the Geneva University Hospital. The goal of phase I trials is largely to evaluate safety, and none of the 25 showed ill effects. Dino Dina, director of virology at Chiron, explained to Rowan that all of the volunteers who received high doses of vaccine produced antibodies against HIV, and all of them, whether they received high or low doses, showed some cellular immunity.

There is little disagreement that Chiron had a strong motivation for wanting to influence public opinion in Canada. Rowan said he assumes the information was provided to him as part of Chiron's effort to win "the hearts and minds of Investment Canada." No one at Chiron told him so directly, he says, but he adds that "the timing suggests it."

Larry Kurtz, Chiron's director of public relations, acknowledged to *Science* that the results were provided for a purpose. "Of course we were trying to convince the Canadian government of our technological merit," he says, but adds that the results of the AIDS vaccine trial had already been discussed with Investment Canada directly. According to Kurtz, Rowan was selected because he had recently done other reporting on Chiron.

Discussions with the *Globe* reporter were kept general so as not to jeopardize journal publication, Kurtz says, adding that a paper summarizing the results on the 25 volunteers has been submitted to a "leading medical journal." Earlier results were presented by Dina at scientific meetings, and Chiron wouldn't have given Rowan the results if they had been "completely out of the blue," Kurtz says.

Rowan believed that with caveats about the data's being unpublished, an accurate and interesting story could be written. "Being a technology writer," he told *Science*, "it was too exciting a story to pass by." On 6 December he wrote a story describing the preliminary results.

The next day Bruce Little, managing editor of the *Globe*'s "Report on Business" section, sat down to read Rowan's story. "Alarm bells started going off," Little says. He adds that "my concern was that these people had a huge axe to grind with Canada, and I was worried about reporting research that hadn't gone through peer review." Little decided not to publish Rowan's article and the story never appeared.

On 13 December Investment Canada announced that both the beefed-up Merieux bid and the CIBA-Geigy–Chiron bid were acceptable to the Canadian government on the grounds of net benefit to the country, and the final decision was left up to the shareholders of Connaught.

Not surprisingly, Connaught's shareholders had already decided (pending government approval) to accept the higher bid, that from Merieux, which amounts to a total of $942 million. As a result, Connaught will now pass into the hands of the Institut Merieux, creating perhaps the world's largest vaccine maker.

But while the corporate questions seem to have been resolved for the moment, some significant scientific issues remain—notably that of the appropriate use of the results of scientific research. Pons and Fleischmann were roundly criticized for offering cold fusion data to the press before it had been reviewed by scientific peers. But in that case the leading question seems to have been scientific priority (although the financial gains from cold fusion, should it prove workable, could not have been far behind).

In the Connaught episode the worldly issues were right on the surface—in the form of public opinion, a decision by a government agency, choices made by stockholders, and the fate of a major corporation. As science and commerce become increasingly intertwined, particularly in biotechnology, such issues will probably crop up with greater frequency. And, since there are no clear guidelines or institutional mechanisms for handling unpublished data, they will not be easy to resolve cleanly.

■ **DOUGLAS POWELL**

Douglas Powell is a science writer based in Toronto.

