Dissecting Legionnaires' Disease

BY JOAN AREHART-TREICHEL

The summer of 1976 was supposed to have been an especially gala one in Philadelphia — a Bicentennial celebration in one of America's oldest and most historic cities. But the festivities were marred by an unexpected medical tragedy: An unknown disease killed 34 persons attending the American Legion convention in downtown Philadelphia and made 187 other conventioneers seriously ill. The mysterious malady was dubbed "Legionnaires' disease."

In the past five years medical researchers have learned a lot about the disease (now called legionellosis). For instance, scientists reported at the recent annual meeting of the American Society for Microbiology in Dallas that although it triggered pneumonia-like symptoms, it was not caused by any of the bacteria or viruses previously known to cause pneumonia, that it was far from an isolated incident and that the disease, with proper equipment and knowledge, can be correctly diagnosed and effectively treated.

Identifying the cause of legionellosis was a real medical challenge. Was it a virus, bacterium or other microbe? A heavy metal or weed killer? An accident or foul play? (A similar malady had struck the Odd Fellows' convention in Philadelphia in 1974, and both the Legionnaires and Odd Fellows had stayed at the same hotel [SN: 8/14/76, p. 102].) No sign of a microbe could be visualized in tissues taken from Legionnaires who had died from the disease.

Nonetheless, in January 1977 two scientists at the Centers for Disease Control in Atlanta, Joseph E. McDade and Charles C. Shepard, found that a bacterium was indeed responsible for legionellosis. They ground up lung tissue from a victim of legionellosis and used it to infect guinea pigs. The investigators injected tissue from these guinea pigs into embryonated eggs. Bacteria that appeared in the yolk sacs of the eggs were exposed to antibodies taken from victims of legionellosis. The antibodies adhered to the bacteria, providing solid evidence that bacteria had caused the disease (SN: 1/29/77, p. 69).

The bacteria are smaller than average (about 2 to 20 microns in length), rod-shaped, Gram-negative (stain pink with Gram's procedure) and, unlike many other bacteria, have ends that tend to be pointed instead of round or squared (SN: 9/17/77, p. 180). At first, the bacteria were not thought to be motile; now they are known to move with the help of flagella, says Albert Balows, one of the leading legionellosis investigators at CDC. And Leo Pine of CDC has found that to grow and survive the bacteria need amino acids and trace elements but not vitamins or carbohydrates.

Scientists are also finding that the bacteria responsible for causing legionellosis are not one previously unidentified species but a whole family. So far, six different species of *Legionella* have been identified, says Balows, ranging from *Legionella pneumophila* (which caused the disease at the Legionnaires' convention) to *Legionella longbeachae* (isolated from a patient in Long Beach, Calif.).

Legionella seem to thrive in water, says Balows. Carl B. Fliermans and colleagues of the Savannah River Laboratory in Aiken, S.C., have isolated *Legionella* from cooling towers, ponds, thermal canals, reservoirs and from clear as well as stagnant water, although the bacteria appear to prefer the stagnant water since it contains blue-green algae, a good source of nutrients for for them. Similar findings for northeastern United States water are reported by Daniel Pope of Rensselaer Polytechnic Institute in Troy, N.Y. The bacteria, says William B. Cherry of CDC, have also been isolated from humidifiers, hot water systems, shower water and even from a shopping mall cascade fountain. The bacteria are capable of surviving in waters of widely varying temperatures, says Fliermans, but appear to prefer water between 40°C and 50°C.

Investigators have also made discoveries about the extent of legionellosis. For instance, since the American Legion convention in Philadelphia, it has struck persons not only in virtually every state in the United States (affecting an estimated 125,000 persons yearly), but all over Europe, and in Canada, Australia, New Zealand, Israel and several African countries. "So we know occurrence of this disease is widespread," says Balows. Legionellosis has also been found to have existed long before the Legionnaires' convention in 1976. A bacterium isolated from the blood of a victim of an unexplained fever in Fort Bragg, N.C., in 1943 turned out to be *Legionella micdadei*, one of the known agents of legionellosis, reports Paul H. Edelstein of the Veterans Administration Wadsworth Medical Center in Los Angeles. Similarly, survivors of the Odd Fellows convention in Philadelphia in 1974 have been noted to have antibodies in their blood that react with *Legionella*, implying that the bacteria were responsible for the disease that struck their convention (SN: 9/17/77, p. 180).

Diagnosis of the disease is now possible, Hazel Wilkinson of CDC reported: Stains that show up *Legionella* in lung tissue have now been developed so that if a lung biopsy specimen is taken from a *Legionella* victim, the tissue can be stained and the bacteria visualized. Such diagnosis is far from ideal, however, since physicians are reluctant to take samples for analysis, and not all labs have equipment to analyze them for *Legionella*. So Wilkinson and her colleagues at CDC are exploring less invasive, easier methods. For instance, they are trying to identify antigenic material from the bacteria in body fluids, since antibodies against the bacteria do not appear in the blood until after the acute stage of the disease is past.

Erythromycin has now been found to be effective in the treatment of legionellosis, an important discovery because the death rate of the disease is 15 to 20 percent if untreated. When the first victims of legionellosis were treated for a bacterially caused disease, Arthur Reingold of CDC says, physicians gave them antibiotics other than erythromycin, which at that time was used mostly on outpatients rather than on critically ill hospitalized patients. A number of *Legionella* cultures were tested in the lab, however, and found to be susceptible to erythromycin. Physicians eventually began trying erythromycin on legionellosis patients and found it to be effective, although the reason has not yet been pinned down.

Researchers are also improving their ability to isolate *Legionella* from the environment. The most effective methods of isolating the bacteria from various water environments to date have been injecting water samples into guinea pigs. If the samples cause legionellosis, then one can conclude that the water sample is contaminated with *Legionella*. Guinea pigs are expensive and the procedure is time-consuming, however, and Richard W. Gilpin of the Medical College of Pennsylvania and Hospital in Philadelphia has designed a technique that promises to be more rapid and less expensive. Antibodies against *Legionella* are attached to solid supports, through which a water sample is run. If *Legionella* are in the sample, they stick to the supports.

Although many biocides do not necessarily kill *Legionella* in water cooling towers, biocides containing Bis (tributyltin) oxide plus quaternary amine seem to do so, Pope reports. Low-level chlorination is effective in removing *Legionella* from large commercial cooling towers and air conditioning systems, studies by Fliermans and his colleagues show.

For the future, Reingold says, "I hope we will understand more about how people acquire legionellosis infection and hopefully will be able to prevent infection." Although there is little that individuals, hotels, office buildings or industries can now do to prevent legionellosis, he says, "It is possible that proper maintenance of air cooling systems may be proven at some point in the future to be efficacious." And as Balows points out, "Ultimately the need for a legionellosis vaccine must be considered." □