RESEARCHERS SYNTHESIZE MATERIAL ESSENTIAL FOR LUNG FUNCTION;
MAY ALLEVIATE RESPIRATORY DISTRESS SYNDROME

LA JOLLA, CALIF. Oct. 25, 1991 -- Scientists at The Scripps Research Institute (TSRI) have synthesized a complete form of surfactant, an essential lung material which keeps air sacs open and prevents respiratory distress syndrome, a major killer of premature babies and adults.

An explanation of how the synthetic surfactant works is published in today’s issue of Science by Charles Cochrane, M.D. and Susan Revak of TSRI’s Department of Immunology.

In the coming months, TSRI hopes to have Federal Drug Administration approval for investigational studies of the synthetic material, Cochrane says, adding that clinical trials will begin early next year. He added that TSRI’s 10 year research agreement with Johnson & Johnson provides that company with the right to license and commercialize this compound.

According to the American Lung Association, 25 percent of premature babies die of respiratory distress syndrome; the mortality rate for adults who acquire the disease is 50 percent.

"It’s possible that one or two administrations of the synthetic surfactant may be enough to allow a baby to recover," Cochrane says.

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Human surfactant is developed in the lungs of a fetus during the last months of pregnancy. It is essential in allowing expansion of the lungs and preventing their collapse during expiration. Annually in this country, about 39,000 premature babies born without surfactant develop respiratory distress syndrome because they are unable to expand their lungs. As a result, they neither receive enough oxygen nor are able to remove carbon dioxide. In adults, the disease strikes about 150,000 Americans annually for a variety of reasons, including injury, surgical manipulation or disease. When the adults' lungs become inflamed, surfactant activity is lost.

Normal human surfactant, which is composed of phospholipids and proteins, is secreted by lung cells, coats the inner lining of the lung, and prevents the lung from collapsing during exhalation.

In four years of research on surfactants, Cochrane and Revak took an interest in the protein components of the substance. They determined that one they called Surfactant Protein-B (SP-B) appeared to play the most important role in working with surfactant phospholipids to keep air sacs open.

In their Science article, the two note that SP-B resists surface tension and collapse of pulmonary alveoli by increasing lateral stability of the phospholipid layer.

"As protein chemists, we looked at SP-B structure and were able to determine how it functioned with phospholipids to produce strength of the layer within the pulmonary alveoli," Cochrane says. "We were also able to synthesize a mimic of the SP-B protein which can be produced simply and inexpensively for potential therapeutic
use. Trials with this synthetic surfactant in fetal monkeys have shown it to be highly effective."

Pending FDA approval for investigational studies, Cochrane and Revak, along with their clinical associates, T. Allen Merritt, M.D., University of California, Davis; Gregory Heldt, M.D., University of California, San Diego; and Mikko Hallman, M.D., University of California, Irvine, plan to begin clinical trials with neonatal patients at several major clinical centers in this country and Europe.

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Surfactant, which lines the air sacs, or alveoli of the lungs, is composed of protein and phospholipids. Both components of surfactant are essential for keeping the air sacs open so that oxygen and other gases can reach the blood stream. This figure represents the protein, SP-B, or a synthetic mimic of SP-B, shown as arches and squares, and the phospholipids, shown as circles with straight, side chains. In the experiments, the portions of the protein represented by the squares, which bear strong positive charges, were found to interact with negative charges located in the circles of the phospholipids; and the arch-portion of the proteins to interact with the straight-line, rigid side chains of the phospholipids. These interactions between the protein and the phospholipids were found to be essential for surfactant activity. The researchers have synthesized a mimic of the protein, which acts identically to the SP-B protein and which, together with synthetic phospholipid, may serve as a therapeutic replacement of surfactant in babies and adults with respiratory distress syndrome.
LA JOLLA, CALIF. Oct. 25, 1991 -- The totally synthetic surfactant has been made and administered to premature monkeys. The graph demonstrates its effectiveness. This monkey was maintained on artificial ventilation for 28 hours after cesarean delivery and remained critically sick as shown by extremely poor lung function. However, shortly after the synthetic surfactant was given at 28 hours of life, lung function rapidly improved, reaching the normal range. The baby monkey, which was ashen gray and still, turned pink and began wiggling and grasping with its hands and feet, typical of normal babies.
Surfactant, which lines the air sacs, or alveoli of the lungs, is composed of protein and phospholipids. Both components of surfactant are essential for keeping the air sacs open so that oxygen and other gases can reach the bloodstream. This figure represents the protein, SP-B, or a synthetic mimic of SP-B, shown as orange arches and yellow squares, and the phospholipids, shown as white circles with straight, white side chains. In the experiments, the portions of the protein represented by the yellow squares, which bear strong positive charges, were found to interact with negative charges located in the circles of the phospholipids; and the orange arch-portions of the proteins to interact with the straight-line, rigid side chains of the phospholipids. These interactions between the protein and the phospholipids were found to be essential for surfactant activity. The researchers have synthesized a mimic of the protein, which acts identically to the SP-B protein and which, together with synthetic phospholipid, may serve as a therapeutic replacement of surfactant in babies and adults with respiratory distress syndrome.