Grains of salt explain cystic fibrosis

For decades, scientists have searched for a thread that could unravel the deadly mystery of cystic fibrosis, a genetic ailment that kills 1 in 2,400 whites and 1 in 17,000 blacks worldwide during what might have been the most productive years of their lives.

Now, researchers may have found just such a thread. Reporting in the April 19 CELL, investigators at the University of Iowa College of Medicine in Iowa City say that their work promises to clear up many stubborn questions about the disease—and that it may ultimately lead to newer, more effective treatments.

The investigators began their work by trying to answer perhaps the most perplexing question about cystic fibrosis: How does a genetic defect turn ordinarily sterile lungs into mucus-clogged breeding grounds for harmful bacteria? They knew that the defect in the *cftr* gene prevents the channel that normally carries chloride ions into cells from forming.

Although the research was remarkably complex—it used lung tissue grown in the laboratory from cells of people with cystic fibrosis and from cells of healthy people—the answer appears to be simple. Cells lining the inner surface of the lung produce a natural antibiotic that works only in a low-salt environment. In cystic fibrosis, the lack of a working chloride gateway results in airway surface fluid that is loaded with salt.

"It's a paradigm shift in our understanding of cystic fibrosis," asserts team member Jeffrey J. Smith. "Now that we have a clear understanding of what the problem is, we can begin asking how we fix the problem and come up with solutions that begin to make sense."

How the water-salt imbalance occurs is a matter of elementary biochemistry. Sodium and chloride, the two components of salt, travel in lockstep. When chloride is unable to enter lung cells, salt accumulates in the airway surface fluid. The natural antibiotic appears unable to combat infection in this brine.

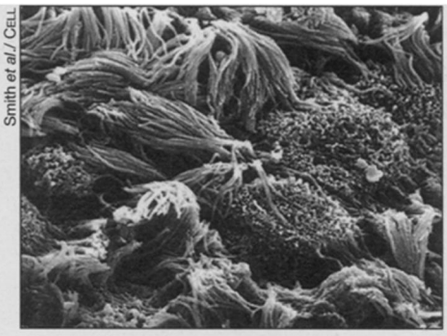
The Iowa researchers placed bacteria on the lung tissues grown in the lab. They found that normal tissue killed the bacteria and that cystic-fibrosis-afflicted tissue did not—until they reduced the amount of salt in the surface fluid.

"My reading of the paper is that this is pretty solid," says Jeffrey J. Wine of Stanford University. "The next thing they'll do is try to identify what the lung secretes that has this antibiotic property, isolate it, modify it so that it is not susceptible to salt, and then give it to people."

Smith agrees. "If we could correct the natural mechanism for killing bacteria, it would lessen the inflammatory process and ultimately lessen damage to the lung."

The action of the natural antibiotic is similar to that of compounds that have been found in insects, frog skin, cow lungs, and human intestines. In the lung fluid, it appears to be effective against several microorganisms and is hardy enough to withstand boiling for 10 minutes, Smith and his colleagues report. Using a synthetic version of the substance found in frogs, Magainin Pharmaceuticals of Plymouth Meeting, Pa., has already begun to make a natural antibiotic intended for the treatment of cystic fibrosis.

Smith plans to look in the human lung and perhaps further afield. "Could there be animals living in the sea that make natural antibiotics that aren't sensitive to salt?" he asks. —*S. Sternberg*



Smith et al./ CELL

Normal lung tissue remains infection-free 41 days after being painted with bacteria.

Family allergies? Keep nuts away from baby

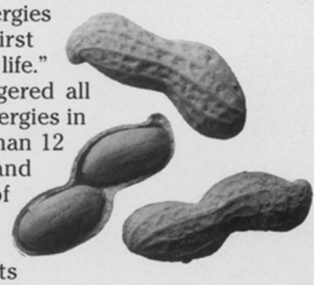
Allergies to nuts figure prominently in the growing number of potentially life-threatening sensitivities to foods. A study now suggests that much of the problem may stem from the recent trend of feeding peanut butter and other nutty foods to very young children.

What makes this practice particularly worrisome, notes Wesley Burks of Arkansas Children's Hospital in Little Rock, is that unlike most childhood food allergies—to milk, eggs, soy, or wheat, for example—allergies to peanuts (a legume) or to true nuts tend to persist into adulthood. Preventing these allergies in young children, therefore, may safeguard susceptible individuals from a lifetime of reactions.

In attempting to understand how and why these especially persistent sensitivities develop, Pamela W. Ewan of the Medical Research Council Centre in Cambridge, England, studied the backgrounds and allergies of all 62 nut-sensitive patients, age 11 months to 53 years, referred to her over a year.

Peanuts proved the commonest cause of nut allergy, occurring in 76 percent of the patients, Ewan reports in the April 27 BRITISH MEDICAL JOURNAL. Brazil nuts, at 30 percent, provoked the second largest number of cases, followed by almonds, hazelnuts, and walnuts. Allergists had thought peanuts and true nuts are so far apart botanically that sensitivity to one would not increase the likelihood of sensitivity to the other. Ewan found, however, that among the 40 percent of patients sensitive to more than one type of nuts, most were sensitive to peanuts.

In 92 percent of the cases, nut allergies developed by age 7—and usually by age 3. Explains Hugh A. Sampson of Johns Hopkins University School of Medicine in Baltimore, "We think the maturation of the immune system and its ability [to tolerate novel substances] is not well established at a very young age. That's why more food allergies occur in the first couple years of life."



Peanuts triggered all cases of nut allergies in children less than 12 months old and 82 percent of those in children under age 3. Ewan points out that "some children reacted to the first known exposure to peanuts, suggesting previous sensitization"—perhaps from breast milk or trace amounts of peanuts in cereals or other foods.

Finally, Ewan observed that among nut-allergy patients, almost all were allergic to other allergens, such as cat dander, pollen, or dust mites. She suggests that "peanut and nut allergy is occurring in a subpopulation with a strong propensity to develop allergies." She concludes that in families where allergies are common, keeping true nuts and peanuts from children, "possibly to the age of 7 years, would be justified."

Though such a ban "has scientific validity, I'm not sure it's practical," says John W. Yunginger of the Mayo Clinic in Rochester, Minn. It's because peanut butter is so tasty and nutritious, he notes, that "most American kids get fed a peanut butter and jelly sandwich long before they're a year old."

In an editorial accompanying Ewan's study, Sampson recommends that breast-feeding mothers in families with allergies should avoid eating peanuts. He argues that these families should also keep foods with true nuts or peanuts from their children until at least age 3. Unfortunately, he concedes, it's not easy identifying which foods contain nuts. Toward that end, he calls on the medical community to "put pressure on governmental agencies" for clear labeling of any foods that contain even traces of peanuts or true nuts. —*J. Raloff*