

Walker's Cay Colloquium Catalyzes Work on Cancer Vaccines and Immunotherapy

3rd Annual Sabin Institute-Sponsored Meeting Convened in March at Walker's Cay, Abaco, Bahamas

Thirty of the world's leading cancer vaccine scientists spent three days in intense, unusually open discussions of their newest research data and ideas at the Sabin Vaccine Institute's Third Annual Walker's Cay Colloquium on Cancer Vaccines in March. Their goal was to accelerate progress toward development of vaccines to treat and prevent various forms of cancer. Most of the renowned scientists reported learning new information that will speed their own research. Several said they formed new, multi-institution collaborations at the meeting.

Ralph A. Reisfeld, professor at The Scripps Research Institute in La Jolla, California, and co-chair

of the colloquium, said the meeting "was a great success since it provided an excellent opportunity for top scientists in the field of tumor vaccines and immu-



Thirty leading cancer vaccine scientists exchanged their latest ideas and data at Walker's Cay. A list of attendees is provided on page 11.

notherapy to learn from each other and to discuss issues that are critical for the improvement of cancer treatments." Jeffrey Schlom, head of the Laboratory of

Tumor Immunology and Biology at the National Cancer Institute also served as co-chair. The Walker's Cay Colloquium follows a peer review format; emphasizing an unusually open discussion of ideas and data so new they have not yet been published. It is multidisciplinary, involving experts in oncology, immunology, microbiology, biochemistry, hematology and several other fields. It differs from most scientific meetings of large numbers of people in a single discipline who

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Don L. Douglas Named President and Chief Executive of the Sabin Vaccine Institute

New President Will Draw Upon Immunization Program Leadership Experience to Increase Institute's Impact

The Albert B. Sabin Vaccine Institute has named Don L. Douglas as its new president and chief executive. Douglas joins Sabin as the scope of the Institute's programs and its influence on public progress and scientific research are growing. His appointment was announced by Institute founder and chairman H. R. "Shep" Shepherd.



Don L. Douglas will serve as Institute President and CEO.

velopment of successful immunization programs," Shepherd said. "He was selected following an extensive search. The Board is confident we have chosen the right person to keep Sabin on its upward trajectory of stimulating development of new vaccines and increasing immunization rates. His extensive international experience enhances the Institute's ability to catalyze global disease prevention efforts."

"Don Douglas brings to the Sabin Vaccine Institute a wealth of experience in organizational leadership and the de-

velopment of successful immunization programs," Shepherd said. "He was selected following an extensive search. The Board is confident we have chosen the right person to keep Sabin on its upward trajectory of stimulating development of new vaccines and increasing immunization rates. His extensive international experience enhances the Institute's ability to catalyze global disease prevention efforts."

Health (PATH) where he served in several positions for 16 years, most recently as country director and Asia regional

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**VIEW
POINT**

The Other Hainan

Hainan Is Home to the Highest Concentration of Endemic Tropical Diseases in China

(This opinion originally appeared in The Advocate, a Stamford, Connecticut newspaper.)

The collision at the end of March between a Chinese F-8 fighter and an American Navy EP-3 electronic reconnaissance plane over the tropical island of Hainan threatens to cast a Cold War-style shadow over diplomatic relations between China and the Bush administration. Yet most Americans may not appreciate that Hainan is also one of China's poorest provinces and among the most destitute regions in Southeast Asia. The province is heavily plagued by a variety of tropical infectious diseases ranging from malaria to mosquito-borne viruses. Our medical parasitology research laboratory has worked in Hainan since 1998 when we first realized that there are more intestinal parasites in Hainan than just about anywhere else on the planet. Based on diagnostic examinations conducted on thousands of Hainan residents during a medical survey of the island in the early 1990s, the Chinese Ministry of Health reported that 94 percent of the population harbors at least one intestinal parasite. This includes more than 60 percent of the population infected with parasitic worms, including *Ascaris* roundworms, *Trichuris* whipworms and *Necator* hookworms. In many cases, it is common to find residents of Hainan who harbor all three examples of this "unholy trinity." All too frequently children are the ones most heavily infected. As a consequence they suffer from malnutrition, physical growth stunting, and intellectual retardation. In many cases, the children of Hainan may experience life-threatening acute intestinal obstruction or perforation that result from the activities of large numbers of these worms.

In order to help alleviate the enormous burden of disease in Hainan, our National Institutes of Health, as well as the March of Dimes Birth Defects Foundation is sponsoring joint research projects

to examine the impact of intestinal parasites on the populations of southern China, especially Hainan. Our work there is being conducted jointly with the Institute of Parasitic Diseases of the Chinese Academy of Preventive Medicine. In an unusually close cooperative effort we are learning why some people living in Hainan might be resistant to these parasites. We are using the information to design a novel vaccine in order to combat parasitic worms. In at least one instance our project took us to Lingshui county—not too far away from where the disabled EP-3 aircraft sits on the tarmac. The work is hard and difficult; it has required lots of mutual give and take on both sides. One of the many benefits of the collaboration is its requirement for regular scientific exchanges to each country. Over the last few years we have built a strong scientific collaboration and close friendship.

Enormous good will has developed between the members of my laboratory and our Chinese friends and colleagues during the last few years. We are driven and touched by the enormous burden of disease that the people of Hainan face on a daily basis. We also recognize that infectious diseases are potential threats to everyone, even in the U.S. The events of the last few days should not distract us from the fact that we have much in common with the Chinese, and much to gain by continued peaceful and meaningful cooperation. We have learned that an anti-worm vaccine makes for a terrific instrument of diplomacy.

—by Peter J. Hotez, MD, PhD, FAAP

Peter J. Hotez, MD, PhD is professor and chair of the Department of Microbiology and Tropical Medicine, The George Washington University, and senior fellow of the Albert Sabin Vaccine Institute. He is also visiting professor of the Institute of Parasitic Diseases of the Chinese Academy of Preventive Medicine in Shanghai.

A Letter from the President



It is indeed a pleasure to be joining the Albert B. Sabin Vaccine Institute. The Sabin name has had a special significance for me since 1964 when my grade school in a small town in South Florida hosted the entire community to receive Dr. Sabin's oral polio vaccine. School was closed that day—a day dedicated to disease prevention.

We have now enjoyed 45 years of protection against polio thanks in large part to Dr. Sabin. The world is full of opportunity now for all those who would have suffered the frightening and seemingly random onset of polio. I vividly remember the leg braces and iron lungs that are forever associated with polio in my generation but thankfully are no longer a prominent part of our mental landscape.

This is truly an exciting time for the science of vaccine development. In the coming years, we can anticipate the introduction of a number of new and improved vaccines that have the potential to further reduce the tragic and unnecessary disease and death associated with vaccine-preventable diseases, and to dramatically improve the quality of life worldwide.

I come to the Sabin Vaccine Institute having worked in public health for the past 21 years, 15 of which were in Southeast Asia. In Thailand, Indonesia, Vietnam, and other countries throughout the region, I witnessed firsthand the challenges of delivering immunization programs in developing countries.

