Biology

Elizabeth Pennisi reports from New Orleans at the Experimental Biology '93 meeting

Healing touch of a liquid breath

Animal tests indicate that a substance being developed as artificial blood (SN: 9/26/87, p.200) may also substitute for the air that moves in and out of lungs. Perfluorocarbon liquid not only provides adequate gas exchange, but also helps heal damaged lung tissue, says Ronald B. Hirschl, a surgeon at the University of Michigan Medical School in Ann Arbor.

Even though ventilators can help people with lung problems breathe, about 40,000 people a year die of respiratory failure in the United States. "We don't have a good way of treating the lungs or [making] them better," Hirschl says.

So he evaluated the performance of this oxygen-carrying liquid in 12 sheep. Hirschl sedated the sheep, damaged their lungs, and made the airways collapse. He then placed six of the animals on typical gas ventilators and six on ventilators that circulated perfluorocarbon through the lungs. He measured how much oxygen entered the animals' blood and, 2½ hours later, examined the lung tissue.

Perfluorocarbon provides two to three times as much oxygen as ventilation with air does, Hirschl reports. In addition, the lung tissue of the sheep treated with perfluorocarbon showed much less hemorrhaging and fluid buildup than the lung tissue of the other sheep.

The liquid seems to flush out "gunk" — fluid filled with proteins and red and white blood cells, which seeps into the lungs and impedes gas exchange, says Hirschl. Perfluorocarbon reinflates collapsed airways and, because it is heavier than air, may cause blood flow to shift to undamaged airways.

Hirschl is seeking permission from the Food and Drug Administration to try this treatment in people.

Custom livers grown in the lab

For babies born with genetic defects known as inborn errors of metabolism, the prospects can be grim. Surgeons can cut a small piece, or lobe, off a parent's liver and transplant it into the sick baby in the hope that the lobe will produce missing enzymes critical to survival. But often that lobe is too big for the tiny body, and the baby dies.

Less than one-tenth of a normal adult liver can provide an adequate supply of the proteins missing in these babies, says Brian A. Naughton of Advanced Tissue Sciences in La Jolla, Calif. To make small enough liver pieces, Naughton and his colleagues have now developed a way to grow liver tissue outside the body.

Although damaged liver regenerates in the body, most liver cells in adults have long since ceased to divide, so they do not multiply readily in laboratory cultures.

Naughton solved that problem for rat liver tissue by creating a more familiar environment for the liver cells. He uses the same approach that he and others developed to grow bone marrow outside the body (SN: 4/3/93, p.214).

"The trick is to use stromal support cells," Naughton says. These include macrophages and fat, endothelial, and fibroblast cells. In the first experiments, Naughton used stromal cells from bone marrow; later, he figured out how to separate support cells from liver tissue and use them instead.

He and colleague Benson Sibanda first sort cells from a tablespoon of liver. They allow the stromal cells to grow on a small nylon screen and then put the enzyme-producing liver cells on top. In about five weeks, these cells fill up the mesh.

The cultured liver continues to thrive when implanted under the skin and in the gut of rats, the researchers report. "You can see the liver forming normal liver structure," says Sibanda. The researchers have also detected enzyme production from these implants.

Some scientists have suggested that liver cell cultures may provide an alternative to using animals for testing the toxicity of substances, but Naughton says his goal is to find ways to grow liver pieces big enough to provide newborns with missing proteins until the babies grow large enough for a donated lobe.

Some 'cage potatoes' don't get fat

Some rodents stay fit even when they get no exercise at all, say scientists who analyzed the muscles of wild chipmunks, deer mice, and ground squirrels kept inactive for a month.

Melanie Thompson and Steven Wickler of California State Polytechnic University in Pomona brought these rodents into the lab and gave them plenty of food and water but no room in which to run. Like inactive people, deer mice (which do not hibernate) and ground squirrels (which fatten up to make it through their winter's sleep) became quite pudgy, Thompson and Wickler say. The animals' muscles shrank and lost some of the proteins involved in using oxygen.

But chipmunks, which hibernate but wake up every so often to eat their cache of food, stayed slim, says Wickler.

He sampled the muscles of 18 chipmunks before and after the experiment. Although the muscles got smaller, the concentrations of an enzyme called citrate synthase increased, indicating that these animals gained aerobic fitness during that period, he says.

Because chipmunks are so active when they emerge in spring, it is important that they stay fit over winter, Wickler adds. He hopes to identify the mechanism behind the chipmunks' ability to resist becoming "cage potatoes," as he calls them. Such knowledge may lead to ways for people to avoid turning into jelly during bed rest, space travel, or inactive periods, he says.

Double duty for donor kidneys

Every week in the United States, about 16,000 people hook up to dialysis machines because their kidneys do not function properly. Only about half of these individuals will get much-needed transplants.

Now, however, physiologists plan to make donated kidneys do double duty by developing a way to divide each organ and transplant each half into a recipient. To investigate this possibility, Dilip S. Kittur of Johns Hopkins University School of Medicine in Baltimore first studied pigs, whose kidneys anatomically resemble those of humans. In early experiments, he removed and split kidneys, then implanted half a kidney back into each 3-month-old donor pig. The pigs thrived for several years, reaching weights of roughly 400 pounds, he says.

Last year, Kittur's team removed the kidneys from another dozen pigs, implanting half of each kidney into the donor and the other half into a different pig. The researchers found that they could successfully hook up a half kidney in a new pig. But because they did not treat the animals with immunosuppressant drugs, these pigs rejected the transplants. In further work, Kittur says, the researchers hope to use immunosuppressants and assess how well a donated minikidney works.

At the same time, Kittur analyzed the anatomy and blood flow of kidneys of deceased humans. Until now, scientists assumed that they couldn't easily divide a kidney because of the arrangement of blood vessels in this organ. But the cadaver studies led Kittur to conclude that he could halve a human kidney if he first altered the connections of two arteries. "It's not too hard to do. It's just the concept that's different," he says.

Other researchers who have evaluated the survival of people who lost all but half a kidney to cancer or some other disease determined that half a kidney can function for at least 10 years. "But they have some amount of damage from having too much work to do," Kittur notes. Also, even small rejection reactions will further impair kidney function. Nonetheless, he thinks the procedure should help relieve shortages of donor organs.