reaction but simply wanted to move molecules inside a crystal and then examine them in their new configuration. In earlier work, other researchers had produced molecular movements with relatively long, single pulses of light. But because such movements take place on a time scale of femtoseconds (10^{-15} second), the workers were not able to examine the details of the motion their lasers induced.

So Nelson and his colleagues recognized that they would have to employ pulses not much longer than femtoseconds. But they also knew that single pulses that are too short can't be selective and will push molecules in several directions at once.

In the MIT/Bellcore work, the researchers exposed a crystal of the organic molecule perylene to a sequence of 75-femtosecond-long laser pulses, timed to 400-femtosecond intervals. That frequency matches the natural frequency of a particular vibration of the crystal in which pairs of molecules move together and apart. Pushing the molecules with a sequence of laser pulses is similar, Nelson says, to propelling a child on a swing by giving the swing a shove each time it reaches its bottom point. The technical difficulty in the experiment, he says, was controlling the laser to produce a dozen incredibly short pulses at precise intervals.

The sequence of pulses moved the perylene molecules less than 0.001 angstrom. That is not very far, Nelson admits, but it is a first step. Eventually, he believes, it will be possible to move molecules by more than 0.1 angstrom with this technique.

Such advances will require improvements in the control of femtosecond lasers as well as a better understanding of molecular dynamics, Rabitz says. The MIT/Bellcore group chose a system that was fairly easy to manipulate, he notes—a crystalline structure limits the types of motion a molecule can undergo. But to "make molecules dance to our tune" will require careful design of the laser input, he says. Chemists trying to use laser pulses to move molecules in precise ways face much the same problem as engineers planning a careful sequence of rocket firings to orient a space station properly, Rabitz says. But the molecular work is even harder because molecules are not rigid and they respond in a much more complicated way to outside pushes.

Still, Rabitz says, the recent development is an important first step. Nelson is more excited. "In the 1980s we saw a revolution in our ability to watch elementary chemical motion [with femtosecond lasers]," he says. "The 1990s will see a similar revolution in our ability to manipulate molecular motion, including motion that leads to chemical or structural change." ■ **ROBERT POOL**

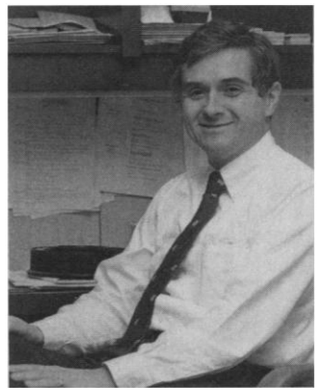
CF Screening Delayed for Awhile, Perhaps Forever

Efforts to develop a test to detect those who carry the cystic fibrosis gene have hit an unexpected roadblock

JUST AS THE MEDICAL COMMUNITY had begun planning for what promises to be the biggest genetic screening program to date—to detect people who carry the abnormal cystic fibrosis gene—new scientific evidence suggests that such a screening program may not be feasible after all, or at least not as quickly as anyone imagined.

The depressing news emerged last week as a panel of geneticists, physicians, genetic counselors, and lawyers met at the National Institutes of Health to craft guidelines to usher cystic fibrosis screening into routine medical practice. But they quickly hit an unexpected roadblock.

It turns out that the cystic fibrosis mutations are far more complex than anyone anticipated. Last summer, when Lap-Chee Tsui of the Hospital for Sick Children in Toronto and Francis Collins of the University of Michigan Medical School found the gene, they identified a simple mutation in it that causes most cases of the disease. About 75% of those who carry the abnormal gene have this particular mutation. The rest have other mutations in the same gene.



Foiled for now. *Arthur Beaudet and other geneticists hope their cystic fibrosis test problems are temporary.*

Almost as soon as the gene was cloned, a handful of biotechnology companies began offering a DNA test to detect this particular mutation. And a more accurate test seemed just around the corner, once the other mutations, expected to number about a dozen, were identified. In a collaborative effort coordinated by Tsui, nearly 70 labs around the world set out to find those mutations. They predicted they would have them—and thus a definitive test—within a year.

But optimism faded last week when Tsui reported that instead of a few common mutations, the investigators have so far turned up more than 20 rare ones. Together, they account for no more than a few percent of the remaining mutations. In fact, most are "private" mutations that occur in just one individual. "These findings bode ill," says Collins. He suspects that there are lots of ways "to mutate this gene to get cystic fibrosis. It is a big gene, and a big target for abnormalities."

Of course, all that could change tomorrow; someone could find one or two much more common mutations, says Arthur Beaudet, a geneticist at Baylor College of Medicine and cochair of the workshop. After all, the researchers have searched through only 10 or 20% of the gene's coding regions, mostly around the site where the first mutation was found. But he and the other assembled scientists agreed with Collins, who professed to a sinking feeling that "we could be here a long time"—and in the worst scenario, forever.

The biggest fear is that once 30, 40, or even hundreds of mutations have been found, 10 or 15% may still be unaccounted for, says Haig Kazazian, a geneticist at Johns Hopkins University School of Medicine who chaired the meeting along with Beaudet. And there is ample precedent for this scenario, Kazazian says: in many of the disorders linked to the X chromosome, including Duchenne muscular dystrophy and hemophilia A, "practically every unrelated person has a different mutation." If that is true for cystic fibrosis, then designing an accurate, cheap, and simple test, with today's technology, is a near impossibility, says Kazazian.

All of which makes the question of whether and when to implement widespread genetic screening even knottier than everyone already thought it was (see *Science*, 5 January, p. 17). The group agreed that for now widespread screening is premature, as the existing test would detect just 75% of the carriers, and thus only half of the couples at risk of having a child with cystic fibrosis. They recommended the test only for those with a family history of the disease.

