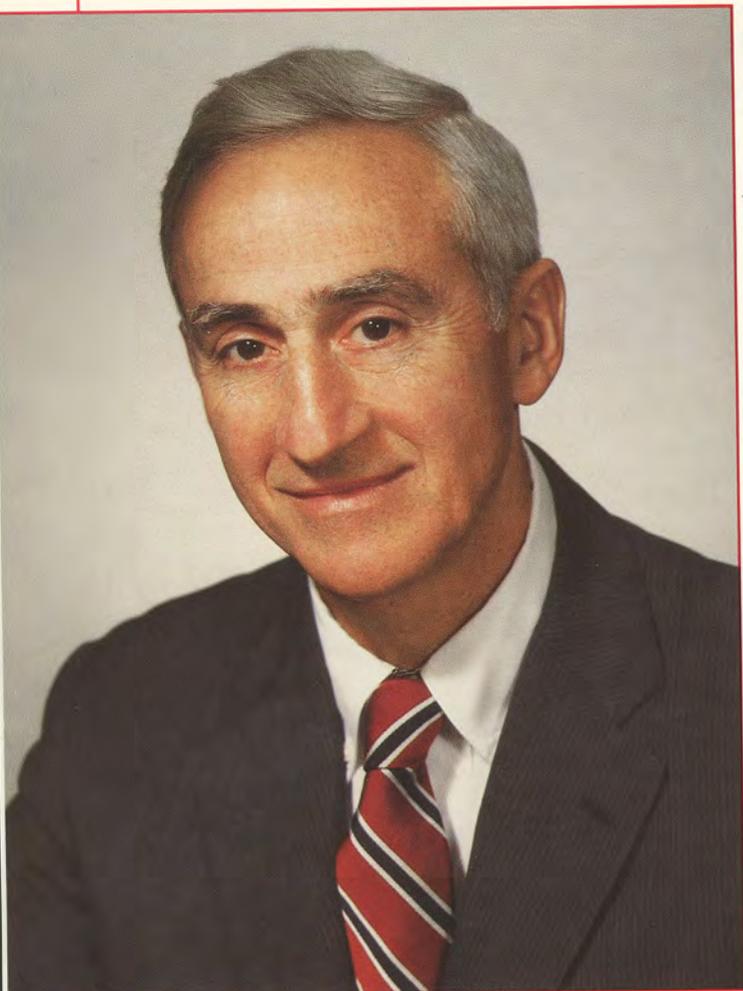


***F**or his extraordinary leadership in biomedical research leading to drugs and other therapeutic agents of direct benefit to mankind, his important influence on national science policy, and for his distinguished contributions to the advancement of knowledge as a teacher and head of one of the nation's outstanding research laboratories, P. Roy Vagelos has been chosen the recipient of the 1991 Maxwell Finland Award.*



P. ROY
VAGELOS, M.D

Maxwell Finland Award Recipient
1991

The never-ending campaign against infectious disease requires the orchestration of many elements in our society, skilled medical care, adequate public health programs, and a societal will to implement them. But the crucial element is the development and manufacture of the tools—drugs and vaccines—needed to do this job. In our society it is the pharmaceutical manufacturer who has traditionally provided these tools.

This year's Maxwell Finland Award acknowledges this contribution. Certainly, it is difficult to talk about this year's recipient, Dr. P. Roy Vagelos, since 1985 Chairman, President and Chief Executive Officer of Merck & Co., Inc., without also recognizing the outstanding contributions the company he heads has made in providing the needed weapons in the war against infectious disease.

Dr. Vagelos came to Merck in 1975 from Washington University School of Medicine in St. Louis where, for nine years he had been chairman of the department of biological chemistry, a position inherited from the Nobel prizewinner Dr. Carl F. Cori.

Discussing how Dr. Vagelos had been selected by Merck's management, John J. Horan, the President and Chief Operating Officer of Merck recalls: "We had had great success with a number of leaders in research, but they were chemists, Dr. Max Tishler and Dr. Lewis Sarett, for instance. We didn't see a life sciences leader in the company."

"To be sure, we did have Dr. Carl Beyer who was one of our leading life scientists but he was nearing retirement.

So we made a conscious decision to start looking for an outstanding man in the life sciences."

The search went on for several years and cast a wide net. The company looked at possible candidates not only within the United States but also Europe. "There were some good prospects but no one that we ended up hiring," says Mr. Horan.

