DNA TAKES THE STAND

Legal and ethical issues abound as the weight of the evidence shrinks to billionths of a gram

By RICK WEISS

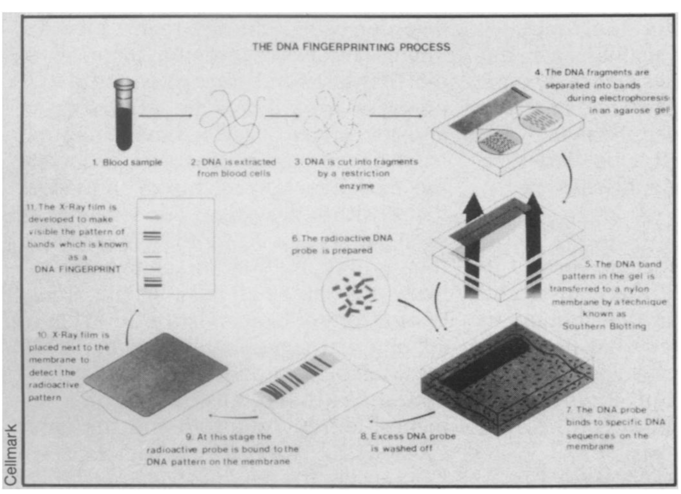
There are plenty of tests one must pass before becoming an agent for the Federal Bureau of Investigation. Starting in June of last year, though, the bureau asked its new agents to submit to just one more exam – a voluntary blood test. Each acquiescing agent received a free T-shirt emblazoned with the motto: "DNA: You leave it, we cleave it."

The blood tests were part of the FBI's fledgling effort to develop a database describing the frequency with which certain genes exist in the U.S. population. The in-house survey represented a crucial step in the bureau's four-year effort to move into the field of forensic DNA testing – an effort that culminated this past March when the agency's DNA laboratory released its first official test results and provided testimony leading to the conviction of a rapist on the Hawaiian island of Maui.

Entry of the nation's premier law enforcement agency into the still-nascent field of DNA testing represents a giant step forward for both the bureau and the science, according to criminologists and molecular biologists. The tests, popularly known as DNA fingerprints, have played a role in approximately 100 criminal cases in the United States. But a recent survey of state and local crime laboratories indicates that thousands of criminal cases per year could benefit from the application of the DNA tests. With unprecedented accuracy, the tests can identify criminals – and exonerate the innocent – by comparing the DNA sequences of crime-scene specimens with those in blood or tissue samples from the accused.

Despite the enthusiasm generated by these tests, however, the jury is still out on the extent to which they should be applied or trusted as legal evidence. Indeed, DNA testing strikes at the heart of some of the most fundamental controversies facing the nation today, including public doubts about the accuracy of scientific testing in general and uncertainty about how the Fourth Amendment's protection against unwarranted search and seizure applies to body fluids and tissue samples.

Recently, experts in the fields of law enforcement, jurisprudence, molecular biology and civil rights gathered at the congressional Office of Technology Assessment (OTA) in Washington, D.C., to sort out the issues surrounding forensic DNA testing. Months will pass and at least one more meeting will be held before the OTA summarizes its volumes of testimony for members of Congress. However, both law enforcement officials and scientists at the meeting cautioned against moving too quickly into the relatively uncharted – and unregulated – field.



Even a tiny drop of blood or the root of a hair provides enough genetic material for forensic analysis. Increasingly, U.S. courts are accepting analyses of DNA from crime-scene specimens as evidence in criminal trials.

The stakes get high when molecular biology comes out of the laboratory and into the courtroom, says Lisa Forman of Germantown, Md.-based Cellmark Diagnostics, one of three major for-profit players in the U.S. forensic DNA field. "We have some very serious issues based on a bunch of bands on a film," Forman says.

The bands Forman describes are charcoal-colored markings on a cellulose gel. This autoradiogram, or "autorad," marks the final result of a procedure in which minute strands of DNA, typically taken from samples of blood, semen or hair, are cleaved, sorted by size and visualized with radioactive, genetic probes. By comparing the specimen's pattern of bands with the pattern from a known source, scientists can determine whether the two are identical.

DNA tests examine highly variable regions of chromosomes – regions so variable they almost totally rule out two people sharing the same exact molecular sequence. When scientists examine and compare several such regions, the chances of coincidental identity can become less than one in several billion, or essentially zero, geneticists assert.