My work involved technology transfer introduction of new vaccines—rabies, hepatitis B and *Haemophilus influenzae* B—and vaccine-related technologies—autodestruct syringes and needles, cold-chain equipment, and vaccine vial monitors. I also worked on regulatory approvals, achieving integra-

tion of new vaccines within the Expanded Programme on Immunizations system, and on solving logistical, economic and management obstacles that hindered the effective delivery of immunization and other public health services.

I look forward to working on the other end of the immunization spectrum at the Sabin Institute—advancing vaccine development, influencing vaccine-related policy, and promoting vaccine acceptance. Please join us in helping make immunization programs more effective and widespread. If you have any suggestions for how we can better serve the vaccine community and general public, please do not hesitate to contact me, or anyone on the staff at the Sabin Institute.

Don L. Douglas, President
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Don L. Douglas Named President and Chief Executive of the Sabin Vaccine Institute

Board Is Confident Douglas Will Keep Institute on Upward Trajectory

Continued from page 1

advisor, based in Jakarta, Indonesia. He has worked 21 years in public health, including 15 years in Southeast Asia (Thailand, Indonesia and Vietnam), where he managed multifaceted programs including trials of hepatitis B and *Haemophilus influenzae* B vaccine, and the evaluation, introduction and technology transfer of auto-destruct syringes, vaccine vial monitors and other immunization-related technologies.

“The Sabin Vaccine Institute has built a track record of accomplishment on several fronts, and I am excited about the opportunity to increase our impact on new vaccine development and increasing vaccination rates in the U.S. and throughout the world,” Douglas said. “Millions of people lose their lives each year to diseases for which vaccines exist or are in development. The biotechnol-

ogy revolution is rapidly giving us new tools to prevent disease. We must work with industry, government, academia and other nongovernment organizations to arm all nations with these weapons against deadly and debilitating diseases.”

In 2000, the Institute embarked upon a substantial program expansion when it launched a program to develop a vaccine to prevent hookworm infection, which afflicts more than one of every five people in the world. Its other programs accelerate cancer vaccine research, stimulate new ideas and policy proposals to make vaccines more accessible in developing countries, and inform Americans about the importance of immunization.

Douglas earned a bachelor's degree at Georgia State University and an MBA from The George Washington University. Following a brief stint in magazine

publishing in Hong Kong and Atlanta, he shifted into public health in 1979, initially promoting health and physical education in the U.S. for a Washington, D.C.-based trade association. He then joined the National Council for International Health (now the Global Health Council) editing *International Health News*. In 1984, he joined PATH, a nonprofit agency that develops and improves access to technologies to improve women's and children's health, primarily in developing countries.

Douglas will work in the Institute's new Washington, D.C. office. The chairman's office and administrative staff are in New Canaan, Connecticut. The Hookworm Vaccine Initiative is managed from the Institute's Rockville, Maryland office, with research conducted at The George Washington University Medical Center and other locations.

Vaccine Developer John B. Robbins Receives Albert B. Sabin Gold Medal

Developer of Vaccines for Meningitis and Pertussis Recognized

John B. Robbins, who played central roles in the development of vaccines to prevent *Haemophilus influenzae* B (Hib), a leading cause of meningitis, and pertussis (whooping cough), is the ninth recipient of the Albert Sabin Gold Medal. The Albert B. Sabin Vaccine Institute awards the medal annually to an exemplary contributor to disease prevention. Robbins is chief of the Laboratory of Developmental and Molecular Immunity at the National Institute of Child Health and Human Development in Bethesda, Maryland.



The Sabin Vaccine Institute awarded John B. Robbins the Albert B. Sabin Gold Medal on April 23, 2001. Philip K. Russell applauds as Dr. Robbins is congratulated by Heloisa Sabin.

LEADING LIGHT FOR VACCINE RESEARCH

“John and his colleagues have been the pointers of the vaccine hunt,” George R. Siber, MD, chief scientific officer of Wyeth Lederle Vaccines, told several hundred scientists at the medal presentation ceremony. “John’s work has led directly to at least three licensed vaccines: the Hib tetanus toxoid conjugate, the Vi-polysaccharide based typhoid vaccine and the pertussis toxoid vaccine. His work also contributed in a major way to

the meningococcal C conjugate vaccine introduced in the United Kingdom in 1999 and to the pneumococcal conjugate which became available to all U.S. children last year and is now being introduced in Europe.”

Siber described the Hib conjugate vaccine as Robbins’ “crowning accomplishment. Hib was the most important cause of bacterial meningitis with terrible complications of hearing loss, paralysis, mental retardation and death. When many of us [physicians] began our training, it was one of the most common and serious infections for which babies were hospitalized. The disease has now essentially disappeared in every country that has introduced the vaccine.”

A MAN ON A MISSION

“John Robbins is an extraordinary physician, scientist and public servant,” said H. R. Shepherd, chairman of the Sabin Vaccine Institute. “His entire career has been devoted to continuing Albert Sabin’s quest to conquer disease with vaccines and immunization.” Shepherd commended Robbins’ “lifelong commitment to disease prevention. At a time in his life when most people sit back and reflect on the past, he is charging ahead to develop several new vaccines. He is a man on a mission and that mission is to protect people all over the world from deadly diseases.”

John B. Robbins—

He is a man on a mission and that mission is to protect people all over the world from deadly diseases.

PHYSICIAN, SCIENTIST, EDUCATOR

Before joining the National Institutes of Health in 1970, Robbins was assistant professor of pediatrics and microbiology at the University of Florida, and associate professor of pediatrics at the Albert Einstein College of Medicine. Between those faculty appointments, he did research at the Weizmann Institute for Sci-



John B. Robbins with Heloisa Sabin following the Sabin Gold Medal presentation ceremony in Arlington, Virginia.

Albert B. Sabin Gold Medal Presentation

Former Winners Return to Recognize Latest Recipient, John B. Robbins

ence in Rehovot, Israel.

Early in his career, Robbins teamed with Rachel Schneerson in 1968. They have worked together on vaccine devel-

opment ever since. Their new vaccine for typhoid fever recently achieved 92 percent efficacy in two-year-old children.

Currently, their laboratory is developing vaccines for non-typhoidal Salmonella, *Shigella*, *Escherichia coli* 0157, *Clostridium difficile* and anthrax. Based on the success of their *Staphylococcus aureus* vaccine in preventing bacteremia in hemodialysis patients, Robbins and Schneerson's research team is planning to develop a vaccine for opportunistic pathogens.

The prestigious prize was presented to Robbins during the 4th Annual Conference on Vaccine Research on April 23 in Arlington, Virginia.



Noted vaccinologist Lance Gordon talks with two Sabin Vaccine Institute trustees, Almedica International CEO Edward S. Neiss, and Lewis A. Miller, CEO of Intermedica, Inc., before the Sabin Gold Medal presentation.



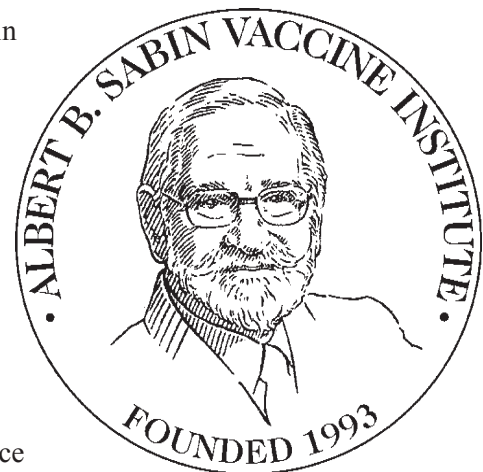
H.R. "Shep" Shepherd with Melinda Moree of the Program for Appropriate Technology in Health and Connie Russell at the Sabin Gold Medal reception.



