SPECIAL ANNOUNCEMENT

Anesthesiology
1999; 91:917–9

Warren Zapol: True-life Adventures in Science, Medicine, and Innovation

Recipient of the 1999 Excellence in Research Award

IN 1962, Warren M. Zapol regained consciousness in a hospital in Rawalpindi, West Pakistan, and gazed up at the hat of a physician nun. He had contracted malaria during the MIT Southwest Asian Expedition, in which he and four other undergraduates traveled from Great Britain to Asia performing research along the way. This venture revealed many of the characteristics that have now led to his selection as the recipient of the 1999 American Society of Anesthesiologists Excellence in Research Award: imaginative, even outrageous, vision; first-class collaborators; adequate, if spartan, funding; disregard for personal safety; complete dedication; and unceasing hard work.

Zapol remained hospitalized for 1 month before regaining his strength. But this experience, enhanced by memories of his childhood family physician, caused him to switch his career aspirations to medicine. He applied to medical school while still in the hospital and has not looked back since. After 1 yr at Boston University, he obtained a scholarship and transferred to the University of Rochester. "I have always had great teachers," Warren has stated. "Early influences included Jerome Lettvin and Patrick Wall at MIT; the great respiratory physiologist Wallace Fenn and Alastair Gilles, who attracted me to anesthesiology at Rochester; and Judah Folkman, Jack Norman, and George H. A. Clowes during my surgical internship on the Harvard Surgical Service at Boston City Hospital."

After his internship, Zapol spent 3 yr at the National Institutes of Health working with Theodor Kolobow, who was working with silicone polymers to develop a novel membrane oxygenator. Kolobow's expertise with biomaterials was a perfect match for Zapol's physiologic interests. They successfully performed long-term perfusions of fetal sheep and studied the control of ductal closure. They transferred this technology to adults and premature babies in some of the first long-term partial perfusions in human beings. This was the first instance of a recurring theme in his career: rapid translation of laboratory studies to clinical medicine.

In 1970, Richard Kitz recruited Zapol to Massachusetts General Hospital and Harvard Medical School as an anesthesia resident. He has been there ever since, at least when not on sabbatical in Oxford or Paris; performing research studies in Antarctica, Korea, or Japan; or treating desperately ill, often famous, patients with acute respiratory distress syndrome (ARDS) anywhere on the globe. During his residency, he developed and led labo-

Warren Zapol at the command console of a deep-diving submarine.

Received from Harvard Medical School and the Department of Anesthesia and Critical Care, Massachusetts General Hospital, Boston, Massachusetts. Submitted for publication July 6, 1999. Accepted for publication July 15, 1999.

Address reprint requests to Dr. Lowenstein: Department of Anesthesia and Critical Care, Massachusetts General Hospital, 32 Fruit Street, Boston, Massachusetts 02114. Address electronic mail to: lowenstein@etherdome.mgh.harvard.edu

Key words: ASCCA; circulatory physiology and hemodynamics; critical care; lung function and disease; nitric oxide; nitric oxide synthase; oxygen; oxygen transport.

ratory and clinical programs in extracorporeal membrane oxygenation for ARDS. He quickly advanced up the academic ladder, achieving professorial status in 1985, being appointed to the Reginald Jenney Chair in 1992, and being selected as Anesthetist-in-Chief at Massachusetts General Hospital in 1994.

Zapol's overarching research focus has been ARDS, both adult and neonatal. He led the National Institutes of Health–supported multi-institutional prospective, randomized study of extracorporeal membrane oxygenation for ARDS. This landmark project proved that the adult lung would not regain function after prolonged venoarterial partial bypass, suggesting that just "buying time" for the lung to heal would not suffice. This led him to initiate a quest to define the mechanisms of ARDS, supported for 10 years (1978–1988) by a National Institutes of Health National Heart, Lung and Blood Institute Specialized Center of Research, which he headed. Together with Michael Snyder, Zapol showed that an elevated pulmonary vascular resistance was characteristic of ARDS. With radiologist Reginald Greene, he demonstrated pulmonary vascular obstruction radiologically. With pathologist Lynne Reid, he showed pulmonary vascular obliteration and remodeling, which at times caused severe right heart failure. After recognizing that complement activation and thrombosis produced the catastrophic pulmonary vasoconstriction of protamine reactions, he showed that similar immunologic events led to pulmonary microthrombosis in ARDS.