But how many chromosomal regions must laboratories compare before scientists, judges and juries can rest assured that chance alone has not produced the final result? "This is a quiz made out of questions . . . and each question has a certain probability of saying 'match' or 'no match,' " says Eric S. Lander of the Whitehead Institute for Biomedical Research in Cambridge, Mass. "It's like a twenty questions game but you get to choose how many questions you want to ask."

So far, scientists propose using anywhere from three to 12 chromosomal sites. But they have yet to reach consensus on an ideal number, in part because they lack sufficient data about the frequency of various genes in the population as a whole. That's why the FBI – and many other research teams – have been gathering blood specimens from large numbers of people, including members of various racial groups. Racial data can be crucial, Lander notes, because a gene that appears in 1 percent of the population overall may, for instance, appear in 10 percent of 10 percent of the population.

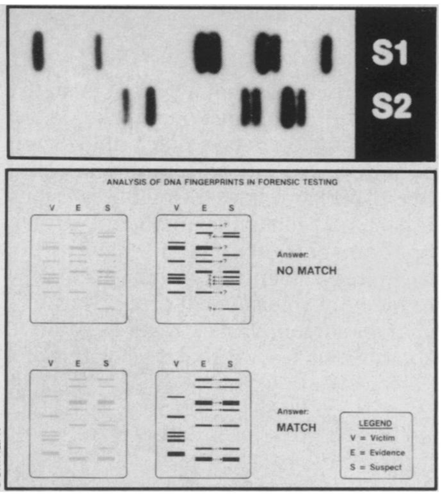
Related to this issue are questions about exactly which genetic loci DNA testing should include. Some chromosomal regions provide more information than others and can be probed more easily. But beyond these technical and statistical factors lie more sensitive considerations, OTA panelists note. For example, although such behavioral associations remain unproven, many researchers see links emerging between certain genes and some criminal behaviors. Should genes that researchers have tentatively associated with psychological or behavioral abnormalities be specifically avoided when tests are being performed for identification purposes?

The use of putative psychological markers, such as those for violent behaviors, in identity testing would be very controversial, says C. Thomas Caskey of the Baylor College of Medicine's Institute for Molecular Genetics and chairman of the OTA panel. Nevertheless, as scientists identify behavior-associated genes, prosecutors may exert pressure to include them in the forensic regimen.

"I don't think many people realize how important character trait is in the criminal law context," says Armando Garcia, a Redwood City, Calif., attorney and OTA adviser. "Most of the time the issue is not 'whodunit' but 'what was the mental state of the actor?' That's basically the difference between murder and manslaughter cases." Garcia and others express concern that unless judges carefully circumscribe the rules for admissibility of DNA evidence for identification purposes, less reliable, behaviorally related genetic evidence may soon creep into criminal prosecutions.

Even if law enforcement officials limit their use of DNA testing to questions of identity, there remain concerns about the technology's potential impact on the civil rights of the accused. For example, what degree of probable cause must law enforcement officials demonstrate before a judge can order DNA blood tests on an unwilling suspect? And can officials use blood specimens previously collected for other purposes—such as for a medical exam—if they later suspect an individual of committing a crime?

Some states already have begun saving DNA test results from convicted sex offenders so that semen samples from future rape cases can be easily cross-matched against DNA records. In some respects, officials say, this is hardly different from keeping "mug book" or fingerprint records of previously convicted



Cellmark

Top: Two nonidentical DNA "fingerprints" appear on an autorad. Each fingerprint consists of a series of bands. Bands help researchers visualize fragments of a DNA specimen that has been cleaved into several pieces with specific enzymes. Those on the left have migrated farthest along a charged gel from the source at right, and thus represent the smallest fragments. Bottom diagram depicts simplified forensic DNA analysis.

burglars or murderers. Already, nongenetic files yield a "great return" in terms of their ability to help nab repeat offenders, notes James J. Kearney of the FBI Laboratory in Quantico, Va. But at what point does using a DNA profile obtained from a person's blood become an invasion of privacy and an unjustified, blanket search of someone for whom there is no particular evidence of criminal activity?

George B. Trubow of the John Marshall Law School in Chicago notes that there's already a trend toward increasing use of institutional databases for storing personal information about U.S. citizens. Next, he and others say, some hospitals may want to run routine DNA profiles on all newborns and store that information in a digitized format. Such a system would allay, for example, growing concerns about nurses inadvertently switching and misidentifying infants in hospital nurseries. Ultimately the DNA-based numbers could serve as a national identity system, much as social security numbers now do.

