

suggesting the need for looser standards.

Other groups say the panel contains the opposite bias and ignores researchers who believe the LNT model is too restrictive. A nonprofit called Radiation, Science, and Health Inc., which insists low doses are harmless, claims that panelist Geoffery Howe, a Columbia University epidemiologist, has “obfuscat[ed] data so as to support the LNT.” Bridge the Gap, meanwhile, finds fault for a different reason, claiming Howe advocates “the premise that low doses of radiation are substantially less harmful than officially presumed.” Howe told *Science* he considers the LNT model “a reasonable assumption not proven.”

NRC hopes to announce any revisions to the panel within a few weeks, Douple says. But that may not quell the fire: If the NRC makes “minor cosmetic changes that do not alter the imbalance of the panel,” Hirsch says, his group may file a lawsuit under the Federal Advisory Committee Act. Revisions to the act in 1997 opened panel memberships to public debate in the first place.

—JOCELYN KAISER

MATHEMATICS

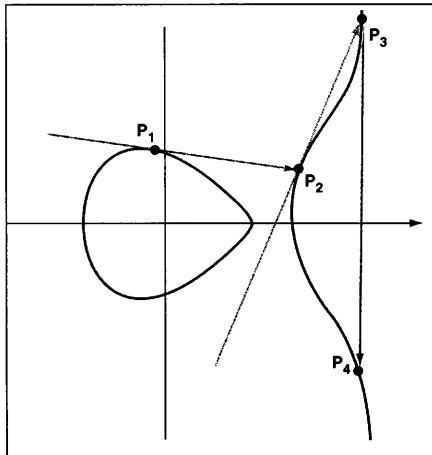
Fermat's Last Theorem Extended

Five years ago, the proof of Fermat's Last Theorem by Andrew Wiles of Princeton University hit the mathematical world like an earthquake, rearranging the landscape and leaving previously unassailable peaks on the verge of collapse. This month, an aftershock has finally leveled the most prominent of these, a 40-year-old unsolved problem called the Taniyama-Shimura conjecture. While it lacks the colorful history of Fermat's 350-year-old unsolved puzzle, this conjecture applies to a vastly broader class of problems.

“Before Wiles came along, nobody even knew how to begin proving the conjecture. Afterwards, there was a widespread belief that it was just a matter of time,” says Brian Conrad of Harvard University, who collaborated on completing the solution with Christophe Breuil of the Université de Paris-Sud, Fred Diamond of Rutgers University, and Richard Taylor of Harvard. “The Taniyama-Shimura conjecture is a wonderful, major conjecture,” comments number theorist Kenneth Ribet of the University of California, Berkeley.

The conjecture, which Wiles partially proved en route to Fermat, states that all elliptic curves are modular. A couple of definitions make the statement a trifle less gnomic. An elliptic curve is not an ellipse: It is the set of solutions to a cubic polynomial in two variables, usually written in the form $y^2 = x^3 + Ax^2 + Bx + C$. If x ranges over all real num-

bers, such equations indeed define curves—mildly wiggly ones that come in one or two pieces. However, number theorists are generally interested only in rational solutions—values of x and y that can be written as fractions. And an elliptic curve is modular if every rational solution can be found with the



Algebra from Geometry. One solution to an equation for an elliptic curve (P_1) can generate many: Just follow the tangents.

help of “modular functions,” a very high-tech version of periodic functions familiar from geometry, like sine and cosine.

In 1955, a young Japanese mathematician named Yutaka Taniyama first suggested using such modular functions to describe all rational points on an elliptic curve. Taniyama, who committed suicide at age 31, never got a chance to work seriously on his problem. However, his contemporary Goro Shimura, now at Princeton University, took this geometric approach to the problem further, strengthening the conjecture into its present form in the early 1960s.

To explain how geometry can be used to solve algebraic problems, Conrad cites the oldest problem in number theory: finding Pythagorean triples. These are sets of three integers such that the square of one is the sum of the squares of the other two: for example, $3^2 + 4^2 = 5^2$. This equation can be rewritten as $(3/5)^2 + (4/5)^2 = 1$. In this way, Pythagorean triples correspond to rational points, such as $(3/5, 4/5)$, on the circle whose equation is $x^2 + y^2 = 1$. And Conrad notes that there's a simple geometric technique for finding all the solutions. First pick one solution—say $(1, 0)$ —and draw any line through that point whose slope is a rational number. That line intersects the circle in a second point, the coordinates of which will be another rational solution.

