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## PASSING THE TORCH: INFECTIOUS DISEASE RESEARCH

*Two hundred years of continuous scholarship, coupled with outstanding people who have taught and studied here, provide the browser in Harvard Medical School history with many accounts of direct lines of research carried forward through several generations of faculty and students. Senior scientists nurture younger ones, who build on their mentors' contributions, and in turn the former protege becomes the next patron. With this issue, Perspectives inaugurates a regular feature highlighting some of the contemporary lines down which 'a torch has been passed' to a current research effort at HMS. This time the subject is infectious diseases, and the torch-bearers are Maxwell Finland '26, Edward Kass, and Dennis Kasper.*

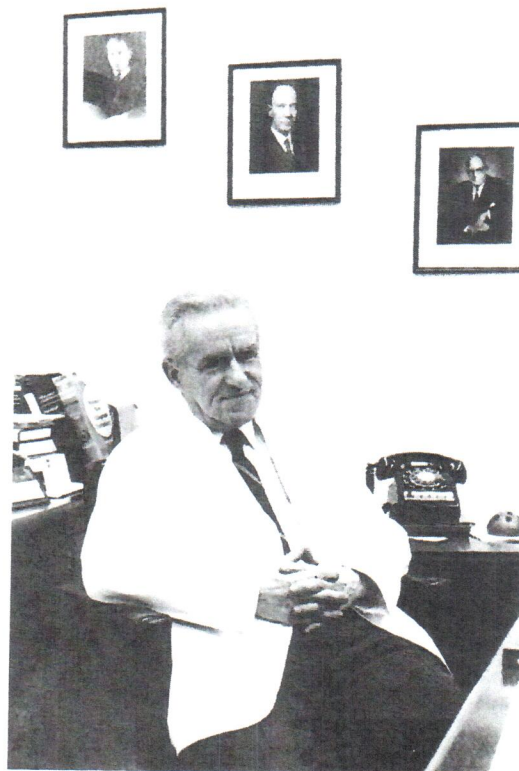
*One way of looking at Max Finland's life is as the quintessential American immigrant's success story.*

There are many ways to praise Maxwell Finland—as one of the greatest infectious disease pioneers, as the supremely dedicated patients' physician, as inspiration and mentor to dozens of younger investigators who have seeded medical research across America, and as perhaps the most authoritative voice on antibiotic drugs. While it is for his benchmark scientific achievements Max Finland will no doubt be remembered, another way of looking at his life is as the quintessential American immigrant's success story.

Born in Russia in 1902, he was brought to the United States as a child. Paying for some of his schooling by teaching at a Hebrew school in his North End neighborhood of Boston, he took his bachelor's degree from Harvard College

in 1922, became a U.S. citizen in 1925, and was awarded his M.D. from HMS in 1926. He worked up through the ranks in the Boston City Hospital's Harvard unit to become, in 1963, George Richards Minot Professor of Medicine and Director of the Second and Fourth (Harvard) Medical Services, thereby succeeding the illustrious William B. Castle as Director of the Thorndike Memorial Laboratory.

He began his extraordinary career in an unprepossessing corner of the pneumonia ward at City Hospital, from which base he lived, slept, worked, and conducted the first in his long series of studies of infectious diseases, a pioneering work in the serum treatment of pneumococcal pneumonia. In that pre-antibiotic era, this disease was treated with individualized antisera, an excruciatingly painstaking process. With great patience and dedication, Max Finland worked out the best methods of serum treatment. (Although he eventually



*Maxwell Finland*

bought a suburban home, he never really occupied it, spending most of his nights for 50 years in a small room at the hospital.)

It was he and his colleagues who recognized the importance of cold agglutinins to the clinical diagnosis of atypical pneumonia. In collaboration with a number of co-workers and fellows, he conducted the early clinical trials of many antimicrobial agents; identified the increasing resistance of bacteria to antibiotics in relation to their usage; recognized the dangerous potential of secondary invasion of the lungs by staphylococci during influenza epidemics; demonstrated the chemical identity of some antibiotics purely on the basis of microbial studies; recognized staphylococcal enteritis as a result of the alteration of the intestinal flora by broad-spectrum antibiotics; and, with Edward Kass, clearly characterized the role of ACTH and cortisone in infection.

