

Panel backs widening net of genetic test

Cystic fibrosis is often considered a bellwether for genetic testing. Besides being traceable to a single gene, this relatively rare disorder is the most common lethal genetic disease in the United States. As more and more human genes are identified, the way genetic testing for cystic fibrosis plays out could determine how other tests are marketed.

Last week, a 15-member advisory panel convened by the National Institutes of Health recommended that DNA testing for cystic fibrosis be "offered as an option," although not promoted, to all couples expecting a child or planning to conceive one.

This marks the first time that the option of a DNA test has been recommended to individuals not already known to be at high risk of a genetic disease. Screening for carriers of the cystic fibrosis gene, or any disease gene, has generally been advised only for people from families with a history of the disease.

"This represents DNA testing coming of age," says medical geneticist Peter T. Rowley of the University of Rochester (N.Y.) School of Medicine.

The panel did not recommend widespread genetic testing for the disease in newborns or for carrier status in anyone except couples who are or may soon be pregnant because of the low overall risk of the disease. Moreover, recent NIH-sponsored studies indicate low public interest in general population screening.

About 25,000 people in the United States are affected to some degree by cystic fibrosis, with about 850 children newly diagnosed each year. There is no cure, although treatments have extended life for some into their thirties.

It's not clear how often screening will be offered to couples, since the advisory panel, chaired by pediatrician R. Rodney Howell of the University of Miami School of Medicine, does not carry the full clout of the federal government.

"Whether it's actually going to change practices much is hard to predict," says Norman Fost, a visiting professor of bioethics at Princeton University.

The panel, which based its recommendations on results from federally funded trials in which free screenings were offered to medical practices, said that insurance should cover the cost of testing. Laboratory costs—up to \$150, according to the panel—do not include the expense of obtaining informed consent. Any such discussion should include the risk of insurance or employer stigmatization that can accompany genetic testing, says Fost.

A key issue, he points out, is whether health insurance will cover the extensive education and counseling that the panel emphasizes should accompany the test. "Those resources are not available," he says. It could take several hours to

explain adequately the nature of the disease, the probability that a child will be born with it, the reliability of the test, reproductive options, and other issues. Howell says relatively few couples, 1 in 900, will test positive and require extensive counseling.

Even though cystic fibrosis stems from a single defective gene, the genetics and clinical outcomes of the disease are not simple. When researchers identified the gene (SN: 9/2/89, p. 149), which codes for a protein involved in the transport of sodium and chloride across cell membranes, a few mutations were thought to be responsible for the disease. But the gene is large, and as more families were examined, more mutations were found (SN: 7/28/90, p. 52).

Today, more than 600 mutations have been identified, some of them resulting in milder forms of the disease than others. Malfunctions of the transport protein lead to the buildup of mucus, especially in the lungs.

Material gives bacterial films the heave-ho

Daily brushing may get rid of plaque, that sticky bacterial film on teeth, but unfortunately for many people, the bacteria that build up on medical implants are not so easily displaced. In a new strategy against the potentially deadly infections that often develop around devices such as catheters, artificial heart valves, and replacement joints, scientists are devising materials that actively prevent bacteria from clinging.

James D. Bryers, codirector of the Center for Biofilm Engineering at Montana State University in Bozeman, described his group's work on such materials at a recent meeting in San Francisco of the American Chemical Society.

Doctors commonly try to thwart infections with high doses of antibiotics. The treatment works well against free-floating bacteria but is often useless against the thick films of bacteria on implants, Bryers says. The antibiotics "may kill the top ones, but they never penetrate down to the depths." Moreover, he has some evidence that the bacteria change genetically when they hit a surface, swapping genes for antibiotic resistance.

To target bacterial films, the researchers added the antibiotic ciprofloxacin to a plastic called polyether urethane (PEU), a staple of medical devices. The treated PEU releases a potent concentration of ciprofloxacin at its surface, killing bacteria that come in contact with it but not providing a high dose to the rest of the body. The problem is that dead cells pile up on the material.

A better strategy, Bryers says, would be to prevent the bacteria from sticking

The standard DNA test now available picks up 32 common mutations. Among people of northern European descent and Ashkenazi Jews, 1 in 29 has one copy of the mutated gene and one copy of the normal gene and thus is a carrier of cystic fibrosis. The odds are one in four that two carriers will have a child with some form of the disease, since the child would have to inherit a defective gene from both mother and father.

"One of the limitations is that the test doesn't pick up all carriers," says Rowley. It identifies about 90 percent of northern European carriers and is less sensitive in other populations, among whom the disease occurs less frequently. The test picks up 75 percent of carriers among African-Americans, 57 percent among Hispanics, and only 30 percent among Asian-Americans.

The American Society of Human Genetics still maintains its 1992 stance, that screening for carrier status be recommended only for people with a family history of the disease, according to Jane Salomon of the Bethesda, Md.-based organization. — C. Mlot

to PEU in the first place. "We'd like to stay away from the whole issue of killing and really orchestrate adhesion," he says. He and his colleagues synthesized a protein that binds to receptors on the bacterium *Staphylococcus aureus*, which often contaminates implants, and then loaded it into PEU.

As it leaches from the plastic, the protein blocks the bacterium's receptors, preventing them from binding tightly to the PEU. Not only did fewer bacterial cells adhere to this treated PEU, but those that did came off the material more readily than they did from the ciprofloxacin-treated PEU. In other words, fewer bacteria stayed to form a film.

Though effective against *Staphylococcus*, this strategy may not impede other bacteria, such as *Pseudomonas aeruginosa*, which is responsible for most urinary catheter infections. "*Pseudomonas* will be a difficult organism to fight in this way because it has so many different types of receptors," Bryers says.

Although PEU releases compounds continuously, materials could also be designed to respond to changes in acidity or other conditions in the body that accompany infection (SN: 9/7/96, p. 159). PEU can release antibiotics for up to a year, says Thomas A. Horbett of the University of Washington in Seattle, one of Bryers' colleagues.

The researchers would also like to engineer materials to promote adhesion of the body's own cells, Bryers says. That way, an implant would "take up residence in your body and not be treated as a foreign object." — C. Wu