Dr. Harry Robinson, Merck's vice president for scientific affairs, suggested Dr. Vagelos. Dr. Vagelos had taken his MD degree at Columbia University's College of Physicians and Surgeons in New York in 1954 after getting his bachelor's degree at the University of Pennsylvania. He did his internship and residency at the Massachusetts General Hospital, Boston. While a young medical student, he had spent a summer working at Merck in Dr. Robinson's laboratory and they had stayed in touch over the years.

"Well, we got him to come in and talk about the position here and I think we were all impressed, I know I was," Mr. Horan says. "Of course he was already well known. He had an excellent research record at the National Institutes of Health and was experienced as an administrator at Washington University.

"The only thing I needed some reassurance about was that he would have an interest in producing drugs. That's our objective after all. We have had experience with university scientists who were of the highest professional caliber who just didn't work out in our environment because not all basic university research is oriented towards a product.

"We talked about this and Roy understood exactly what I meant. He said he had done academic research and was interested in science. But he said he was just as interested in seeing a drug developed as a result of that research and the excitement that comes with it."

"In addition," Mr. Horan says, "Roy is personable. He's good with people, certainly he sold himself to me totally."

For his part Dr. Vagelos says the job

offer at Merck was an exciting challenge for him. "I had been doing basic research for 19 years. Yet my original plan was to be a clinician, a cardiologist as a matter of fact. I wanted to work against disease, to try and do something important in taking care of patients.

"When Merck called, I felt that this was the challenge for me to put my brains where my mouth was. Use my understanding of basic research and apply it to trying to make an important drug."

In 1956 Dr. Vagelos went to the National Heart Institute, part of the National Institutes of Health (NIH) in Bethesda, Maryland. He planned to spend part of his time in the Clinical Center taking care of patients and part of his time in a research laboratory.

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But while he was in Boston he met Dr. Paul C. Zamecnik, a researcher who had done pioneering work on protein synthesis. It was Dr. Zamecnik who suggested that Dr. Vagelos might enjoy working at the NIH, and further suggested he try to work with Dr. Earl Stadtman, then head of an enzyme section in the laboratory of cellular physiology and now one of the Heart Institute's leading biochemists.

It was on Dr. Zamecnik's recommendation that Dr. Stadtman accepted the

young physician but with some doubts. "Quite frankly," says Dr. Stadtman, "I was only a young PhD myself at the time, but I didn't have much confidence in the possibility that a physician could do the kind of work we were doing. Roy was the first MD that I took into the laboratory."

In Stadtman's laboratory Dr. Vagelos worked on several aspects of long chain fatty acid synthesis. There he discovered the acyl carrier protein, a critical intermediate in the synthesis of fatty acids.

During this period one of Dr. Vagelos's associates was Alfred Alberts. Mr. Alberts never troubled to obtain his PhD, despite Dr. Vagelos's injunction that he do so. But when Dr. Vagelos went to St. Louis in 1966, Mr. Alberts went with him and he eventually became a full professor at the University. When Dr. Vagelos went to Merck, Mr. Alberts again moved with him and here he discovered Merck's now famous lipid-lowering drug Mevacor.

Dr. Stadtman recalls that while Dr. Vagelos was with him Dr. Vagelos was offered a job back at the Massachusetts General Hospital which he was very tempted to take since there he felt he could make a real contribution to medicine. But, at the time Dr. Stadtman was going to work in Europe for a year and needed someone to look after his laboratory. He asked Dr. Vagelos to postpone his decision until his return, and Dr. Vagelos agreed.

"I told him," says Dr. Stadtman today, "that out of a hundred biochemists, there was only one or two that were really good and had a feel for biochemistry and that he was one of them."

While he was at NIH, Dr. Vagelos took a sabbatical year at the Pasteur Institute in Paris working with the Nobel prizewinner Jacques Monod. They became close friends. "I was doing biochemistry and enzymology with Dr. Stadtman; at the Pasteur I learned bacterial genetics and it changed the direction of my work," he says.

"Using bacterial mutants we looked at

fatty acid biochemistry. Later when I got to Washington University we had the notion of trying the same thing in mammalian cells, and found that you could make a mutation in just one enzyme and thereby turn off cholesterol biosynthesis.

"This gave me the idea of working on cholesterol as a major project. In turn, this led eventually to the development of Mevacor.

It's interesting how things turn out," Dr. Vagelos says. "You can trace Mevacor back to Monod who got me into genetics and to Stadtman who got me into biochemistry."