Through the years, Dr. Finland has been showered with awards and honors, and in 1982, the year of the Harvard Medical School Bicentennial, Harvard University conferred on him an honorary Doctor of Science degree.

*Edward Kass and colleagues showed the probable cause of the association between toxic shock and highly-absorbent tampons.*

Not all of the promising young investigators tutored by Dr. Finland scattered to other locales. Edward H. Kass, now the William Ellery Channing Professor of Medicine and Director of the Channing Laboratory, is one who remained with Harvard. His years with Dr. Finland began when the Channing Laboratory was a part of the Boston City Hospital. One of their earliest projects together was to work out the role of the corticosteroids in resistance to infection.



*Edward Kass*

Dr. Kass's research interests have been broad-ranging, but his best-known work is on urinary infections. He was one of the first to suggest a quantitative approach to the study of urinary infections, developing a simple, inexpensive technique for such study, and using it in extensive epidemiological and experimental studies. One series demonstrated the high incidence of bacteriuria in asymptomatic patients, especially females. He showed most pyelonephritis of pregnancy could be prevented by adequate treatment of asymptomatic bacteriuria. A preventive effect on neonatal mortality and low birth weight was also demonstrated.

An interest in hypertension led Kass to explore various facets of its epidemiology, developing evidence suggesting that it may begin in early childhood. Other work helped to show that even mild hypertension in adults should be treated to prevent detrimental effects

on organ systems. Later investigations broadened to include the familial nature of hypertension, and the late consequences of relatively asymptomatic infections.

Dr. Kass was a founding member of the Infectious Diseases Society of America, and founding editor of the *Journal of Infectious Diseases (JID)*. In 1979 he launched a new journal, *Reviews in Infectious Diseases*, and as a parting tribute, the JID dedicated the December 1978 issue to him, with Maxwell Finland as guest editor, and papers from Kass' former colleagues and fellows.

This year he stirred national attention by providing a scientific explanation for the association of toxic shock syndrome with the use of menstrual tampons. His group identified the magnesium-binding capability of certain highly-absorbent tampon fibers as the key to the phenomenon, and showed that production of staphylococcus toxin is maximized in the low-magnesium vaginal environment created by these magnesium-binding fibers.

Dennis Kasper, an emigre from Illinois, came to the Peter Bent Brigham Hospital as senior resident in 1972. He

*Dennis Kasper*



began work with Dr. Kass at the Channing Laboratory, becoming Associate Director within a few years and head of infectious diseases at Beth Israel Hospital in 1981. He is the 1985 winner of the Squibb award to the outstanding infectious disease investigator under 45. He has made major contributions to understanding bacterial pathogenesis and the importance of various components of bacteria to the immune response and to the causes, prevention, and treatment of infectious diseases.

In collaboration with Dr. Carol Baker, he developed a vaccine against group B Streptococcus, which causes meningitis in 2,000-15,000 newborns yearly, death in 35-40 percent of those cases, and serious neurological disorder in many others. A preliminary test in humans of a vaccine against one strain of group B Strep, published in 1978, proved to be safe and to raise antibodies against the organism. Since then, they have developed vaccines for the other four strains of group B Strep, which have been used in Phase I FDA trials on human volunteers.

Dr. Kasper's other major work has been on the anerobic bacterium *B. fragilis*, a common cause of sepsis and abscess in trauma victims and surgery patients. He has examined its virulence, its structure, and the requirements of a vaccine that could protect those at high risk for infection with it, such as military recruits.

His work has changed basic thinking about this class of bacteria and the regulation of immune mechanisms against it, shed light on bacterial structure in general, and showed which fraction of *B. fragilis* is responsible for the infection. Surprisingly, immune studies showed that antibody to *B. fragilis* was not protective, but that T cells from immune animals conferred protection.

Dr. Kasper was just appointed to Professor of Medicine at HMS.