Mending a torn screen in the lung

Replacing a protective protein that stops potentially harmful enzymes may slow lung-tissue destruction in a hereditary disease associated with emphysema, suggest recent human trials at the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, Md. But researchers caution that deciding whether the replacement therapy would be clinically useful in large numbers of patients will require years of testing.

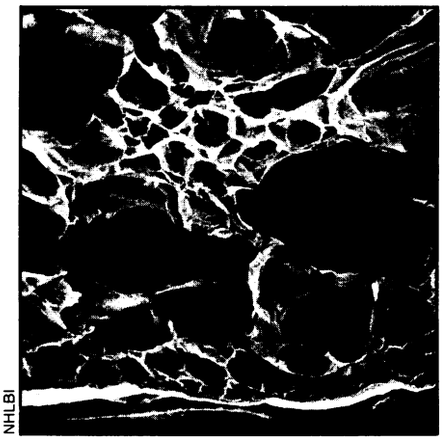
Destruction of the lung's alveoli (sacs in which oxygen and carbon dioxide are exchanged between blood and inhaled air) causes the shortness of breath characteristic of emphysema, which affects millions in the United States. Scientists believe an imbalance between enzymes called proteases and molecules that inhibit those proteases is responsible for the progressive breakdown of tissue, much of it due to the protease elastase. When there is a shortage of the liver-produced blood protein called alpha$_1$-antitrypsin, elastase is free to attack the connective tissue in alveolar walls. Although a healthy pair of lungs contains 300 million alveoli, once any are lost, they are gone forever.

Nearly all cases of emphysema can be linked directly to smoking, says Ronald G. Crystal, chief of NHLBI's pulmonary research, who described the latest findings at a briefing last week. But 2 percent – an estimated 20,000 to 40,000 patients – of the U.S. emphysema cases are people who have inherited from both parents the gene for alpha$_1$-antitrypsin deficiency.

Serum levels of the protein in patients with alpha$_1$-antitrypsin deficiency are as low as 10 to 15 percent of normal, thus exposing their lungs to abnormally high elastase activity; 85 percent of those with this deficiency eventually die from emphysema. "The obvious approach to therapy would be to reestablish that protective screen," says Crystal.

In the NHLBI study, described in the April 23 NEW ENGLAND JOURNAL OF MEDICINE, 21 patients were given alpha$_1$-antitrypsin commercially purified from pooled donor blood. (Researchers elsewhere are making synthetic forms of the protein for similar use.) Because the protein does not remain long in the body, weekly infusions are required.

Data prove the "biochemical efficacy" of the replacement treatment, with minimal side effects, says Crystal. In other words, infusion of the protein apparently maintains a patient's blood concentrations of the protein at near normal. Also, samples taken of lung fluid indicate that alpha$_1$-antitrypsin levels there are essentially normal, as well as the anti-elastase capacity of the protein found in the lung.



NHLBI

A scanning electron micrograph shows the destructive erosion of the lung's air sacs seen in emphysema patients.

This particular treatment, which would be a preventive measure rather than a cure, is limited to the hereditary disease, according to Crystal. Nevertheless, he says that learning about this relatively uncommon type of emphysema "charts the directions to research that has implications for the garden variety of the disease." *– D.D. Edwards*

Altered bacteria released

Last week, scientists sprayed bacteria designed to protect plants from frost on a strawberry field in northern California. It was the first authorized outdoor release of genetically altered bacteria in the United States. The experiment, conducted by Oakland-based Advanced Genetic Sciences, Inc. (AGS), took place after a California Superior Court judge refused to issue a preliminary injunction blocking the test at the request of environmental groups.

By splicing the genes in the bacterium *Pseudomonas syringae*, scientists at AGS and elsewhere had developed bacteria that retard ice crystal formation on plants. Plans to test the bacteria in field trials several years ago started a continuing controversy over the safety of such a release and where it should occur (SN: 1/25/86, p.56). The Environmental Protection Agency had fined AGS for injecting the bacteria into trees growing on a laboratory roof in 1985, but AGS's field-testing permit recently was reissued. Similar tests planned by the University of California at Berkeley have hit an equally rocky road to approval (SN: 6/7/86, p.366).

In Brentwood, where the test took place, the frost season is long gone, but scientists will study how the new bacterium survives "in the wild" – also a primary concern of a coalition of groups, led by the Foundation on Economic Trends in Washington, D.C., which has filed repeated suits and petitions to stop the test. □

Lead *in utero*: Low-level danger

Exposure to small amounts of lead before birth, even at levels considered safe for children, appears to slow important aspects of mental development in the first two years of life, according to a study described in the April 23 NEW ENGLAND JOURNAL OF MEDICINE. The project will follow lead-exposed children beyond 2 years of age to see if these effects persist, say David Bellinger of Children's Hospital in Boston and his colleagues.

In a previous study of 300 low-income families in inner-city Cincinnati, pregnant women exposed to low levels of lead had an increased chance of bearing children with low birthweight and somewhat slowed neurological development (SN: 9/13/86, p.164).

The Boston researchers studied 249 infants from middle- and upper-income families. They determined prenatal lead exposure by taking samples of umbilical-cord blood at birth. Children were divided into three groups: those with less than 3 micrograms of lead per deciliter in their blood, those with 6 to 7 micrograms per deciliter and those with 10 to 25 micrograms per deciliter. Blood lead levels higher than 25 micrograms per deciliter are deemed unacceptable for young children by the federal Centers for Disease Control.

For two years after birth, the babies were periodically given a standard mental development test that includes measures of simple problem-solving, perception, memory, learning and coordination. The group of children with the highest lead levels consistently had the poorest scores. By the age of 2, those with the highest exposure had a markedly lower average score on the development test than those in the other two groups. Infants with high lead levels still performed slightly above the population average.

Since only socially advantaged families were studied, the observed link between lead and mental development may be a conservative estimate, note the researchers. Lead's adverse effects can be amplified in an impoverished environment, they say, by factors such as poor nutrition.

Leading sources of lead exposure, say the researchers, are automobile exhaust and lead-based paints. They add that studies based on umbilical-cord blood samples indicate that more than one-fourth of the newborns in urban areas have lead levels of more than 10 micrograms per deciliter.

If their finding is repeated in further studies, the investigators say that the current federal standard for acceptable blood levels in young children should be lowered for fetuses. *– B. Bower*