Maine Case Deals Blow to DNA Fingerprinting

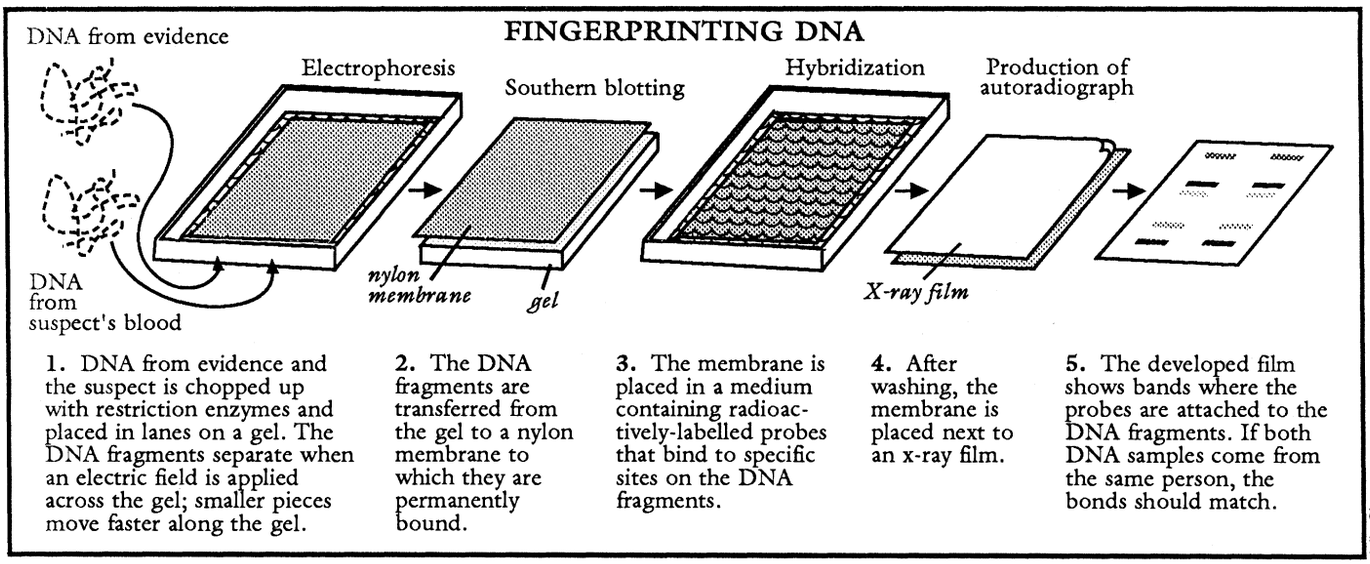
DNA evidence was withdrawn after the defense challenged the validity of a method to correct the data

A FEW HOURS after a 5-year-old girl was sexually assaulted behind a school in South Portland, Maine, the police had identified a prime suspect. Not only did he match a description given by the victim and two older girls who had been with her, but he admitted that he had been in the area at the time. Moreover, he had tissues in his pockets similar to one left at the scene of the crime that had apparently been used to wipe semen from the girl's leg. Case closed?

Not quite. To nail down the suspect's culpability, the police sent the semen-stained tissue and a blood sample from the suspect, referred to as David G., to Lifecodes Inc. in Valhalla, New York, for DNA typing. Three months later, on 18 August 1988, the results came back: David G.'s DNA did *not* match that of the semen on the tissue. He was not the assailant, Lifecodes concluded.

On its face, this criminal investigation provides a dramatic demonstration of the power of DNA fingerprinting—in this case, possibly saving an innocent man from jail. But what happened next has put the technology in a much less flattering light; indeed, it could cause difficulties for prosecutors in future cases when the DNA data are not crystal clear.

The very day the negative results were reported for David G., the South Portland police got a warrant to draw blood from a second suspect, a man named Kenneth McLeod. McLeod had a history of charges involving child molestation, and he had been living in Portland at the time the assault took place. But McLeod is short and fat and the victim and her friends described the assailant as tall and thin. He may not have looked the part, but, on 17 November 1988, Lifecodes reported that McLeod's DNA matched that of the semen sample.



The case against McLeod then moved inexorably toward a trial—until last week, when it was stopped dead in its tracks. After 5 days of testimony at a pretrial hearing to determine whether the DNA data could be admitted in court, the prosecution withdrew the Lifecodes evidence and subsequently dropped the charges against McLeod.

This extraordinary turn of events came after McLeod's lawyer, Gene R. Libby, had exposed a problem with the way the company had tried to correct for a phenomenon known as bandshifting that, according to one expert, arises in perhaps 30% of DNA fingerprinting cases. In addition, the prosecution's own expert witness, Calvin Vary of Idexx Corporation in Portland, advised the prosecutor, deputy district attorney Laurence Gardner, that he would be unable to testify in support of a key piece of evidence because it was "uninterpretable."

During cross examination of Michael Baird, director of forensic testing at Lifecodes, and Lisa Bennett, the scientist who conducted the tests, Libby also uncovered some irregularities in the way the data were handled. For example, an autoradiograph was mislabeled and an independent check was not done to confirm the result of one probe. Says Joseph Nadeau, a geneticist at Jackson Laboratory who was serving as an expert witness for the defense: "The whole experiment wasn't done with the kind of rigor you would expect."

This is the second time in recent months that DNA fingerprinting evidence presented by Lifecodes has been rebuffed in the courtroom. In a widely publicized murder trial in the Bronx, New York, a judge refused to allow DNA evidence indicating that a blood spot on the watch of the defendant, Joseph Castro, came from the victim (*Science*, 2 June, p. 1033). The data and Lifecodes' procedures had been thoroughly picked apart by expert witnesses in a pretrial hearing. (Castro nevertheless later pleaded guilty as part of a plea bargain.)