From left, Philip K. Russell, Heloisa (Mrs. Albert B.) Sabin, George R. Siber, and John B. Robbins.



Two previous recipients of the Albert B. Sabin Gold Medal, Giro A. de Quadros (2000), of the Pan American Health Organization, and Myron M. Levine (1988), of the University of Maryland School of Medicine, compare notes on vaccine research and development.



PREVIOUS RECIPIENTS OF THE ALBERT SABIN GOLD MEDAL

- D.A. Henderson
Johns Hopkins University
- Robert M. Chanock
National Institutes of Health
- Joseph L. Melnick
Baylor College of Medicine
- Maurice R. Hilleman
Merck & Co., Inc.
- Myron M. Levine
University of Maryland
- Allen C. Steere
Tufts University
- Philip K. Russell
Johns Hopkins University
- Ciro A. de Quadros
Pan American Health Organization

Institute to Honor Bertrand and Rowe for Humanitarianism and Leadership

Awards Dinner in New York City to Benefit Sabin Research and Education Programs

The Sabin Vaccine Institute will present its two highest non-science awards to Jean-Jacques Bertrand, chairman and chief executive officer of Aventis Pasteur, and John W. Rowe, MD, chairman, president and chief executive officer of Aetna Inc. Bertrand will receive Sabin's Humanitarian Award and Rowe will receive the Institute's Lifetime Achievement Award at a May 31 dinner at the Pierre Hotel in New York City.

Bertrand will be recognized for his "career-long leadership to improve human health," according to Institute Chairman H. R. Shepherd. This leadership is exemplified by his company's role in the global polio eradication campaign. "Mr. Bertrand and Aventis Pasteur have taken extraordinary measures to ensure that the polio vaccine reaches all of the people who need it, even the least fortunate in the farthest corners of the world," Shepherd said.

Rowe was chosen for successfully leading Mt. Sinai NYU Health through major changes in healthcare economics that cast many academic medical centers into dire straits, and for bringing a commitment to preventive health care to the helm of Aetna, which manages health and related benefits for over 19 million Americans. Rowe was president and CEO of Mt. Sinai NYU Health prior to joining Aetna in September 2000. "Jack Rowe is widely regarded as a special leader with a clear vision and the ability to articulate it and get others to support it," Shepherd commented.

Before the global polio eradication campaign began in 1988, about 1,000 children a day were paralyzed from polio, according to the World Health Organization. Thanks to immunization, the number today is less than 20. Over the same period of time, the number of

countries reporting polio cases has dropped from 125 to about 20, mostly in Asia and Africa. The disease has been eradicated from the Americas and Europe. Still, as long as the disease exists and is transmitted in any country, all countries must continue to vaccinate their entire populations against the easily transmissible disease.

Aventis Pasteur has donated approximately 90 million doses of oral polio vaccine (OPV) to African countries since 1997 to support the global eradication effort. In October 1999, the vaccine research and manufacturing company committed to donate 50 million doses of OPV to five war-torn countries—Angola, Liberia, Sierra Leone, Somalia and South Sudan. The size of the donation was designed to cover those countries' entire vaccine needs for national immunization days during which every child in a country under age five is vaccinated.

The WHO and its global polio eradication campaign partners set 2005 as their new goal to rid the world of the paralyzing and sometimes lethal disease. As with smallpox, which was eradicated in 1979, once polio is wiped out, vaccination is expected to be discontinued around the globe.

"For Jean-Jacques Bertrand, the bottom line is measured not just in dollars, francs or euros, but in terms of impact on humanity," Shepherd said. "Mr. Bertrand's company has played a vital role in the ongoing effort to rid the world of polio, as a major producer of the vaccine for sale throughout the world and as a major donor of the vaccine to economically-challenged countries." But it was not just the donation of tens of millions of doses that impressed the Sabin Institute. "At a time of intense pressure from Wall Street for pharmaceutical companies to limit capital outlays,

Mr. Bertrand committed to add manufacturing capacity for polio vaccine—a vaccine that the world will stop using in a few years, after the global eradication campaign is completed. Shepherd called Bertrand's decision "extraordinary" and worthy of note by world leaders.

Senior officials from several of the countries and agencies involved in the polio eradication effort will attend the dinner in Bertrand's honor.

As president of the Mt. Sinai Hospital and the Mt. Sinai School of Medicine, Rowe steered the New York City institutions through a period of financial distress for most academic medical centers brought on by managed care, restrictions on federal medical care reimbursements and increased costs associated with research, teaching and patient care. He established the Mount Sinai Health System, which grew to be the largest integrated healthcare system in the greater New York region.

Rowe led the successful merger of Mount Sinai with NYU Medical Center in 1998, becoming president and CEO of the five-hospital organization, which has \$1.8 billion in revenue and 31,000 employees. He is a distinguished physician, having founded the Division on Aging at Harvard Medical School and served as chief of Gerontology at Beth Israel Hospital in Boston

before going to Mount Sinai. He is a member of the Institute of Medicine.

When Aetna announced Rowe's appointment as CEO, then-chairman William H. Donaldson called Rowe, "an outstanding choice to help Aetna accomplish its strategic goal of improving its financial performance by remaking its business model to meet consumer demands for choice and flexibility, and en



Jean-Jacques Bertrand



John W. Rowe

Continued on page 15.

Conference on Vaccine Research Features Exciting Developments

Sabin Vaccine Institute, NIAID, CDC, FDA, ISV, USDA, WHO Collaborate on NFID-Sponsored Vaccine Conference

Nearly 500 scientists who participated in the Fourth Annual Conference on Vaccine Research on April 23 to 25 in Arlington, Virginia heard both expected and unexpected reports. They expected epidemiological and clinical confirmation of the lifesaving effects of both familiar and new vaccines and they were not disappointed. They may not have expected the important advances reported in the broad

application of vaccines to diverse noninfectious diseases such as cancer, atherosclerotic cardiovascular disease, inflammatory autoimmune diseases such as multiple sclerosis and even gastric ulcers. They were informed of news as different as the activation of dendritic cells in an anti-tumor vaccine by a glycolipid extracted from sea sponges off the coast of Japan, oral vaccines from a transgenic line of potatoes, to the very successful development of a new conjugate Meningococcus Group C vaccine by a public-private sector consortium that has immunized the 15 million target youthful candidates in the United Kingdom with a dramatic impact on reduction of Group C meningococcal disease and mortality.

Nonetheless, it was recognized again that despite steady progress in the sciences upon which vaccinology is based, an effective vaccine for HIV remains unavailable. Progress in molecular biology has been prodigious and these advances have permitted new understanding which has translated into HIV vaccine clinical trials: 70 Phase I clinical studies are now in process, five Phase II clinical evaluations and two Phase III clinical trials with novel HIV vaccines

now exist. Albert Sabin understood well the problems with developing an effective HIV vaccine and was skeptical about the possibilities of developing one. In this regard, Gary J. Nabel, director of the NIH Vaccine Research Center said that Sabin “was right on.” “He knew that the genetic variability of HIV was a huge problem and

Dr. Sabin’s words are still true,” Nabel said. “Fortunately we now have technologies that were totally unavailable at his [Sabin’s] time and these new tools permit us to do things in crafting novel vaccines that were only dreamed of at an earlier time.”

