New test developed for early detection of cystic fibrosis

The infant boy showed his first disease symptoms at six weeks of age: slowed growth, persistent diarrhea and labored breathing. But the symptoms came and went, and the child's parents and doctors chalked his illness up to a series of bad colds. By the time he was three years old, and finally diagnosed as having cystic fibrosis — the most common lethal genetic disease among whites — the little boy had tallied 26 visits to doctors and three costly hospitalizations.

"All the while, inappropriate therapy was performed and appropriate therapy was withheld," complains Keith Hammond, a researcher at the University of Colorado in Denver. Currently, 30 to 40 percent of the children born in the United States with cystic fibrosis (CF), which can masquerade as asthma, bronchitis or pneumonia, are not properly diagnosed in their first year of life. About 20 percent remain undiagnosed by age three. Doctors still don't know what specific genetic defect or defects cause the disease, which strikes 1 in every 2,000 children born in the United States, and are divided in their ideas about optimal treatment. But intuitively, Hammond says, most would agree that the earlier the correct diagnosis, the better the general health of the patient.

At the meeting of the American Association for Clinical Chemistry in Washington, D.C., last week, he described promising results from a two-year study of a fairly simple blood test that could help doctors detect the disease in the first few weeks after birth, before clinical symptoms surface.

"The test is not yet at a stage that it should be implemented in screening labs all over the country," Hammond told SCIENCE NEWS, and the Cystic Fibrosis Foundation, which funded Hammond's study, agrees. The idea of screening all newborns for a disease for which there is no known cure raises medical, ethical, psychological and economic questions that still need answers, they say. But, reports Hammond, the assay for the pancreatic enzyme trypsin has earned a strong midterm report card.

Trypsin is one of several digestive enzymes produced by the pancreas. In cystic fibrosis patients, the same thick mucus that clogs airways and eventually leads to fatal lung disease also plugs pancreatic ducts, obstructing the flow of enzymes to the intestine. The blocked trypsin "back-leaks" into the bloodstream, Hammond explains, where it can be detected by the "immunoreactive trypsin assay" or IRT. In IRT tests of 109,505 infants (virtually all the infants born in Colorado between the springs of 1982 and 1984), Hammond and colleagues detected 34 cases of cystic fibrosis.

The IRT test can be performed on the same small blood sample that most states now require for detecting the enzyme deficiency phenylketonuria, or PKU. A single positive IRT finding is not enough for reliable diagnosis of cystic fibrosis, Hammond says, but is an important first step in detection. When infants with a positive initial assay are tested again at four weeks of age, a second positive result is indicative of disease in about 80 percent of the cases. At that point, the children are given a confirmatory "sweat test," a quantitative measure of the high salt content characteristic of the perspiration of CF patients.

While the sweat test is much more accurate than the IRT when performed by experienced personnel, it is too expensive ($40 to $60 per test, compared to the IRT's 95 cents) to be used in mass screening, Hammond says. Currently the sweat test is performed only after symptoms arise, or when an infant has an older sibling with cystic fibrosis.

But does knowing that a healthy-looking baby will go on to develop disease improve the child's prognosis? It is too soon to be certain, but results from a preliminary study at the University of Wisconsin in Madison indicate a tentative yes, probably because nutritional supplements can be started at an earlier age.

Because of the loss of digestive enzymes, most untreated CF patients suffer some degree of malnutrition. Philip Farrell, Elaine Mischler and Wisconsin coworkers compared the growth rates of 36 one-year-old CF babies fed various diets. While most of the infants diagnosed late in their first year were stunted in weight and size, all 19 diagnosed before they were six months old and immediately placed on a diet of predigested formula had normal heights and weights at one year. Normal growth is important, Mischler says, to optimize the development of healthy lung tissue and a strong immune system.

A careful follow-up of Hammond's work to more specifically determine test reliability and to study the impact of neonatal screening on the parent-child bond needs to be done, says Mischler. Pending funding by the CF Foundation, the Wisconsin group hopes to begin just such a study next autumn. Early diagnosis won't prevent cystic fibrosis, she says, but it might ameliorate its severity. "Hopefully we'll look down the road and see a healthier bunch of kids in seven years," she says. *— D. Franklin*

Severe depression may last for years

Severe depression is, by and large, a recurrent — not a constant — illness. The approximately 10 million people in the United States who suffer from the disorder tend to alternate between valleys of despair and hopelessness and peaks of normal or near-normal mood. Scientists conducting a nationwide study now report, however, that about one-fifth of a group of patients who sought treatment at several university medical centers do not have periods of emotional calm; they remain severely depressed for at least two years despite being given antidepressant drugs or electroconvulsive therapy (ECT).

"There is a group of hardcore depressed patients who don't respond to standard treatments and don't have cyclical depressions who we're just beginning to understand," says project participant Gerald L. Klerman of Massachusetts General Hospital in Boston.

Klerman and colleagues from collaborating medical centers in Chicago, Iowa City, New York City and St. Louis followed a total of 97 severely depressed patients for two years. Twenty of them did not recover and remained severely, or for short periods moderately, depressed. The rate of recovery among the rest of the patients was highest in the first three months of the study. It dropped sharply after one year. Treatments for the hardcore group varied; half received high doses of antidepressants or ECT for at least two months, five were given low drug doses for six months and five received little or no medication.

Several factors predicted persistent depression, note the researchers in the Aug. 10 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION: a long period of depression before entering the study; being in a hospital at entry; low family income; a history of other psychiatric disorders, particularly alcoholism; and, surprisingly, an intact marriage. Contrary to some reports, persistent depression was not more common among older patients.

The study is limited by the lack of a control group, say the investigators. Depressed patients who do not seek treatment or who are seen by general practitioners may have less risk of being hardcore, they add.

But it is clear that not all depressions come in cycles, says study participant Philip W. Lavori of Massachusetts General Hospital. "The longer a depressed patient has been sick, the slighter is the probability of recovery," he notes. "The problem for the clinician is that it's difficult to identify in advance the patients who won't recover." *— B. Bower*