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4 Winners of Lasker Medical Prize

By LAWRENCE K. ALTMAN

Two surgeons who developed prosthetic heart valves that have prolonged the lives of millions of people are among the winners of this year's Lasker awards, widely considered the nation's most prestigious medical prizes.

Drs. Alain Carpentier, 74, of the Georges Pompidou hospital in Paris, and Albert Starr, 81, of the Providence Health System in Portland, Ore., are among three American and one French scientists to win the awards, the Albert and Mary Lasker Foundation announced yesterday.

The third, Dr. Ralph M. Steinman, 64, of Rockefeller University in Manhattan, discovered a cell that starts a cascade of immune responses that defend the body against microbes. The cell is now the basis of experimental therapies for cancer and many other diseases.

The fourth winner, Dr. Anthony S. Fauci, 66, is an internationally known immunologist who is being honored as the principal architect of two major Bush administration programs: the President's Emergency

Plan for AIDS Relief, or Pepfar, and Project Bioshield, which seeks to improve countermeasures against potential bioterror agents.

Dr. Fauci, who has directed the National Institute of Allergy and Infectious Diseases since 1984, marshaled scientific evidence to construct the United States' responses to these two global crises. The Lasker Foundation also cited Dr. Fauci for his role "in explaining issues of great concern like the science behind emerging biological hazards" to the public.

Mechanical heart valves did not exist 50 years ago. But the valves developed by Drs. Starr and Carpentier and then by others have made such replacements the second most common heart operation in this country, after coronary bypasses. An estimated four million valve operations have been performed worldwide on patients of all ages, and about 300,000 are performed in the United States each year.

Valves control the flow of blood through the chambers of the heart. The valves can become damaged from long-term complications of infections, rheumatic fever and birth defects.

In 1960, Dr. Starr, working with the late Lowell Edwards, an engineer, implanted the first successful artificial heart valve. The patient died 10 years later after falling from a ladder.

Earlier, Dr. Starr and other surgeons and engineers had tested valves designed to mimic the mitral valve's natural leaflets. (The mitral valve is situated between the upper and lower chambers of the left side of the heart.) But the devices failed because blood clots commonly formed, often leading to strokes.

Dr. Starr and Mr. Edwards chose a different design — a free-floating ball inside a cage that resembled a bottle stopper patented in 1858 — that hardly resembled a real heart valve. To help prevent strokes and other complications, they prescribed long-term anticoagulant drugs.

The two scientists and other researchers also went on to develop newer valves with leaflets instead of a caged ball.

Mr. Edwards founded what is now Edwards Lifesciences of Irvine, Calif., to make the valves. It was a time when the Food and Drug Administration did not regulate devices.

Because the inventors wanted accurate information about the safety and effectiveness of their valve, they created what the Lasker Foundation said was the first clinical-research tracking system for long-term follow-up of patients carrying implanted medical devices. The researchers restricted sale of the valve to medical centers specializing in heart surgery. The centers, in turn, reported any adverse reactions.

A few among the initial recipients of the valves lived for at least 40 years with those valves, the foundation said.

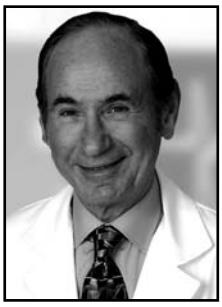
In part to overcome the need for anticoagulant drugs, Dr. Carpentier began research on use of human cadaver valves and adapting pig valves for human use in 1964. He also earned a Ph.D. at the University of Paris to learn ways to strengthen animal valves to increase their durability.

Dr. Carpentier found that a liquid chemical, glutaraldehyde, was better than other substances in sterilizing the tissue, reducing its propensity to cause adverse immunologic reactions and lengthening the valve's use. He also combined the animal tissue with a Teflon coating to create a device that could be produced in large amounts and kept on hospital shelves and that can avoid the need for anticoagulant drugs. Animal tissues account for an increasing percentage of valve replacements that almost equals mechanical ones, the Lasker Foundation said.

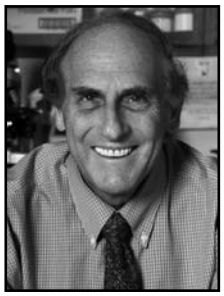
Dr. Carpentier went on to devise a ring that stabilizes and reshapes the area around the damaged valves so they can be repaired, not replaced.

In the 1970s, when most scientists were studying how the body reacted after an invasion by a microbe, Dr. Steinman began focusing on the initial steps of invasion. He discovered a rare cell in mouse spleens that moved in a distinctive way under laboratory conditions. The cell acted differently from other immune cells. For example, long projections emerged

Dr. Anthony S. Fauci



Dr. Albert Starr



Dr. Ralph M. Steinman

Dr. Alain Carpentier

from the cells and floated before they retracted, creating a starlike pattern. He named them dendritic cells after the Greek word for tree.

Although dendritic cells comprise only 1 percent of mouse spleen cells, Dr. Steinman found that they were the most powerful cell in priming the immune system. The dendritic cell can adjust the body's defenses by stimulating different T immune cells.

"No one had anticipated that any cell could so efficiently goad T cells into action," said Dr. Joseph L. Goldstein, the chairman of the Lasker jury and a Nobel laureate from the University of Texas Southwestern Medical Center in Dallas.

Dr. Steinman found that as dendritic cells mature, they migrate from the skin and other tissues to nearby lymph nodes. He and other scientists found that dendritic cells provide a safe haven for the AIDS virus and can transmit it to lymph nodes, helping to spread H.I.V. instead of killing it.

Scientists have found ways to produce large numbers of dendritic cells and are testing their use among cancer patients in 70 trials, Dr. Goldstein said. Scientists are also exploring use of dendritic cells for allergies, autoimmune diseases and in preventing rejection of transplanted organs and tissues.

Dr. Steinman and Dr. Fauci will each receive $150,000 and Dr. Starr and Dr. Carpentier will each receive $75,000.