In many ways the conference was summarized by Stanley A. Plotkin when he discussed the 10 most important discoveries in vaccinology of the

past decade. He could have extended the list to 15 or 20 seminal events and the meeting transactions related to his ten and more. Among these are:

- The development of the acellular pertussis vaccine which was shown to be equivalently effective to the British whole cell vaccine and sparing of morbidity.
- The creation of sufficient community (herd) immunity in developed countries to permit transition from the oral polio vaccine (OPV) to inactivated polio vaccine thereby avoiding the rare OPV-associated neuropathy.
- Varicella-zoster (chicken pox) vaccine—the first vaccine for the herpes group virus.
- Live influenza vaccine which uses old attenuated strains and is 92% effective against influenza A strains in pediatric age infections.
- Rotavirus which, despite the recall associated with gastrointestinal intussusceptions, has clearly demonstrated that this major cause of high global mortality can be controlled by vaccination; safer rotavirus vaccines are currently in development

- Combination vaccines for infants which are widely used outside of the U.S. and may be licensed here.
- Protein conjugation of bacterial polysaccharides which was earlier shown to be advantageous with the *Haemophilus influenzae* B (Hib) vaccine and is the approach used in the effective pneumococcal and meningococcal conjugated vaccines.
- Attenuated vectors which are based on the insertion of genes into attenuated viruses (e.g., canary pox) or bacteria (e.g., attenuated salmonella or shigella) results in a high stimulation of B-cell response in addition to the T-cell responses.
- Naked DNA has been used extensively to identify protective antigens in research on new vaccines.
- Transgenic plants which produce vaccine antigens and are orally administered via a food such as banana or potato.

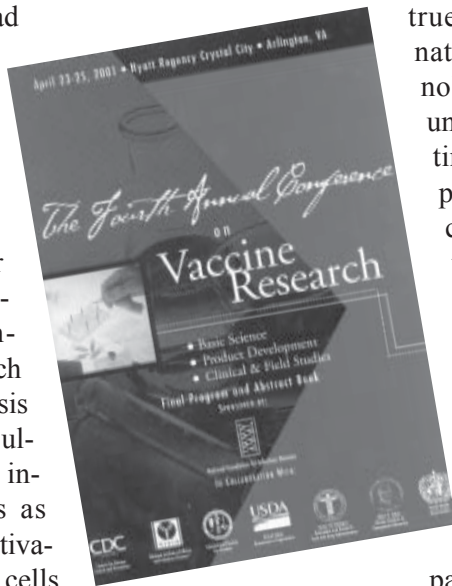
The three-day meeting covered all of the above developments as well as advances in vaccines against malignancies and chronic diseases (therapeutic vaccines), vaccines for bioterrorism candidate agents and other dangerous exotic disease and selected issues in vaccine safety.

The Albert B. Sabin Vaccine Institute was a collaborator in presenting the conference, together with the Centers for Disease Control and Prevention, National Institute of Allergy and Infectious Diseases, International Society for Vaccines, U.S. Department of Agriculture, FDA Center for Biologics Evaluation and Research and the World Health Organization. The National Foundation for Infectious Diseases was the Conference sponsor.

The Fifth Annual Conference on Vaccine Research will be held in Baltimore on May 6-8, 2002.

—by Edward S. Neiss, MD, PhD

Edward S. Neiss, MD, PhD is vice chairman and CEO of Almedica International, Inc. He is a member of the Sabin Vaccine Institute Board of Trustees.



Anatoli Alexandrovich Smorodintsev and Albert B. Sabin

—Partners in Vaccinology and Vaccine Diplomacy

“Vaccine diplomacy” is beginning to gain attention from vaccine scientists, healthcare agencies, academicians and diplomats. An essay on the topic by Sabin Vaccine Institute senior fellow Peter J. Hotez, MD, PhD, appears in the May/June issue of *Foreign Policy* magazine. But half a century before the term began to gain currency, vaccine diplomacy was being practiced by two giants in the field of vaccinology: Albert B. Sabin, MD, of the United States and Anatoli Alexandrovich Smorodintsev, MD, PhD, of the Soviet Union. These physician-scientists joined forces to combat several deadly diseases. Their efforts transcended the deep philosophical, political and military divides between the two nuclear superpowers. Most *Sabin Vaccine Report* readers are familiar with Sabin’s role in developing vaccines against polio, Japanese encephalitis and other diseases. But Smorodintsev’s work and contributions to humankind may be less well known. Following is an account of the Russian’s achievements written by his son, Alexander A. Smorodintsev, MD, PhD.

HERO OF MEDICAL SCIENCE

Anatoli Alexandrovich Smorodintsev was a giant of virology, founder of vaccinology in Russia, a member of the Russian Academy of Medical Sciences. He was also an honorary member of the American Society for Microbiology (1947), honorary life member of the New York Academy of Sciences (1956) and honorary member of the Royal Society of Medicine in Great Britain. For many years, Smorodintsev was a permanent member of the Committee of Virology in the World Health Organization in Geneva, Switzerland. His friendship with many American scientists in the field of virology helped to build a solid bridge between our countries during World War II, and opened a hole in the Iron Curtain during the Cold War in the 1950s which lasted to the end of his life.

Smorodintsev was born in Birsk in the Bashkirian Republic on April 19, 1901. The son of a physician, he earned his medical degree at the University of Tomsk in 1923. He served as a medical doctor in the Red Army in Central Asia, moved to Leningrad in 1925, and joined the Institute of Obstetrics where he became a director of the Bacteriological Department. In the early 1930s he began to work in Leningrad’s Pasteur Institute and in the Institute of Experimental Medicine. He proved in 1933 that the influenza agent was a virus, not bacteria. The publication appeared in the *Lancet* simultaneously with the paper of Smith and Laidlow from England. His early work in tick-borne encephalitis in the Far East in 1937-1940 gained him a national reputation in the Soviet Union.

He was honored with “Stalin’s Prize” in 1941 and was decorated with the Gold Medal of First Degree for the discovery of viral agents which provoked spring-summer tick-borne and autumn (Japanese) encephalitis in the Soviet Union.

Smorodintsev visited the United States more than 20 times during his life. His first scientific visit took place in 1944 during World War II when he was invited as a special guest of the U.S. Typhus Commission and the Rockefeller Foundation. It was during this period that he met Albert B. Sabin who was working on vaccines against dengue fever and Japanese B encephalitis at the Rockefeller Foundation Laboratories in Princeton, New Jersey. They shared many mutual interests in vaccine devel-

opment and its activities. For two months, Smorodintsev met and exchanged information with more than twenty virologists in the U.S. and Canada. Visiting Harvard, Yale, Johns Hopkins, the Rockefeller Institute and the National Institutes of Health, Smorodintsev created the first bridge for future Soviet-American scientific exchanges in the field of virology and for the future alliance in fighting against poliomyelitis in the 1950s.