A similar idea works for elliptic curves. Given one rational solution, called a “generator,” you can get another by drawing a tangent to the curve at that point and looking for its other intersection with the curve. By repeat-

ing this procedure (and a variation of it) over and over, you can get lots of solutions—but only if you have one to start with. Sometimes, no such “generator” exists. In other cases, no single generator can produce all the rational solutions. The current record-holder is a curve that requires at least 23 of them. At present, modular functions offer the only hope for predicting the number of generators.

Indeed, number theorists have proven quite a few results about modular elliptic curves, including how to tell if they have only one generator. But until now, they didn't know which elliptic curves would turn out to be modular. Wiles, in effect, found modular traces for many elliptic curves. Now, Breuil, Conrad, Diamond, and Taylor have proved that such modular functions exist for all the rest.

“It is very aesthetically pleasing that now the full conjecture has been proved, rather than just ‘most’ of it,” says Berkeley mathematician Hendrik Lenstra. “It is just as with stamp collecting ... having a complete collection is infinitely more pleasing than having all but one.” Lenstra and other mathematicians note, however, that they have not yet been able to judge the correctness of the proof, which so far has been presented only in public lectures. “I hope a complete draft will be ready by the end of the summer,” Conrad says.

—DANA MACKENZIE

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GENETIC TESTING

Beryllium Screening Raises Ethical Issues

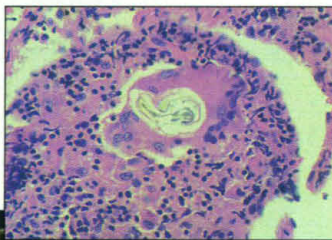
Analytical chemist Reed Durham finds himself at the cutting edge of an ethical debate over research on genetic risks in the workplace—but not as an investigator. Instead, Durham has become a significant data point in an effort to understand why a small percentage of people exposed to the metal beryllium—element number four on the periodic table—develop an incurable and sometimes fatal lung disease. And he's not happy about being removed from his job after testing positive for a sensitivity to the metal that is believed to be caused by a genetic variation. “I have been excluded from anything that has to do with beryllium,” says Durham, who does not have the disease. “All the expertise that I've gained over the past 30 years working with these materials, I can't use any more.”

Durham spoke about his plight at a 24 June meeting outside Washington, D.C., on the ethical problems of conducting workplace health studies. His case illustrates the “troublesome aspects” of using a test without clear benefits to those taking it, one that not only produces lots of “wrong” answers but that also monitors a condition that cannot be

treated until symptoms appear, says Donna Cragle, director of epidemiological studies at the Oak Ridge (Tennessee) Institute for Science and Education. Cragle, who is helping the Department of Energy (DOE) build a registry of workers exposed to beryllium, says the value of a robust database must be weighed against the psychological impact of a positive test, the threat to an individual's health insurance, and the disruption at work.

Durham has spent his career in an area of the Y-12 plant at the Oak Ridge National Laboratory, where beryllium-containing nuclear weapons components are handled. Recently, he received word that a blood test for an immune reaction was positive, which fingers him as at greater risk for developing chronic beryllium disease (CBD), also known as berylliosis. As a consequence, Durham has been banned from certain areas of the factory where he might be exposed to beryllium, although the value of removing such workers is not clear.

He is just one of nearly 10,000 beryllium workers who have been screened by DOE, which sponsored the meeting. The practice is also in use at the Cleveland, Ohio-based Brush Wellman Co., which mines, refines, and sells beryllium for uses that range from electronics to golf clubs. Both organizations are using blood test results, offered on a voluntary basis, to warn employ-



Exposure. Workers handling beryllium ceramic wear respirators to reduce risk of developing granulomatous lung tissue (inset).

ees about their immunogenicity status and to keep "sensitives" away from high-exposure areas. And both are developing sophisticated new molecular assays—including potential genetic tests—to more reliably identify workers who may become ill. DOE researchers say this may be the first major attempt to screen for an employment risk based on genetic susceptibility.

