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HERBERT L. DUPONT, MD

Recipient of the 2007 Maxwell Finland Award for Scientific Achievement

ext to respiratory infections, diarrhea is one of the most commonly reported illnesses in the US. By one estimate it occurs about four times a year in most individuals. Travelers world wide are plagued by the problem—estimated to affect 20 million persons a year. In underdeveloped coun-

tries, diarrhea is the leading cause of deaths in children under five years of age—over 1.5 million a year.

These figures illustrate the magnitude of the disorder, and in turn, measure the impact of the research into its causes and treatments that have been the central focus in the career of Herbert L. DuPont, MD, this year's Maxwell Finland Award recipient. "While documenting the efficacy of antimicrobial agents in the treatment and prevention of travelers' diarrhea, he has, nearly sin-

gle-handedly, kept one step ahead of antibiotic resistance emerging in the developing world," says Charles D. Ericsson, MD, head of clinical infectious disease at the University of Texas Medical School, Houston.

Dr. DuPont became interested in infectious diseases in 1966 while he was a resident at the University of Minnesota under the supervision of Dr. Wesley Spink. "Dr. Spink's studies convinced me to pursue infectious diseases as a career. He taught me the concepts of hard work, productivity, and excellence in research," Dr. DuPont comments.

He recalls what it was like to analyze data in the precomputer age. One of his jobs was analyzing the medical records of 860 patients with gram negative sepsis. "I had the clinical information on unisort cards, the data for each patient punched on the edge of the card. Using a long needle inserted through the various holes of these cards I determined which patients were positive for a

> particular finding. It was quite a task to count the various cards accurately, by each parameter, by hand!"

> At that time, when physicians were subject to the draft, Dr. DuPont, as did many physicians in training, fulfilled his service obligation by joining the Centers for Disease Control and Prevention as an Epidemic Intelligence Officer. "I was interested in a career in academic medicine" he says. "I felt this was a better experience than military service."

He was assigned to the Division of Infectious Diseases at the University of Maryland in Baltimore, where he worked on the pathogenesis of bacterial and viral diarrhea and on the epidemiology of enteric infectious diseases, topics that have become the central focus of his career. As a member of the CDC's team of investigators, he traveled to sites of emerging epidemics around the world and helped develop vaccines for infec-

"Our research was aimed at answering practical and clinically useful questions," he says. "We worked on a

tious causes of diarrhea.

group of low dose diarrheal pathogens such as *Escherichia coli*, typhoid fever, *shigellosis*, *cryptococcus*, and Norwalk virus as well as the immunology of diarrheal diseases."

His studies demonstrated the development of significant acquired immunity to *E. coli* and the usefulness of fecal leucocyte studies as a method of diagnosing inflammatory diarrhea among children living in developing countries.

"Dr. DuPont has been a pioneer in this field," says Dr. A. Clinton White,

professor of infectious diseases at Baylor College of Medicine in Houston, Texas. "He has played a critical role as a mentor to numerous leaders in infectious diseases and in travel medicine."

After completing his CDC service in 1969, Dr. DuPont joined the faculty of the University of Maryland, initially as an Instructor and later as Associate Professor of Medicine in the University's Division of Infectious Diseases.

In 1973 he went to the University of Texas Medical School in Houston, where he became the first director of

a new program in infectious diseases and clinical microbiology. He assembled a team of laboratory scientists, pediatricians, and internists to work on various aspects of diarrheal diseases. In 1995 he became Chief of the Internal Medicine Service at St. Luke's Episcopal Hospital and joined Baylor College of Medicine as Vice Chairman of the Department of Medicine—positions he holds today.

Dr. DuPont describes his approach to research in infectious diarrhea as a coupling of laboratory research tech-



niques to field population studies. His work has taken him to Mexico, Peru, Egypt, Jamaica, Zambia, Kenya, and India. In Houston, he established a volunteer program to study the immunology and pathogenesis of enteric infectious diseases in humans.

Dr. DuPont's international studies, which have major public health implications, have focused on the epidemiology, immunology, clinical features, prevention, and therapy of diarrheal diseases.

The outcome of these studies has

been a series of ground-breaking papers on diarrhea, its causes, diagnosis, and treatment. Every year Dr. DuPont takes a team of graduate students to Mexico where they work on the causes and prevention of diarrhea. In studies of the development of immunity to *Shigella* and enterotoxigenic *E. coli*, they showed that individuals acquire immunity to the agents that are circulating in the geographic areas in which they live for a period of time. "These studies and others served as the basis of current vaccine strategies for both these enteric infections," Dr.

DuPont says.

In Mexico, Dr. DuPont and his associates showed that very low doses of *Shigella* and *Crytosporidium* could infect healthy individuals, explaining the tendency of these two organisms to spread by person-to-person transmission. Dr. DuPont noted that the dosage data he obtained from the *Cryptosporidium* studies could be used to set adequate and safe water treatment standards in the US.

Tap water in Mexico was identified as the main culprit carrying viral pathogens including rotaviruses and the cause of diarrhea in Mexican infants and children, mimicking the diarrhea that travelers, not just to Mexico but also to countries such as India and Kenya, frequently experience.

His studies showed that bacterial agents are responsible for approximately 85% of cases of traveler's diarrhea, and that contaminated food was the main source of these pathogens. In addition, they found that water accounted for 10% of cases of viral gastroenteritis and that samples of tap wa-

ter were contaminated with enteric viral pathogens. Current recommendations on the treatment and chemoprophylaxis for traveler's diarrhea are based on these studies.

Over the years, Dr. DuPont developed a body of knowledge on what is popularly called traveler's diarrhea, the most common health problem among travelers from industrialized countries visiting developing countries.

Diarrhea has long been a problem for civilian and military travelers alike because they often have no immunity

to the pathogens to which they are exposed. Between 50% and 70% of visitors to countries such as India and Kenya where there is a high risk of exposure to pathogens will acquire diarrhea and 45% will become incapacitated.

Traditionally the condition has been treated with antimicrobials, but since the 1980's there have been reports of the development of resistance to these agents. When Dr. DuPont and his associates showed that a semi-synthetic antibiotic, rifaximun, that does not result

Dr. DuPont has been a pioneer, as well as a mentor to numerous leaders, in infectious diseases and in travel medicine in the development of resistance can be used to treat traveler's diarrhea, it was a major advance in the treatment protocol. Unlike other antibiotics, rifaximun remains in the gastrointestinal tract, so organisms causing diarrhea do not develop resistance. In a number of studies in Mexico, the Caribbean, Africa, and India they showed that rifaximun can be used to treat traveler's diarrhea caused by a number of different organisms. The drug was approved by the Food and Drug Administration in 2004.

In a study among US students in Mexico Dr. DuPont showed that less than 15% of a group given a daily dose of rifaximun experienced diarrhea compared with over 50% of a placebo-treated group. The effectiveness, lack of side effects, and ability of rifaximun to avoid the development of resistance, indicates "that rifaximun is an ideal drug for the prevention of traveler's diarrhea," Dr. Dupont says. His work on traveler's diarrhea led, it seems logically, to his interest in the general health of travelers, and he was one of the founders of the International So-

ciety of Travel Medicine and its first president.

Dr. DuPont has received numerous awards and honors for his contributions to scientific research and infectious diseases and has served on the boards of many prestigious organizations. He was a member of the National Foundation for Infectious Diseases Board of Directors from 1981–2002 serving as President from 1997–1999, and is a Past President of the Infectious Diseases Society of America.