Smorodintsev organized the Ivanovski Institute of Virology in Moscow in 1948, but soon moved to Leningrad to study the “double-waves” of meningo-encephalitis. In 1950 he isolated the virus, and proved that it was the cause of the deadly illness in Northwestern Russia. He organized a laboratory at the Pas-



Among a group of colleagues are Anatoli Smorodintsev, standing at left, and Albert B. Sabin, sitting at right in foreground (circa 1956).

teur Institute in Leningrad, where he began studying the isolation and attenuation of measles and mumps viruses for future vaccine production.

SOVIET-AMERICAN COLLABORATION KEY TO CONQUERING POLIO

As a member of the Soviet Poliomyelitis Team A, Smorodintsev visited the United States in January and February of 1956. Both the United States and the Soviet Union had very large polio epidemics in the 1950s. The mission had many contacts with Jonas Salk, and for three days they visited Albert Sabin in his laboratories in Cincinnati, Ohio.

Soviet-American Collaboration Was Key to Conquering Polio

Effective Vaccine Effort Achieved After Visits and Exchanges on the Common Research Front

Smorodintsev decided to organize the research work with Sabin's live polio strains, and asked Sabin for some of his newly attenuated strains of poliovirus for testing on children living in orphanages in Leningrad.

During Sabin's visit to the Soviet Union in the summer of 1956, Smorodintsev presented him with attenuated strains for live virus vaccines against mumps and measles.

Sabin sent all three types of attenuated polio strains to Smorodintsev in Leningrad for further human tests in November 1956.

Smorodintsev then organized experiments with Sabin's strains on adult volunteers, proved the stability of attenuated strains and demonstrated that all three types of live vaccine were safe for the children. His granddaughter, Helena, was one of the first children to be immunized against polio in the Soviet Union by Sabin's live vaccine.

In 1957-1959, Smorodintsev organized the mass production of live polio vaccine in Leningrad, and immunized three million children in various regions of the Soviet Union. As a result, poliomyelitis disappeared from these huge territories. From January 1959, the production of live polio vaccine started in Mikhail Chumakov's Institute of Poliomyelitis in Moscow and during that year, Smorodintsev and Chumakov immunized nearly 10 million children by live oral polio vaccine prepared from Sabin's strains.

Chumakov and Smorodintsev were awarded the "Lenin Prize" and a Gold Medal in 1963 (the highest awards in the USSR) for the organization of mass production of polio vaccine and eradication of child paralysis from the Soviet Union. Their victory was also a victory for Sabin who in 1962 received a license for industrial production and sale of the live oral polio vaccine he developed. As a re-

sult, by the end of the 1960s, the Sabin vaccine had become the primary medical intervention for the prevention of polio in the United States, and polio became virtually non-existent in the United States by 1970. The live, i.e., oral, polio vaccine began to be widely used by the World Health Organization for complete eradication of the disease from our planet.

AFTER POLIO: COMBATING OTHER DISEASES

Like Sabin, Smorodintsev was not content to rest on his laurels. Fresh from his success against polio, Smorodintsev pressed forward to prevent other deadly diseases. He developed and introduced in Russia the live vaccine against measles by 1967. It was produced from the strain "Leningrad-16." This vaccine was safely used in Russia for 34 years and today measles is virtually eliminated. In 1975 he developed and introduced the live vaccine against mumps from the strain "Leningrad-3." This vaccine is also successfully used in Russia.

In 1967, Smorodintsev established the Research Institute of Influenza in Leningrad and was its director until 1983. During this period, the Institute became a world center for many foreign researchers, especially from the United



Anatoli Smorodintsev among village children in rural India.

States. The Soviet-American committee of advisors gathered annually and many researchers from around the world involved in the study of this widespread infection and other respiratory viruses visited the Institute and worked there. This Institute became the initiating facility for many strains for live influenza vaccine production.

The Russian virologist published more than 700 scientific papers in various journals around the world. Many of his books were published in the field of virology and antiviral immunity. He was the director of the Leningrad Scientific School of Virology in Russia. More than half of the vaccines widely used in Russia and in the countries of the former Soviet Union were developed and introduced by Smorodintsev and his scholars. Under his scientific supervision more than 120 researchers received their MD and PhD degrees.

—by Alexander A. Smorodintsev, MD, PhD

Alexander A. Smorodintsev, MD, PhD, is director general and CEO of Antivirus Smorodintsev, a joint-venture company in St. Petersburg, Russia. As laboratory chief at the Soviet State Influenza Research Institute from 1967-76, he was Russia's official coordinator of Soviet-American collaborative research on influenza, concerned with interferon development and application of interferon-inducers during influenza epidemics. From 1976-85, he coordinated Russian-Finnish collaborative studies on human interferon. He earned his MD from the Medical University of Leningrad, 1954, and his PhD in virology, immunology and vaccinology in 1970.



H.R. Shepherd and Alexander A. Smorodintsev at the Sabin Gold Medal Reception in April 2001.

**BOOK
REVIEW**

Evolution of Infectious Disease

—by Paul Ewald



Paul Ewald's book *Evolution of Infectious Disease* is a seminal work that convincingly makes the case for the urgent need to integrate a modern understanding of evolutionary processes into both medical education and patient care. He maintains that despite superficial appearances this has not been adequately done, and as a result our society acts in ways that undermines rather than promotes long-term health prospects of our population. Ewald also contends that to the limited extent that evolutionary ideas have influenced medical thinking, they have involved outmoded concepts which have fostered an unjustified confidence in our future prospects.

For example, Ewald dismisses as a dangerous myth the widespread belief that there is a natural tendency for microbes over time to adapt to humans by becoming less virulent. He says that less pathogenic microbes will replace more pathogenic ones, only if conditions make it more likely that their offspring (and thus their genes) successfully infect new hosts. If conditions make it more likely that increasing virulence will produce that favorable result, then evolutionary processes will select for such an outcome. In other words, pathogens can become more as well as less dangerous over time depending on the environment that they experience.

According to Ewald, human beings often create conditions through their cultural, economic, and medical activities that favor the evolution of more rather than less dangerous microbes. He believes that only the use of modern evolutionary concepts can reverse this destructive tendency. If evolutionary ideas are not used, or if they are only given lip service while alternative, and inferior theoretical perspectives are emphasized, the results could be dire.

Ewald believes that just such a dangerous misconception of where the danger to humanity lies has recently occurred. The scientific community has

lately been alerted to the danger of "emerging diseases." Stephen Morse, one of the most effective people in raising public awareness of the problem, has closely linked new diseases to what he calls "viral traffic." This idea attributes the appearance of new diseases primarily to trade, exploration, new settlements and civil disturbances, where the movement of people, goods or animals create physical contact between groups that had previously been geographical isolated. Morse indicts a large variety of social activities as the chief causes of increased human vulnerability, especially those that result in ecological disruption. As a result, Morse argues that "the essential first line of defense" against such threats is the creation of a series of early warning surveillance systems, many of them aimed at distant and exotic places, where viral traffic (i.e., exposure to novel viruses) might originate through ecologically unsound human activities. Morse further maintains that the emergence of new diseases from human activity has one significant positive aspect because it makes counter measures possible; if new diseases resulted simply from random genetic mutation of microbes, then there would be little humans could do to protect themselves except sit and wait for misfortune.