There's a "nagging beauty" to such a system, Trubow says — beautiful for its simplicity, nagging for its abuse potential. But some people are more than nagged. They say storing such records in centralized databases might tempt police to perform wholesale computerized searches for the owner of a hair, blood or semen specimen left at the scene of a crime. Such a widespread search without some evidence linking the individuals in question to the scene of the crime may well represent a violation of constitutional guarantees of due process and privacy, civil libertarians say. "You don't just set up a database because it sounds like a good idea," warns Janlori Goldman of the American Civil Liberties Union in Washington, D.C.

Robert E. Stevenson of the American Type Culture Collection in Rockville, Md., a database-oriented institution whose primary function is to maintain and catalog immense numbers of preserved microbial specimens, notes another problem with computer databases: They are easily scanned and retrieved by individuals or agencies who gain access to the computer systems, making confidentiality difficult to maintain. "The question is who should control the database," Stevenson says. "There is a history of hanky-panky with databases."

Fears about large-scale consolidation and abuse of DNA data appear a bit premature, if for no other reason than the lack of agreement among researchers and law enforcement agencies regarding standardized methods for DNA testing and information storage. Each of the major U.S. forensic DNA laboratories using enzyme techniques (Cellmark, the FBI Laboratory and Lifecodes in Valhalla, N.Y.) uses different enzymes to cut DNA into different-sized pieces and has custom-matched probes to identify those pieces. In addition, Cetus Corp. in Emeryville, Calif., has developed an entirely different method, the polymerase chain reaction, to obtain DNA profiles from even smaller specimens than those used in enzyme-based methods.

In part, these differences persist because each lab remains wary that others may take advantage of proprietary technology. But that may be rectified once the technology becomes more widespread. "Nothing is routine yet," says Cellmark's Forman. "It's all too new."

So far, methods of quality control remain similarly unstandardized — a fact that worries some of the technology's critics. As with many new technologies, the greatest risk of reaching an incorrect conclusion stems not from any inherent fault with the methods themselves but from undetected human error.

Preliminary quality-control surveys have already revealed some serious errors in DNA labs, which would probably have resulted in unjustified acquittals and convictions, researchers concede. "I know in my lab we screw up," says Lander of the Whitehead Institute. "Load the same [specimen] in both lanes and you get identity."

There also remains the question of who, if anyone, ought to regulate or oversee the emerging science. The FBI is developing quality-control guidelines that may eventually become widely adopted, says John W. Hicks of the FBI's laboratory division in Washington, D.C. But ultimately, he adds, the bureau would prefer to decentralize the monitoring of forensic DNA laboratories – much as the National Institutes of Health delegates many of its oversight responsibilities to Institutional Biosafety Committees at individual universities and research centers.

Issues of accuracy and regulation may prove particularly contentious because a single DNA test often consumes all of an available sample. Researchers disagree about the importance of this detail. If scientists perform the test accurately the first time, they note, then the autorad, unlike many other types of tests, remains as a permanent record and is available for corroborative inspection by any number of experts. In a sense, says Caskey, "you've not used up the DNA; you've immortalized it." Others, however, express frustration that the tests cannot be run from scratch a second time.

The quality-control debate touches upon questions of computer correction as well as human error. In basic research laboratories, scientists routinely use computer algorithms to "clean up" autorad records by digitally compensating for slightly variable migration rates in different parts of the gel. But when a slightly altered autorad might mean the difference between life imprisonment and walking free, these corrective techniques stir intense controversy. Some say that revealing the use of such techniques during a trial may inspire a jury – rightly or wrongly – to mistrust the data as a whole.

Indeed, one of the biggest unknowns in the debate about DNA forensics is just how big an impact the high-tech evidence will have on juries. Experience to date suggests that most people are easily swayed by the apparently incontrovertible – and not easily understood – nature of DNA evidence.

"With a [standard] fingerprint you can put it up on the wall, you can blow it up, follow the ridges – great, it matches," says Douglas P. Rutnick, an Albany, N.Y., public defender. However, he says, an average juror looking at an autorad doesn't know what it is. "I've looked at it, and I couldn't understand it for beans."

Ultimately, Rutnick suggests, it may be lawyers who have the most difficulty adjusting to this newest kind of evidence. Even Perry Mason might fail to see the flaws in a molecular biologist's testimony that restriction enzymes, polymorphisms and gel electrophoresis indicate a defendant's guilt.

"How do you cross examine [such a witness]?" asks Rutnick. "What do you do?"

He shakes his head.