Stimulated by the late Myron Laver, Zapol searched for a selective pulmonary vasodilator. In 1987, other investigators identified endothelial-derived relaxing factor as nitric oxide, and Warren immediately recognized its potential. He performed whole animal, cellular, molecular, and genetic studies of low-level exogenous nitric oxide. Within 1 yr of starting animal studies of inhaled nitric oxide, he and coworkers Claes Frostell and Jesse D. Roberts began work in severely hypoxemic newborns and soon demonstrated clinical efficacy in meconium aspiration, persistent pulmonary hypertension, and several other causes of neonatal respiratory distress. He takes great pride in noting that since 1992, the number of neonatal extracorporeal membrane oxygenation perfusions have declined by half as nitric oxide inhalation together with other advances has been used in hypoxemic newborns. Other studies followed those of neonatal inhalation with William Hurford and Luca Bigatello, demonstrating efficacy in many adults with ARDS. Along with collaborators Alvin Head, Marc Semigran, and Kenneth Bloch, Zapol has now expanded his studies of nitric oxide to other important diseases, including sickle cell anemia, congestive heart failure, and ischemic heart disease. The trajectory of his research productivity continues to accelerate.

As if this were not sufficient to keep one person occupied, he has made noteworthy contributions to comparative and environmental physiology and has led nine expeditions to Antarctica. He has been particularly fascinated by the Weddell seal, which can hold its breath for over an hour on dives up to 600 m deep beneath the ice, and has pursued the innovative question of whether the ability of this animal to function while severely hypoxemic might provide clues to enhance the care of humans. His elegant studies have provided many insights into the mechanisms by which this remarkable mammal can stay submerged and physically active for long periods, can surface rapidly without suffering the bends, and why the seal fetus is not harmed when its mother dives. For example, he and his coworkers demonstrated that the metabolism and circulation of the seal responds differently to "laboratory dives" (submersion of the head) than to free dives, that the spleen acts as a contractile reservoir of oxygenated red blood cells to increase arterial oxygen content during dives, that the combination of a flexible rib cage (which allows the lung to collapse at high pressures) together with a rigid tracheobronchial system keeps blood nitrogen content sufficiently low to avoid nitrogen narcosis at depth and prevent nitrogen bubbles (bends) upon ascent. Characteristically, after investigations in marine mammals, he performed comparable studies of human female "Ama" breath-hold divers of Korea and Japan. His interdisciplinary, international Antarctic research teams have included young investigators Robert Schneider, Roger Hill (physics), Jesper Qvist (Denmark), Konrad Falke (Germany), and numerous others. He is now planning his 10th Antarctic trip for the austral summer of 2000, this time in unaccustomed luxury as a guest lecturer accompanied by his wife, Nikki, on a cruise sponsored by the Harvard Museum of Comparative Zoology.

Warren has influenced and expanded the research horizons of mature scientists such as G. C. "Monty" Liggins (obstetrics/gynecology); Peter Hochachka (comparative biochemistry), and Su Ki Hong (physiology), and has attracted young people from many disciplines to initiate research careers as his disciples. He speaks eloquently of the need to foster "the youngsters" and exemplifies the model of a mentor. He has won many honors, including the United States Antarctic Service Medal and election to the Felix Fleishner Radiology So-

ciety and the Explorers Club of New York. The most selective peer-review processes have funded his research; his scientific articles are published in the most discriminating journals. He is an indefatigable editor who has produced seven books, including three in the series "Lung Biology in Health and Disease" and a textbook of critical care in its second edition, and serves as contributing editor to *The Biologic Foundations of Anesthesia*. He heads one of the world's great academic departments of anesthesiology with passion and commitment.

In his 1983 Rovenstine lecture, Arthur Keats stated, "Anesthesiology is at its best when the observations it makes contribute benefits to medicine at large." Warren Zapol's research admirably demonstrates this trait. It is therefore no surprise that he has been chosen to receive this year's award.

Edward Lowenstein, M.D.
Henry Isaiah Dorr Professor of Anaesthesia
Professor of Medical Ethics
Harvard Medical School
Provost
Department of Anesthesia and Critical Care
Massachusetts General Hospital
Boston, Massachusetts