On the other hand, Ewald contends that emphasizing evolutionary processes rather than "viral traffic" is a far more productive way of looking at the problem. For him, the key to understanding the emergence of virulent pathogens is not the existence of mutations per se, but rather the forces that select which mutations are successfully passed on, and which are not. According to Ewald, the range of human activities that unintentionally affect microbial evolution is far wider than simple disruption of the natural environment, and it is in specifying the basic principles that govern

that evolution and then using that knowledge in practical situations that our most effective defense against emerging diseases lies.

What are some of those evolutionary rules that Ewald sees as vital to understand? A key one is that pathogens carried directly from one person to another tend to be less lethal than

those transmitted by non-human carriers. The logic of the situation is quite simple: if the microbe is spread by a mobile person, then incapacitating that host will lower the likelihood that its offspring will be successfully passed on to a new host. For example, if a cold virus is to be effectively spread, it is best that it not force the victim prematurely into bed. Virulent cold viruses that tended to immobilize people would face selective pressure that favored less virulent strains which allow people to carry on their daily lives.

On the other hand, if a mobile human is not necessary (for example in a vector-borne disease such as yellow fever), then the virus can be considerably more virulent without paying any cost in its ability to successfully pass on its genes.

It is not only insect-carried diseases that are more likely to be deadly. Water often acts as a vector for disease transmission. Cholera incapacitates its host but because of the infected bodily discharges that the disease induces, even the immobilized individual can contaminate the ground water and through it spread the bacteria to new victims. Thus, the host can quickly die with little or no impediment to the pathogen passing its virulent genes on.

In the same way, other forms of water-borne dysentery have evolved toward more virulent forms because there is little or no price to be paid if it immobilizes or kills its host. Ewald says that the existence of vectors encourages the selection of strains that reproduce faster over those that reproduce slower — and those strains tend to be more virulent and destructive.

Ewald also points out that society by its practices can artificially create a "cul

Continued on page 14.

Walker's Cay Colloquium Puts Spotlight on Cancer Vaccines and Immunotherapies

Ideas and Data So New They Have Not Yet Been Published

Continued from page 1

make prepared presentations, one after another, with little time for serious discussion.

"The format resulted in all attendees presenting their latest data, and some of it was absolutely striking," according to Philip O. Livingston of Memorial Sloan Kettering Cancer Center in New York. He described revelations of cellular responses to particular cancer vaccines with high correlations in experimental treatments of humans as "revolutionary." According to Livingston, this should result in rapid progress in the development of more effective cancer vaccines. It will immediately change the focus of immunogenicity monitoring among the colloquium attendees and, very quickly, the biomedical research field.

A NEW CHAPTER IN THE WAR ON CANCER

The colloquium was conceived by Sabin Vaccine Institute chairman H. R. "Shep" Shepherd and his friend, Robert H. Abplanalp, CEO of Precision Valve Corporation. Abplanalp owns Walker's Cay, a small island in the northern Bahamas that his close friend, former President Richard Nixon, visited frequently to relax and contemplate major issues. It was during a stay at Walker's Cay that Nixon decided to declare "war on cancer," and make the search for a cure a national priority. Nixon increased funding for basic research at the National Institutes of Health that paved the way for today's experiments with vaccines to shrink and even prevent cancerous tumors.

Shepherd and Abplanalp

believed that creating a venue where the world's leading cancer vaccine scientists could candidly exchange their latest ideas and data could speed scientific progress in this field. In 1999 the Sabin Vaccine Institute held its first Walker's Cay Colloquium on Cancer Vaccines and Immunotherapy. According to the scientists, Shepherd and Abplanalp's hunch was correct.

W. Martin Kast, director of the Cancer Immunology Program at Loyola University Chicago's Cardinal Bernadin Cancer Center, found "the challenging discussions and information flow far exceed that of any normal scientific meeting."

"The size of the meeting and the venue were very conducive to excellent discussions, both inside and outside the conference room, and to cross-fertilization between disciplines in the field," said Jay A. Berzofsky, chief of the Molecular Immunogenetics and Vaccine Research Section at the National Cancer Institute. "This kind of interchange and cross-fertilization has been seen historically over and over again to be critical for many major advances in science."

Esteban Celis of the Mayo Clinic in Rochester, Minnesota, put it succinctly: "This setting facilitated strong scientific interactions between groups which are certain to translate into cancer therapy breakthroughs."

ACCELERATING PROGRESS FROM BENCH TO BEDSIDE

The colloquium mission is to speed up the conversion of scientific knowledge into therapies that are available to treat patients. A new class of therapeutic vaccines

could supplement or even replace conventional cancer treatments such as chemotherapy, radiation, and surgery. The vaccines have the potential to attack tumors themselves, without the collateral damage to other cells and parts of the body caused by the conventional treatments.

"It was particularly helpful for cancer researchers such as myself who are beginning to translate their laboratory findings into clinical trials to be able to get input from investigators who have already done this," said Yvonne Paterson, professor of microbiology at the University of Pennsylvania School of Medicine in Philadelphia. "I always come away from this meeting with new ideas for my own research," she added.

CATALYST FOR COLLABORATION

Another colloquium goal is to encourage development of new collaborations between researchers at multiple institutions.

Jeffrey B. Ulmer, senior director of Vaccine Research at Chiron Corporation in Emeryville, California, said that at last year's colloquium, he "set up several collaborations to test our gene delivery technologies in cancer models. This year's meeting allowed me to build on those collaborations and several others are being contemplated."

Reisfeld reported, "I started two scientific collaborations at the meeting and I am certain that I was not the only one to do this." Kast said he "will literally embark on three research collaborations that otherwise would not have been possible."

Albert LoBuglio, director of the Comprehensive Cancer Center at the University of Alabama at Bingham, summed up a sentiment expressed by most of the colloquium participants. "I had heard very good things about it and the meeting surpassed my expectations."

—by John M. Clymer

John M. Clymer is the Sabin Institute's Vice President of External Affairs (john.clymer@sabin.org).

