# Robert Austrian, M.D.

Recipient of the 2001 Maxwell Finland Award for Scientific Achievement

There are some scientists who tower over the results of their work, no matter how significant. There are others whose work towers over them. This year's recipient of the Maxwell Finland Award for Scientific Achievement, Robert Austrian, MD, is a member of the second group.

Self-effacing, almost to a fault, Dr. Austrian, Chairman Emeritus of the Department of Research Medicine at the University of Pennsylvania School of Medicine, is nevertheless widely known, not only because of his distinguished career in research medicine, but also because of his single-minded pursuit of a single bacterium — *Streptococcus pneumoniae* and the diseases it causes, as well as the development of a pneumococcal vaccine and the subsequent controversies over its efficacy.

*S. pneumoniae* took over Dr. Austrian's professional life. He became known as "Mr. Pneumococcus," epitomized by the title of a collection of his published papers, *Life with the Pneumococcus*. In 1986, the late David Rogers, MD, then President of the Robert Wood Johnson Foundation said, "Dr Austrian has stuck, single-mindedly, indeed almost fanatically, to work on this organism and the human illnesses it produces."

Dr. Austrian's work with the pneumococcus is of course well known to this audience, but it is worth summarizing if only because it demonstrates the value of questioning accepted dogma: Things are not always what they seem. This, certainly, was the situation in 1952 when Dr. Austrian came to Kings County Hospital-Downstate Medical Center in Brooklyn from Johns Hopkins School of Medicine. Dr Austrian had become interested in the pneumococcus while a resident at Johns Hopkins. He

decided to pursue its study despite concern from colleagues stating that they saw only three or four cases of pneumococcal pneumonia a year, and that such pneumonia was no longer a significant problem, thanks to the sulfonamides and penicillin. Indeed, largely because of the advent of the antibiotics, two hexavalent pneumococcal vaccines had been taken off the market by the manufacturer the same year that Dr. Austrian went to Brooklyn.

Dr. Austrian remembered that, when he was at Johns Hopkins, he hadn't seen any dramatic fall in the incidence of pneumonia and doubted the situation in Brooklyn was very different. "I was convinced the disease wasn't being recognized," he says. He set to work training the house staff to take blood and sputum cultures from patients with pneumonia before treating them. Over the next decade they identified approximately 200 cases of presumed pneumococcal pneumonia a year. To Dr. Austrian, this was clear confirmation of his contention that the disease was not being recognized.

In 1962, ten years after coming to Brooklyn, Dr. Austrian and his associate, Jerome Gold, MD, analyzed their proved cases of bacteremic pneumococcal pneumonia. They found that, while there was a striking reduction in mortality among those patients treated with penicillin, there was a significant number of patients who had been given antibiotics who died within a few days after the onset of disease, even though they were bacteriologically cured. The patients, especially the elderly, were dying because of irreversible damage that occurred early in the infection. The exact mechanism still remains unknown. "Over 100 years after the organism was first identified we still don't understand fully how it causes death in humans," Dr. Austrian says.

Dr. Austrian reported these findings in 1963 at the annual meeting of the Association of American Physicians. Dr. Rogers called it a "bombshell." Dr. Austrian did more than draw attention to an unsuspected situation. To him the message was clear: To prevent the disease there had to be a revival of interest in a vaccine. At that