And they agreed that when and if there is a test capable of detecting 95% of the carriers, it should be offered to everyone of reproductive age, perhaps 100 million people in the United States. Even then, they said, screening should only begin if a counseling program for education is in place.

But what happens if the test is never able to detect more than, say, 80 or 85% of the carriers? Should it be denied to the large number of couples who could nonetheless be helped? Hopkins geneticist Neil Holtzman, for one, is not so sure. Even now, with today's limited test, it is a tricky call, he says. "The problem with not screening with a 75% test is we miss the opportunity to reduce the disease in 50% of those affected." Cystic fibrosis is now the most common lethal genetic disease, affecting 1 in 2500 newborns.

Robert Williamson of St. Mary's Hospital Medical School in London agrees with Holtzman: "We have to learn how to deliver it to the 50 to 60% of the population who can benefit. I don't think we have a choice."

Others, like Michael Kaback, president-elect of the American Society of Human Genetics and chairman of the pediatrics department at the University of California, San Diego, Medical School, fear that screening with an imperfect test will do more harm than good, especially for those couples who receive inconclusive results. For now, if one partner is positive and one negative, there is no way to tell if the negative one actually does carry the disease gene, but with one of the as yet unidentified mutations. With today's test, 1 in 15 couples will be left in this genetic limbo, and Kaback suspects their anxiety will be tremendous and that some may even end up aborting healthy fetuses.

After grappling with the issue for a day and a half, the NIH panel reached no conclusion on what to do if trapped in this murky middle ground. Nevertheless, they managed to agree on some guidelines for population screening, if and when it comes about: that it should be voluntary and confidential; that it should be available to all who want it, though they advise against testing newborns and children; that informed consent be required; and that laboratory quality assurance begin immediately. They put the onus on health care providers to ensure that adequate education and counseling are available before they offer testing.

The group also recognized that the demand for testing is likely to continue to grow, even if a near perfect test can never be developed. Consequently, they called for pilot programs, to start right away, to determine how best to deliver a cystic fibrosis test and to measure just how much anxiety it produces. ■ LESLIE ROBERTS

Ozone Destruction Closer to Home

Researchers appear to have forged another link in the chain connecting man-made chlorofluorocarbons (CFCs) to losses of protective ozone over the populous mid-latitudes of the Northern Hemisphere. From Oslo to New Orleans, the ozone screen has thinned about 5% during the winter months of the past 10 years. The question: Is the ozone being destroyed by CFCs, in which case things could get worse, or are less sinister, natural variations behind the decline?

The finger of suspicion pointed to the CFCs a year ago when an airborne expedition probing the Arctic stratosphere found an abundance of ozone-destroying chlorine from CFCs (*Science*, 24 February 1989, p. 1007). But expedition researchers had their hands full showing that the chlorine was actually destroying the Arctic ozone. Now it may have finally been caught in the act.

The first direct evidence against CFCs as the culprit comes in a series of papers published in this month's *Geophysical Research Letters*, a special issue devoted to results from last year's expedition. As summarized in a prologue by atmospheric physicist Richard Turco of the University of California, Los Angeles, and others, the papers show that "the initial phases of a widespread ozone depletion apparently were observed."

The Arctic losses are a far cry from those seen every October in the Antarctic ozone hole, however. In the Antarctic, as much as half of all the stratosphere's ozone has been destroyed in some years, with the losses reaching more than 95% at some altitudes. Over the Arctic, total ozone destruction probably did not exceed a few percent and the hardest hit layers, those at and just above 20 kilometers, might have lost only 15 to 20% of their ozone.

Pinning down such small losses was not easy. For example, during the 39 days when the 1989 Airborne Arctic Stratospheric Expedition, as it is officially known, was collecting data, ozone concentrations within the 3000-kilometer-wide vortex of winds that swirl around the Arctic stratosphere actually increased below 20 kilometers as high-altitude, ozone-rich air sank into the vortex. So the challenge was to see whether the ozone increase was less than it should have been.

Participants in the Arctic expedition approached this problem by using the concentration of nitrous oxide, a relatively stable gas, as a benchmark against which to measure any loss of ozone. By determining the relative ozone and nitrous oxide concentrations, a multi-institutional group headed by atmospheric physicist Mark Schoeberl of NASA's Goddard Space Flight Center in Greenbelt, Maryland, found an ozone loss at around 20 kilometers of 15 ± 10% (95% confidence limits) during the expedition.

There was another detection of apparent ozone destruction, this one by a group headed by Edward Browell of NASA's Langley Research Center in Hampton, Virginia. Browell's group detected two patches of air that had up to 17% less ozone than the surrounding air. The nitrous oxide data again seemed to require chemical destruction of ozone. In addition, the altitude range of the patches, 17 to 23 kilometers, coincided with that of the polar stratospheric clouds. In the Antarctic ozone hole, these icy clouds catalyze the production of ozone-destroying chlorine. The coincidence of ozone loss and clouds in the Arctic implies the same may be happening there.

Despite this evidence, there are still doubters, but the link between CFCs and ozone loss was buttressed by calculations by three different groups of the amount of ozone that should have disappeared during the expedition, given the chemical state of the atmosphere at its start. Although the groups all used different modeling approaches, the results agreed "quite well with the limited observations of actual Arctic ozone variations," note the authors of the special issue's prologue.

Now that new evidence has been found that CFC-derived chlorine is destroying ozone within the Arctic vortex, the next step is to find out whether the Arctic vortex is exporting ozone-depleted air and ozone-destroying chlorine to the mid-latitudes. Such atmospheric transport could be behind the decreased wintertime ozone there. Making this connection will be particularly difficult, however, and politicians considering whether to decrease ozone destruction by further reductions of CFC emissions will probably have to settle for less than a perfect chain of cause and effect.

■ RICHARD A. KERR