Colloquium Attendees

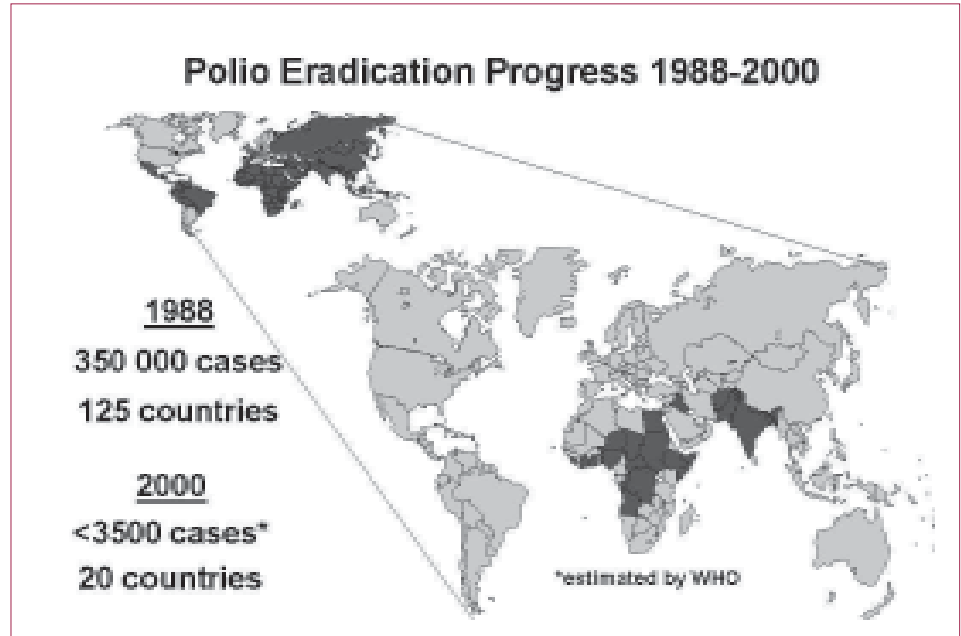
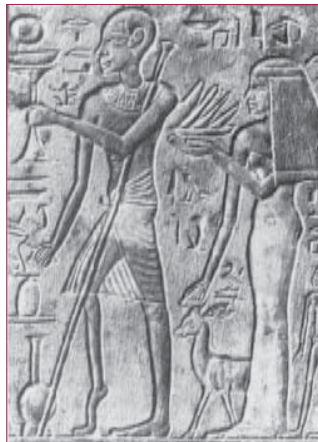
Jay A. Berzofsky, Claudine Bruck, Esteban Celis, Richard B. Ciccarelli, Edgar G. Engleman, Olivera J. Finn, Eli Gilboa, Allan L. Goldstein, Lance K. Gordon, John Gutheil, Jane C.I. Hirsh, W. Martin Kast, Larry W. Kwak, Philip O. Livingston, Albert E. LoBuglio, Grant D. MacLean, Lewis A. Miller, Malcolm S. Mitchell, Dennis Panicali, Yvonne Paterson, Ralph A. Reisfeld, Philip K. Russell, Jeffrey Schlom, Steve Schoenberger, Alessandro Sette, Walter J. Storkus, James Tartaglia, and Jeffrey B. Ulmer

Realizing the Dream: Closing In on the Conquest of Polio

A Hard-fought Battle Against the Disease That Crippled Millions over the Course of 3,000 Years

Polio. Ask an older American about it and they will guess it began in the first part of the 1900s: a fair assumption since it had hardly ever been documented. By the second decade of the 20th century it gained a national reputation, because future president Franklin Delano Roosevelt had it. As the century turned 40 and 50, there was nowhere left to run from it and few people's lives would remain untouched in some way. Those growing up in the last few decades of the second millennium knew little about it and probably never even saw it firsthand. But ask medical and social historians about it and they will point to ancient Egyptian stone engravings and reference 16th century paintings by artist Pieter Brueghel. They will explain, interestingly enough, improved hygiene and sanitation throughout the years only encouraged it by eliminating the chance for children to acquire immunity. And they will also tell you, with guarded excitement, *its days—polio's days—are numbered.*

It has been exactly 40 years since the Sabin oral polio vaccine (OPV) was licensed in the United States and many other countries. In other words, since the Sabin vaccine became available in 1961 and an intravenous vaccine was licensed before that, polio has been preventable for more than 40 years! It is hard to believe then, in some respects, that it has taken that long for poliomyelitis, the disease that has crippled millions for at least 3,000 years, to be on the verge of global eradication. Part of the reason is that although incidences of polio have been declining since 1988 (*see map*), as the disease itself dwindles so does the momentum on the part of governments and ordinary citizens to combat the remaining pock



World Health Organization map depicts the recent progress in the conquest of polio

ets of contagion. The dream of a polio-free world is being brought to fruition. Now is the crucial time before that dream is fully realized and it necessitates extra vigilance and commitment. Because of its high rate of infection and contagion, *any* amount of remaining poliovirus is still a threat and could potentially regain a

foothold. *Most important is the fact that polio is preventable, but there is no cure.*

—by Veronica Korn

Veronica Korn is a research associate at the Sabin Vaccine Institute (veronica.korn@sabin.org).

Images that reflect the human impact of poliomyelitis.



Photos courtesy of Roosevelt Warm Springs Institute for Rehabilitation.

In Memoriam—Three Research Champions in the Conquest of Polio

Joseph L. Melnick, PhD, DSc (1914-2001) 1966 Sabin Gold Medal Awardee

On January 7, 2001, the modern virology world lost one of its principal founders, Dr. Joseph L. Melnick, who died in Houston, Texas at age 86. In 1996, Dr. Melnick was awarded the Albert B. Sabin Gold Medal for his many contributions to the study of polio and vaccines to prevent the disease that affected as many as 57,000 people a year in the 1950s in the United States alone. For more than 30 years, he served on the World Health Organization Expert Panel on Virus Diseases and was active in WHO programs concerned with poliomyelitis.



Joseph L. Melnick

Dr. Melnick was founding chairman of the Department of Virology and Epidemiology at the Baylor College of Medicine from 1968 until 1991, when he was named dean emeritus. During this time, he was also Dean of Graduate Sciences. He wrote the virology section of a standard textbook on microbiology, now updated and in its 22nd edition, and was chief editor of three scientific textbooks. He was formerly the chief biologist at the Division of Biological Standards at the National Institutes of Health.

Dr. Melnick proved himself to be an international leader in identification and control of virus diseases, especially polio. His work on the poliomyelitis virus included his demonstration that the poliovirus usually invades the intestines of the host rather than the long-held belief that it invaded the host through the central nervous system. In 1960, Dr. Melnick demonstrated that the Sabin oral polio vaccine (OPV) produced less damage to the nervous system than the competing intravenous vaccine. In addition, he headed the team that developed thermostabilized live vaccines. By adding magnesium chloride to vaccines, such as the Sabin OPV, the need for deep-freeze storage facilities was eliminated which enabled the immunization of millions of people worldwide. This had, and continues to have, an invaluable and far-reaching effect on those living in the least developed countries.

Upon Dr. Melnick's death, Sabin Vaccine Institute Chairman, H.R. Shepherd said, "Joseph Melnick was an extraordinary scientist, mentor and colleague who will never be forgotten."

Dorothy Horstmann, MD (1911-2001) Made Significant Contributions to the Sabin Oral Polio Vaccine

The death of Dorothy Horstmann, MD came only four days after the death of her colleague and collaborator, Joseph L. Melnick, PhD, DSc. They worked together at Yale University, co-authoring scholarly papers and conducting research during the polio epidemics in New Haven, Connecticut throughout the 1940s and 50s.

Horstmann was an epidemiologist, virologist, and at mid-career became a pediatrician. During a polio outbreak in 1943 in New Haven, she joined the Yale Poliomyelitis Study Unit and decided at that time to devote much of her research to infectious diseases. She was not only



Dorothy Horstmann and Albert B. Sabin.

the first woman professor at Yale, but in 1969 also became the first woman there to receive an endowed chair which was named after her mentor and renowned polio expert, Dr. John R. Paul.

Among Horstmann's many contributions in the fields of epidemiology and infectious diseases, her major scientific achievement in polio was one which upset scientific dogma in the middle part of the last century. She disproved the widely held belief that the poliovirus grew only in nerve cells by showing that in fact the virus reached the brain by way of the blood. Scientists of the time thought that because their efforts to isolate the virus from the blood of paralyzed patients failed, the virus directly attacked the nervous system. Horstmann's team rationalized this failure when they detected polio in the blood of infected apes—before paralysis occurred. The team found that by the time the apes were paralyzed, antibodies had already eliminated the poliovirus from the blood. What was at first viewed as a scientific upset, later became to be viewed as somewhat of a relief that indeed poliomyelitis acted like other infectious diseases.

