country has acculturated to a more western lifestyle, exposure to the environmental factor has declined," Spencer argues. He concludes that high levels of exposure led to the most serious symptoms, ALS, which are so debilitating they mask any parkinsonism or dementia. A lower level of exposure and the ALS symptoms drop away; still lower levels leave only the dementia.

Of course, that explanation would be more convincing if someone could identify the toxin. And the trend toward a diminishing disease means there may not be many more opportunities. "We may only have 10 or 20 more years at the most to conduct studies and store brain tissue for analysis in the future," Kurland says. So he and others on the NIA grant intend to leave no stone unturned: Aside from compiling the remaining cases of ALS-PDC, they're performing brain scans and blood tests on Chamorros to look at everything from levels of parathyroid hormone (implicated as a player in the aluminum hypothesis) to levels of superoxide dismutase, an enzyme implicated in familial ALS.

This NIA study may be scientists' last, best chance to catch the killer, and no one thinks it's going be easy: "If it was what we expected, we'd have found it already," Kopin asserts. But the fact that the search has been difficult has only helped to raise the stakes. "ALS-PDC is the Rosetta Stone of neurodegenerative diseases," says Perl. "Whoever provides a translation will win the Nobel Prize."

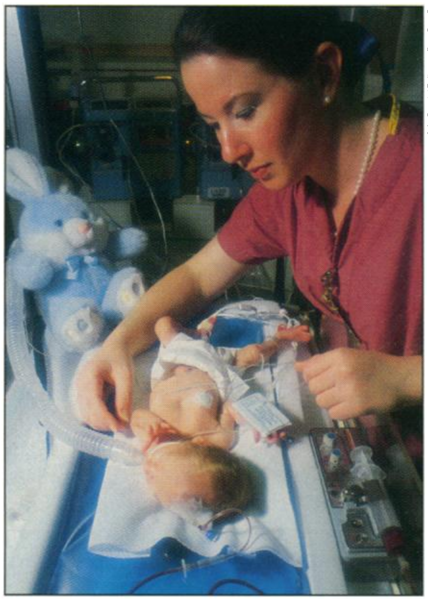
–**Richard Stone**

PULMONARY PHYSIOLOGY

Helping Premature Lungs Breathe Easier

The next time you're on the basketball court and stop to fill your lungs, you should offer up some silent thanks to a little known benefactor: your lung surfactant. What's that, you ask? Lung surfactant is the foamy material, blended of fats and proteins, that lines the inner surface of the lungs. Why give thanks? Well, without surfactant, catching your breath wouldn't just be hard—it could well be impossible, since this lubricating substance helps your lungs expand to draw in air after exhaling.

Lack of surfactant is just the problem faced by the 65,000 premature infants born each year in the United States with "respiratory distress syndrome." Their immature lungs can't produce the material, and until recently, when researchers learned to synthesize surfactant substitutes or get them from animals, as many as 10% of the babies died. But the substitutes could be improved, which is where a paper in this issue of *Science* comes in. On page 453, biochemist Alan Waring of the University of California, Los Angeles, and his colleagues explore the role of a surfactant protein known as SP-B. Though SP-B is a small part of the surfactant complex, it is crucial to its functioning; it is also expensive and difficult to obtain. Though not all in the research community are convinced by the results, Waring's group hopes their data will lead to improved replacements for SP-B, and hence to better treatments for premature infants.



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A better start. Surfactant therapy has revolutionized premature infant care.

Not that current treatments are disastrous. On the contrary, Ivan Frantz, chief of newborn medicine at the New England Medical Center, says surfactant substitutes, which are already cutting the death rate in half, constitute "the most important therapeutic advance in the care of premature infants in 20 years." But investigators feel they can make even more effective replacements once they puzzle out the inner workings of how the surfactant lubricates the lungs. The goal is to simplify the recipe for a replacement surfactant, thereby reducing the cost of treatment, which can be as high as hundreds of dollars per dose.

The current recipe for surfactant starts with large amounts of a phospholipid known as dipalmitoylphosphatidylcholine (DPPC). DPPC is extremely effective at reducing surface tension within the alveoli (the lung's many air sacs), which is the key step in carrying out the surfactant's function. But the substance needs help to do the job. When prepared in solution, DPPC tends to form bilayers or globules, instead of the molecular monolayer needed to coat the alveoli, and thus can't be administered by itself into the lung. Additional ingredients, such as palmitic acid, SP-B, and other proteins found in natural surfactant, must be added. Palmitic acid, which is a negatively charged molecule, apparently acts to "spread" the DPPC into a monolayer, thereby helping it line the alveoli.

Understanding SP-B's role in all this might make it easier to design a better synthetic surfactant, which is one reason Waring and co-workers performed their study. By measuring the surface tension of various solutions of palmitic acid and synthetic peptide mimics of SP-B, they deduce that the positive charges on the protein interact with the negatively charged palmitic acid, locking it into place in the surfactant complex. Without the protein, the palmitic acid would be "squeezed out" of the surfactant monolayer, thus reducing its capacity for decreasing surface tension. "The proteins appear to hold the palmitic acid in a monolayer with low surface tension," says University of California, Santa Barbara, chemical engineer Joseph Zasadzinski, a co-author on the report.

Not everyone in the small surfactant research community agrees, however. "There's just insufficient data. I think they're missing the important function of SP-B," contends Charles Cochrane of the Scripps Research Institute, who published his own theory about the protein's role in *Science* 2 years ago (*Science*, 25 October 1991, p. 566). Cochrane points out that the amount of free palmitic acid in surfactant is quite small. So although SP-B may indeed interact with the fatty acid, Cochrane maintains that the primary role of SP-B is to strengthen the phospholipid monolayer composed of DPPC. In this scenario, he says, rather than locking in the palmitic acid, SP-B provides greater stability to the monolayer, like reinforcements that buttress a bridge.

The Waring group responds that they're confident that SP-B associates predominantly with palmitic acid, although Zasadzinski admits, "it's a complicated affair." He suggests that new experiments they have under way to explore the "squeeze-out" phenomenon may show whose interpretation is correct. But what intrigues Zasadzinski and his colleagues is that their experiments show that simple polymers like polyethylenimine, which bear similar charges to SP-B but are otherwise unrelated in structure, can have the same impact on palmitic acid as the protein. If preventing squeeze-out is truly SP-B's only important function, then such polymers may provide a superior alternative to the synthetic peptides being used now in surfactant replacements. And if that's the case, then even more premature infants, and their parents, might breathe easier.

–**John Travis**