"One would have thought. . .that after. . . *People v. Castro*, Lifecodes would have taken to heart the lessons learned there," Gardner, the prosecuting attorney, wrote in a stinging letter to John K. Winkler, Lifecodes' senior vice president, on 15 December. But, because of the problems that subsequently came to light in the McLeod case, Gardner wrote, "the use of DNA identity testing in criminal trials throughout the country has been further undermined."

In virtually every case in which DNA evidence has been challenged, including the Castro case, judges have ruled that the theory behind DNA fingerprinting is scientifically well established and that the technology can produce evidence that is admissible in court. The practice has, however, occasionally been found wanting.

The theory is straightforward. Chop up a person's DNA with a restriction enzyme, and you get millions of DNA fragments of varying sizes. Restriction enzymes cut DNA only at specific sequences of base pairs, but because in each individual these sequences occur in different places along the DNA, the pattern of fragments generated provides markers that allow you to discriminate between individuals.

First, sort the fragments according to their size by electrophoresis—smaller pieces migrate further along the electrophoresis gel than larger ones—then transfer the DNA from the gel to a solid membrane (see diagram). The pattern of the fragments can be revealed by washing the membrane with a radioactively labeled probe that binds to a specific sequence of bases in the DNA. Depending on where the restriction enzyme cuts the DNA, that sequence may be part of a large fragment from one person's DNA and a small fragment from another's. To see where the probe attached, simply place the membrane next to an x-ray film. The developed film, called an autoradiograph, shows a pattern of bands that corresponds to the fragments carrying the probe. A second autoradiograph can be generated by chemically removing the first probe and using another that binds to a different sequence of bases. To determine whether two DNA samples came from the same person, compare autoradiographs.

It sounds straightforward, but it involves precise measurements of fragment sizes and it can be a tricky process to get right—especially when one of the DNA samples is limited in quantity and quality.

Lifecodes reported that four different probes produced bands from McLeod's DNA that are identical to those from the DNA in the semen sample. The odds of this occurring by chance are 13.5 million to 1, the company said.

But there was one problem: The bands did not line up. The pattern was the same, but it was displaced in one direction, like badly hung wallpaper. On its face, this indicated that the fragments lit up by the probes in McLeod's DNA were all slightly larger than the equivalent fragments in the DNA from the semen.

Lifecodes' explanation was that the DNA from the semen sample ran faster along the gel than McLeod's DNA, causing a problem known as bandshift. Researchers have long known that bandshifting can occur, and they have recognized that one way to check for it is to use a probe that attaches to a fragment of DNA that is the same in every person. These so-called monomorphic probes generate bands that should always be in the same

place. If they are displaced, bandshifting has occurred.

Lifecodes demonstrated this in the McLeod case with a probe that attaches to a constant fragment on the X chromosome. Then it went one step further. From the displacement, it calculated that the size of the fragments in the semen sample should all be corrected by 3.15% to account for the bandshifting. Once this was done, the differences between the bands from the semen and those from McLeod's DNA all fell within the threshold required to declare a match. The conclusion: The two DNA samples came from the same person.

Armed with that evidence, the prosecution went into a hearing before Judge Kermit Lipez on 5 December to determine whether the DNA data could be used in McLeod's trial. It was the first such procedure in Maine involving DNA typing.

The most devastating cross examination came on Friday, 8 December. The issue: Is a single monomorphic probe sufficient to calculate the degree of bandshifting, and can one correction factor be applied to all the fragments from one sample?

Baird, of Lifecodes, testified that the 3.15% correction for bandshifting could have been determined from any monomorphic probe, and he stated that all the bands should be adjusted by the same percentage. Libby, the defense attorney, then presented a sheet from Lifecodes' own documents that cast doubt on these assertions. Lifecodes had in fact used a second monomorphic probe, one that attaches to a constant fragment on the Y chromosome, along with the monomorphic X probe. The sheet Libby produced contained a calculation that Baird himself had made showing that this Y probe gave a bandshift of 1.72%, not the 3.15% derived from the X probe. If the smaller percentage were used as a constant correction, two out of nine bands would differ by more than the threshold required to declare a match. Lifecodes had not included this document in the evidence it presented.