Dr. Vagelos says that Dr. Stadtman has trained hundreds of good biochemists including Dr. Michael Brown, who with Dr. Joseph Goldstein (who trained in another NIH laboratory) won the 1985 Nobel Prize for their work on the cholesterol receptor site. The two Nobelists worked with Merck as consultants during the development of Mevacor.

In addition to Mr. Alberts, last October another Stadtman-trained biochemist Dr. Benjamin Shapiro joined Merck. "So we at Merck now have two of the top people that Dr. Stadtman trained," says Dr. Vagelos.

"His scientific judgment plus his management skills are a unique combination in the pharmaceutical industry."

A research-driven organization staffed with scientists of the highest caliber, Merck is considered to have among the most productive laboratories in the industry. Today, the company has 18 products in nine therapeutic classes—each with

annual sales of \$100 million or more.

Dr. Vagelos himself says the most exciting part of his job is discussing science, evaluating data and understanding experiments. The discovery, development, and testing of Mevacor is naturally one of Dr. Vagelos's favorite topics, he doesn't hesitate to describe Merck's achievements in producing agents useful in the treatment and prevention of infectious diseases.

Among the agents developed since he came to Merck, he cites Mefoxin, a leading antibiotic used in hospitals; Primaxin, which he describes as the broadest spectrum antibiotic in the world; and Mectizan for the treatment of the tropical disease onchocerciasis, river blindness.

For years Merck has been a leader in the development of the ever-lengthening list of vaccines which have all but banished childhood infections like measles, mumps, rubella and Hemophilus influenzae. Recently the company has also created agents against adult infections like hepatitis B and pneumococcal pneumonia.

While many pharmaceutical concerns were demolishing or severely cutting back the manufacture of immunizing agents, Merck continued not only to supply and improve established vaccines but to expand the development of new ones.

Recently, three new vaccines have also been developed: a plasma-derived agent against hepatitis B and subsequently the world's first successful recombinant vaccine against this disease; Pneumovax, a vaccine against the common forms of pneumococcal pneumonia; and a just-licensed vaccine against the bacterial disease Hemophilus influenzae which protects infants as young as two months of age.

The now retired Dr. Maurice Hilleman, Merck's champion vaccine developer, gives credit to Dr. Vagelos for these successes. "His scientific judgment plus his management skills are a unique combination in the pharmaceutical industry from what I've seen," he says. In a high technol-

ogy organization and in a highly competitive business you have to create useful products. Having a manager who understands the science and can make decisions on the future of a product with some confidence is invaluable, and Dr. Vagelos has certainly done that."

When Dr. Vagelos came to Merck, he came back to where he grew up. He was born in Westfield N.J. in 1929. Like Maxwell Finland, for whom this award is named, his parents were immigrants, in this case from Greece.

The Vagelos family ran a restaurant in Rahway, only a few blocks from the company their son now heads. "My mother did the cooking, my dad ran the place, my sisters and I helped out. I was jack of all trades, waiter, soda jerk, the lot," Vagelos says. "Being so near Merck we got to know a lot of Merck people. My sister married a Merck chemist."

Part of Merck's commercial success lies in applying the principle that good people attract other good people. Dr. Vagelos, in biochemical terms, describes the process as "autocatalytic. Once you get key top people, they attract others; get good people and you get more good people."

This encourages innovation says Dr. Edward M. Scolnick, Merck's head of research and development: "If you have bright, highly motivated people who feel responsible for their work they will discover great things."

But today the 61-year-old Dr. Vagelos worries about America's scientific future: "Finding these good people is getting harder and harder. The supply is not what it was. Science has become less attractive because it is not being funded as it used to be.

"This is painful to those of us who trained in science in the golden years. At the time people my age were getting their training the sky was the limit. All you needed was a good idea and automati-

cally there would be space, equipment and funds. This stimulated people to go into science, science was exciting, our understanding of molecular biology was just taking off, and even more important, science was being adequately supported.

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So those who decided to become scientists knew they would have a job."

As a company Merck demonstrates its concern with this situation through support of scientific education. In 1990, alone, it gave over \$11 million. The company has always looked towards the future and the need for high quality scientific innovation, so the possibility that needed scientific talent may some day be unavailable is troubling. "It isn't good for this industry, or this nation's competitive position in world markets," Dr. Vagelos says.

"It's better to have universities and institutions of higher learning growing and prospering. They bring people to science, produce more ideas to work from, and train more people that we can recruit." ❏