"What you get is deadly. But I couldn't read [the autorad]. I couldn't at all." □

Continued from p.73

likely toss.

Rivier believes that a system in statistical equilibrium must obey a rule called the Aboav-Weaire law, which applies not only to froths but also to crystals and cells. This law relates the number of sides of each polygon to the number of sides of its nearest neighbors. Glazier likens the law to the tendency of electrical charges to hide or "shield" each other: Negative charges surround an extraneous positive charge in such a way that the positive one eludes detection from a distance. In a soap froth, the number of sides greater or fewer than six would correspond to a bubble's charge. For example, a seven-sided bubble is like a +1, while a four-sided one is like a −2. The Aboav-Weaire law, then, predicts the way in which few-sided bubbles will congregate around many-sided ones, and vice versa.

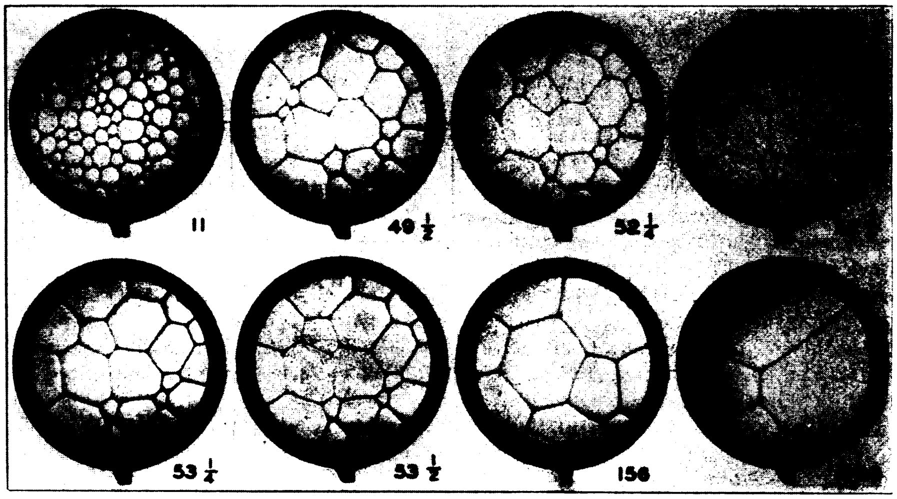
Rivier thinks statistical equilibrium implies that the system also follows another rule, called Lewis' law, which predicts that the area enclosed within an individual two-dimensional bubble grows in a linear relation to the bubble's number of sides. F.T. Lewis formulated this law in 1928 while studying the skin of a cucumber. It seems to hold for biological cells but not as well for soap froths. Glazier observed that many-sided bubbles roughly follow Lewis' law, while fewer-sided ones deviate from it. Rivier says the deviation may stem from subtle differences between the physical properties of an actual network of bubbles and the theoretical ideal – just as real gases stray from ideal gas laws.

In his journal paper, Glazier highlights several ways in which froths stray from theoretical ideals. He says the real system contradicts the long-held assumption that all sides of the bubbles in a froth join in 120° vertices. Bubbles tend to bend their edges to accommodate the mechanically favored 120° joining angle, but according to Glazier, they don't always achieve that goal. He notes that earlier calculations, including Von Neumann's law, rest on the 120° angle assumption – but the bubbles don't seem to notice, violating the angle and following Von Neumann's law all the same.

Such bubble puzzles haven't kept researchers from grasping froth evolution well enough to simulate it on computers. Glazier is now working with Gary S. Grest of Exxon Research and Engineering in Clinton, N.J., to create computer froths that become disordered in much the same way as real ones. In the simulations, individual picture elements, or "pixels," on the borders between bubbles switch their allegiances to neighboring bubbles according to programmed-in physical laws. To an untrained eye, the computer froths appear indistinguishable from the real ones.

Natural froths, of course, come in a more complicated three-dimensional network. Nonetheless, Glazier says the two-dimensional rules may extend to the three-dimensional world, noting that cross sections of 3-D froths look like the squashed 2-D ones.

Real froths can be useful, too. Petroleum engineers use them to force oil from the ground, while brewers strive to achieve the perfect beer foam. Indeed, Glazier says the U.S. government has shown interest in using them for the unfrothy purpose of making hydrogen bombs. Yet the beauty of froth patterns alone would seem sufficient to entice scientists to investigate their filmy, ephemeral world. □



Cyril Stanley Smith's original froth photos show how flattened bubbles grow and disappear over a period of 225 minutes.

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