Confronted with his own calculations, Baird reversed his earlier testimony. He said that there may not be a constant correction factor because the bandshifting appeared to vary throughout the gel. In that case, different correction factors may be required for different sized particles.

"In actuality," said Baird, "if you want to apply the monomorphic probe with more exactness, you would apply the number you generate for the size range you are looking at." Asked why he used just the correction derived from the X probe, Baird said he considered it gave the appropriate correction for the range he was looking at.

Baird was unavailable for an interview with *Science*, but Lifecodes spokesperson Karen Wexler says the company "does not use the Y probe to document bandshifts, but to give a yes or no answer on whether the DNA is from a male." (Females do not have a Y chromosome, so the probe would not bind to female DNA.) The position of the Y band in the McLeod case was determined in "a routine sizing, but it was difficult to see where the bands were," Wexler said.

Gardner, the prosecutor, met the next day with his independent scientific expert, Calvin Vary, and got another bit of bad news. Vary said he could not testify in support of the bandshift correction claimed by Lifecodes. Well before the hearing began, Vary had been shown the autoradiograph with the monomorphic X and Y probes on the semen sample and he told Lifecodes it was "uninterpretable." Vary told *Science* that there was too much background interference to measure the bands precisely. He asked Lifecodes to repeat the test using just the monomorphic X probe, and Lifecodes had done this, producing what Vary describes as a clean autoradiograph that "quantifiably shows the shift" at about 3%. It emerged during the hearing, however, that Lifecodes had not conducted an independent sizing of the bands on that autoradiograph, so it was useless as evidence.

"The right place to address these questions is in scientific journals rather than in courtrooms."

—Eric Lander

Gardner, who said in an interview that he was never told by Lifecodes that there may be different bandshifts in different regions of the gel, had no alternative but to pull the evidence. "They should have alerted me that there was a different way of looking at it," he says. Gardner also says it is inexplicable that Lifecodes failed to measure the bandshift when it repeated the experiment Vary called for. Had this been done, "it would have made the case," Gardner claimed. Libby shoots back: "That still doesn't do anything to the bottom line here. Lifecodes selected one [correction factor] that supported their data and discarded the other one."

Because there was no ruling on the admissibility of the evidence, the case will have no legal precedent, but it could make it hard for prosecutors to argue future cases in which bandshifting occurs. Baird testified that bandshifting is sometimes seen when DNA is been degraded, which happened in the McLeod case. Daniel Garner, the head of forensic testing at Cellmark—Lifecodes' chief commercial competitor—says contaminants and even the amount of DNA being tested have also been found to alter the rate at which DNA runs in a gel.

There seems to be general agreement that when bandshifting does occur, the displacement may indeed vary throughout the gel. George Sensabaugh, a forensics expert at the University of California at Berkeley, says that based on limited experience in his lab, "there is a rubber band effect—[bandshifting] that occurs to different degrees for high molecular weight fragments compared to low molecular weight fragments."

The implication is that several different correction factors may be required for the same gel when bandshifting occurs. Indeed, Lifecodes, Cellmark, and the Federal Bureau of Investigation (FBI) are all working on systems involving several monomorphic probes that would pick up fragments that range in size and would therefore provide a check on bandshifting throughout the gel. In the meantime, Bruce Budowle, an expert on DNA typing at the FBI, says that if bandshifting pushes the bands outside the limit required to declare a match, there are really only two alternatives: Declare that the samples don't match or that the evidence is inconclusive.

To some observers, Lifecodes' attempt to correct bandshifting in the McLeod case represents the premature introduction of the technique into a forensic case. "There's little scientific literature on the nature of bandshifting—even on such fundamental points as whether the shifts are constant or nonconstant," says Eric Lander, an expert on DNA typing at the Whitehead Institute. "The right place to address these questions is in scientific journals rather than in courtrooms. This is an extremely powerful technology, but there has got to be a better way to ensure that it is used properly."

That's where the National Academy of Sciences comes in. Responding to questions raised by the Castro case in New York, the academy this week appointed a committee to draw up guidelines for DNA fingerprinting. Chaired by Johns Hopkins University geneticist Victor McKusick, it is expected to report by the end of 1990.

In the McLeod case, the technology worked perfectly in excluding the first suspect, David G. All three expert witnesses who reviewed the data told *Science* that the evidence excluding David G. was conclusive. But the case also suggests that basic scientific research is still required on some aspects of DNA fingerprinting technology.

■ **COLIN NORMAN**