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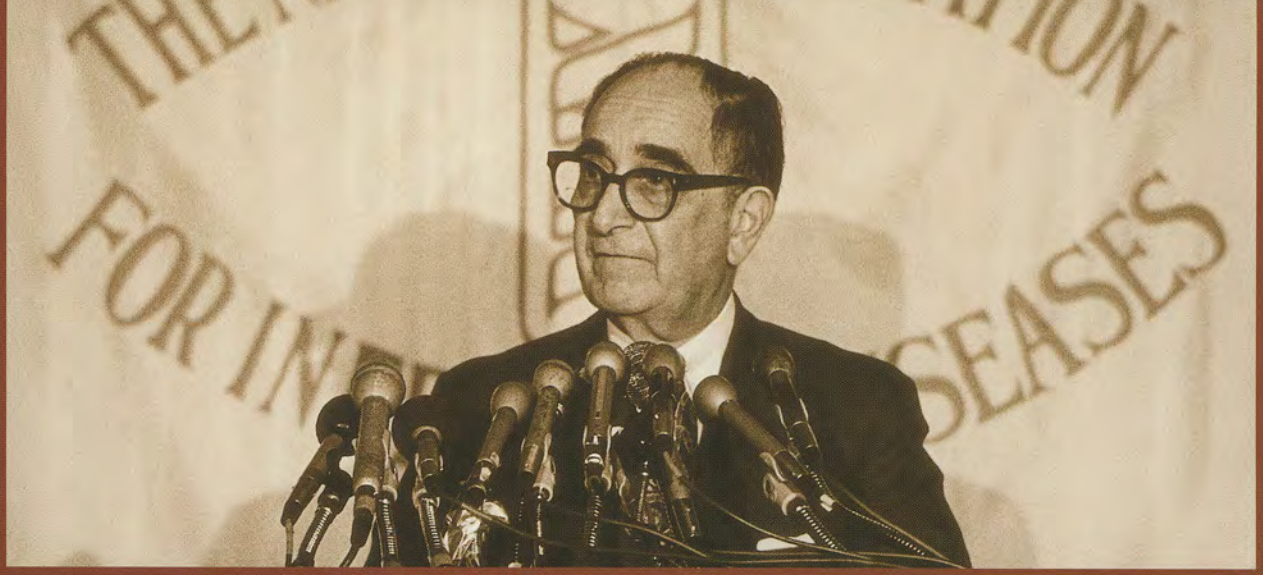


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meeting he suggested how it might be formulated. He had recognized that, of the 80-odd different pneumococcal serotypes, only a relatively few caused most of the disease. As a result, Dr. Austrian concluded that it was feasible to immunize those groups known to be at high risk of death after infection with a vaccine of a limited number of identifiable pneumococcal types.

It took several more years to convince the medical world that making a vaccine was desirable and necessary. Fortunately, once alerted, other investigators found similar evidence that, despite antibiotics, pneumococcal pneumonia was still a serious disease. Faced with this situation, in 1967 the National Institute of Allergy and Infectious Diseases decided to fund vaccine development.

The Institute let a contract to Eli Lilly and Company and the company developed a vaccine incorporating 12 of the most important serotypes. Dr. Austrian tested the vaccine in field trials among South African gold miners where the disease was endemic. At the same time, Dr. Maurice R. Hilleman of Merck and Company did a similar study on another group of gold miners using a 14-valent vaccine that Merck had developed. "The two studies showed remarkable effectiveness against the serotypes occurring in the mineworkers. On the basis of this and some other studies we got a license in 1977," Hilleman recalls. Subsequently Merck developed a vaccine containing 23 serotypes. This vaccine, Pneumovax, was licensed in 1983 and is still in current use. It covers between 85% and 90% of the pneumococcal pneumonia in the US.

One might conclude that this was the end of the story. A vaccine was now available to prevent a major disease. But as it turned out, it was only the beginning of a prolonged debate, occupying much of the 1980's, over the effectiveness of the vaccine and its value in different age groups.

Some of the criticisms were based on ignorance of what could be reasonably expected from the vaccine. For

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example, there were reports of death from pneumonia among vaccinated individuals. However, if the disease was caused by serotypes not present in the vaccine it could hardly be expected to be protective. "It took three years to get that idea across," comments Dr. Hilleman.

In the US, pneumococcal pneumonia is predominantly a disease of infancy and of the elderly, but the South African gold miners, in whom the vaccine was tested, were young adults. The vaccine, therefore, would not protect the most susceptible population, they said. Then there were inconclusive results from controlled trials. However, notes Harvey Friedman, MD, professor of medicine at the University of Pennsylvania, "the study groups were too small to evaluate protection against bacteremic disease and the vaccine's effect on non-bacteremic disease could not be properly evaluated because the diagnostic tests to establish the cause of infection were not definitive."

The critics were often shrill and contentious, but Dr. Austrian responded with cool precision and the greatest courtesy. "He kept that vaccine alive," comments Dr. Hilleman. His quiet, unassuming manner, and his arguments expressed in fastidious English are models worth study by any researcher engaged in similar debates. Eventually, of course, Dr. Austrian won the day. In 1991, the New England Journal of Medicine published a case control study that, says Dr. Friedman, conclusively established the protective efficacy of the pneumococcal vaccine.

After the pneumococcal vaccine was licensed and immunizing patients with it had become a routine part of medical practice, Dr Austrian was asked what would he do next. He replied: "the pneumococcus has housed, clothed and fed me throughout out my life. I will not forsake it now."