The current screening program is based on a relatively straightforward blood test vali-

dated 7 years ago by researchers at the National Jewish Medical Research Center in Denver, Colorado, who demonstrated that lymphocytes from certain workers exposed to beryllium proliferated rapidly in the presence of beryllium salts. That indicated their immune systems had become "hypersensitized" to the metal and were attacking the lungs. Patients with full-blown CBD test positive on this assay, and recent studies have shown it is predictive as well: About 45% of the people with positive results also develop CBD.

These findings, plus health surveillance results based on the blood test, point to the disheartening conclusion that the rate of CBD among exposed workers, despite a decades-long effort to reduce ambient beryllium dust in the workplace, is "about the same as it was in the 1930s and 1940s," says Paul Wambach, an occupational medicine officer at DOE's office in Germantown, Maryland. The new research also turned up an alarming incidence of CBD among clerical staff and workers outside the beryllium work zones—raising the possibility that very small amounts of dust might trigger the disease process in "sensitives." As a result, DOE and Brush Wellman have expanded their screening programs and introduced new measures to reduce dust, including protective gear for those subject to greatest exposure.

Now researchers are seeking a genetic marker more predictive than the lymphocyte proliferation test. Babetta Marrone and colleagues at the Los Alamos National Laboratory in New Mexico have built upon work on the major histocompatibility complex gene to identify a rare allele and a pattern of homozygous inheritance of a common allele that appear to be strong predictors of disease risk. About 85% of CBD patients in a small study were positive for one of these markers, Marrone says, compared with only 16% of beryllium-exposed workers without CBD.

Genetic information like this may soon make possible more accurate predictions of which prospective employees would be harmed by exposure to beryllium. Officials at both DOE and Brush Wellman say that genetic tests are not being used in the work place today because they are not yet considered good enough predictors of health and because they have been denounced as discriminatory. Of course, the whole point of diagnostic testing is to discriminate. Reed Durham has learned that lesson firsthand, and his reaction suggests that the issue is likely to remain controversial. "I cannot recommend that anyone ever take that test," he says. "If they'd ask me again, I'd say no."

—ELIOT MARSHALL

ScienceScope

Tax Relief A move to give companies a permanent tax break for R&D investments is gaining momentum. Over the last decade, the White House and Congress have backed only temporary renewals of the \$2 billion-a-year R&D tax credit. But last month a congressional panel said the projected budget surplus makes it a good time to put the subsidy on firmer footing, and last week—just as the rebate expired—the White House changed its tune, endorsing legislation for a permanent credit.

Company officials claim the incentive may loosen up an extra \$40 billion for R&D by 2010. Congress could vote on the issue as early as next week.

Bone Tired The Kennewick Man drama seems set for a long engagement. Last week, the Interior Department announced that a scientific panel appointed in February has been unable to conclusively date the controversial remains. The government now must negotiate with five Native American tribes that lay claim to the remains for permission to destroy a bit of bone for radiocarbon tests.

Scientists believe Kennewick Man, found 3 years ago in the bank of Washington's Columbia River, could offer insights into the peopling of the Americas. After extensive legal wrangling, Interior set up a panel to decide whether the bones qualify as Native American—defined by the government as anyone in the United States before the Europeans (*Science*, 26 February, p. 1239).

Scientists earlier had got an age of 9300 years after carbon dating a finger fragment. But with only nondestructive testing now allowed, the Interior panel had to try to date organic matter in sediment adhering to the bones. They failed to find any scraps bearing carbon-14.

Even if tribes assent to a new test on the bones, a firm date won't settle the dispute: Assuming the remains are ancient, Interior must still try to figure out if Kennewick Man has any biological or cultural link to a modern tribe.

Meanwhile, scientists who have filed suit to gain access to the bones aren't optimistic about getting a look. Says plaintiff Robson Bonnicksen of Oregon State University in Corvallis: "This one's going to drag on a long time."

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Casting of Kennewick Man's skull.