These findings and contributions led to the licensing of the Sabin oral polio vaccine (OPV). While the OPV was being tested on millions in the former Soviet Union, other countries, including the United States, were not wholly convinced of its effectiveness. Horstmann was asked by the World Health Organization to study polio incidences in vaccinated areas; concluding that the Sabin vaccine was safe. It was subsequently licensed in the United States.

Other honors during her career include election to the National Academy of Sciences. In the mid-1990s, when she was in her eighties, Horstmann was a member of the International Commission of the Certification of Poliomyelitis Eradication.

Charles Mérieux (1907-2001) Jacques-François Martin Remembers a Mentor Committed to the Health of the Poor

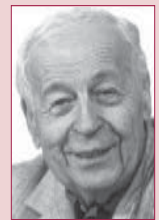
Charles Mérieux, vaccinologist, born January 9, 1907, died January 19, 2001. Strongly influenced by Louis Pasteur's approach (his father had been assistant to Emile Roux and to Pasteur), Charles Mérieux gave his whole life to preventive medicine: it was he, together with Jonas Salk, who coined the term "vaccinology."

Charles Mérieux, who liked to say that there is no boundary between the two branches of medicine, industrialized modern virology in veterinary medicine. By culturing cells in-vitro, he enabled the large-scale production of a vaccine for foot-and-mouth disease. He then applied this approach to the development of human vaccines against polio and measles.

In the 1970s he developed the first vaccine against meningococcal meningitis, which found an unexpected application in Brazil when the entire population was immunized in 1975. That campaign was a precursor to the National Immunization Days which were introduced, again by Brazil, for polio, paving the way for eradication of the disease.

His family life was not unmarked by hardship, but he never failed to demonstrate the strength that sprang from hope. Resolutely turned towards the future, he taught us to believe in the impossible because in his case, the impossible was no match for his determination.

(First published in the March 2001 *Immunization Focus: the newsletter of GAVI: Global Alliance for Vaccines and Immunization.*)



Charles Mérieux

**BOOK
REVIEW**

Evolution of Infectious Disease

Continued from page 10

tural vector.” A striking example of this is found in hospitals where doctors and nurses ignore good hygiene practices and carry pathogens between immobilized patients. In this situation the pathogen is free to evolve into more lethal forms since its ability to spread is not dependent on leaving its victims mobile.

The implications of this situation are rather striking because it casts light on why hospital-acquired infections tend to be more lethal than community-acquired ones. Ewald hypothesizes that the growing problem of deadly infections in hospitals may have less to do with the fact that patients are very sick and have weak immune systems than that healthcare workers can and do spread pathogens between bedridden hosts. Thus, according to Ewald, tighter enforcement of hygienic standards should work as an “evolutionary” pressure to lower the virulence of hospital-acquired infections. If health professionals don’t carry microbes between non-mobile patients then the more lethal ones will die out, and those that require direct contact between ambulatory patients will be favored.

In the same way, according to Ewald, if water acts as a vector to increase microbial virulence, cleaning up the water supply and protecting it against contamination should put evolutionary pressure on microbes to be less lethal. Many people believe that cleaner water totally eliminates pathogens, but actually it acts as a selective agent in producing more benign strains of existing microbes. This has been the case in the United States where deadly forms of dysentery have been replaced by more benign strains as the water system has been upgraded over the years.

Ewald says that it is not only dysentery that has been positively affected by changes in water quality. The same thing has happened in the case of *Vibrio Cholerae*. The milder “El Tor” strain replaced the more virulent classical form throughout the world during the 1960s.

The countries that first experienced this phenomenon tended to be the ones that had made improvements in their drinking water. Most observers have not been able to adequately explain this replacement situation. However, if one looks at the question of changing cholera strains from an evolutionary perspective, one can understand both why the El Tor type made little progress in replacing the classical strain in the 50 years before 1960, and then almost completely substituted for it within a single decade. The classical strain of cholera bacteria possesses a toxin-producing gene that makes it a more efficient pathogen than the El Tor strain which lacks it, in places where contaminated water is abundant. But where water supplies become cleaner, the El Tor strain, which can be passed directly from person to person without using water as a vector, has a selective advantage over its more lethal competitor.

Ewald argues that a similar situation potentially exists in the case of malaria, and it should be exploited. The fact that the disease is carried by mosquitoes means that different strains of it can evolve into more virulent forms despite immobilizing its victims. Thus, cultural patterns which expose bedridden people to mosquitoes help spread the most virulent forms of the disease. This implies, however, that a health intervention that makes it impossible for mosquitoes to bite severely ill people (e.g., screens on houses, or bednets) would favor the spread of less severe strains that leave infected people healthy enough to move around. In this case both screens and bednets would function as an “evolutionary device” not just as direct protection for uninfected individuals as most public health workers assume.

The theme of the book is that we can use evolutionary principles and inter-

ventions to put pressure on microbes to evolve in ways that are better for us, or we can ignore such principles and inadvertently help select for more virulent and deadly pathogens. In the case of antibiotic resistance, our health practices have been disastrous working against our long-term interest and threatening to return us to the pre-antibiotic age.

While Ewald argues the importance of using evolutionary theory, it is nevertheless full of provocative practical interventions that may make healthcare better.

For example, one of the more important ideas in the book is that the symptoms a pathogen produces in the body may either be a “defense” by the host or a “manipulation” by the microbe. In the case of diarrhea, the symptom is often the way that the body tries to rid itself of a pathogen. Other times, the diarrhea is a way for the pathogen to contaminate the environment and be successfully spread to other victims. It is important for us to recognize this distinction.

If the symptom is a defense of the body, then we do not want to take medicine that will prematurely stop the diarrhea; to do so may be dangerous or even lethal because it keeps the pathogen inside the intestines. On the other hand, if the diarrhea is a “manipulation” by the pathogen, it may be necessary to counter the symptom to protect other people.

The same situation holds in the case of “fever” — sometimes it is a defense by the body and sometimes it is a manipulation by the pathogen that allows it to thrive better. According to Ewald, knowing the difference between a defense and a manipulation will aid in the treatment of illnesses that are now frequently mishandled.

Ewald’s use of evolutionary theory also has a major application in the area of emerging diseases. One of the key questions that he asks is how can we know which types of new diseases are most dangerous to us? He believes that illnesses like Ebola, Marburg, and Lassa Fever which cause the most public and governmental anxiety because of their



The author, Paul Ewald.

Continued on page 16.

INSTITUTE NEWS

Sabin Institute Honors

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hancing relationships with doctors and hospitals.”

Shepherd praised Rowe as “a leader with the experience, skill, vision and passion to lead his company through a major set of challenges. He is the right person at the right time for Aetna. And he is helping Aetna share his commitment to preventive healthcare, including disease prevention.” Shepherd noted, “The Sabin Vaccine Institute had important affiliations and dealings with various academic medical centers during all of the upheaval in the ‘90s. We saw research scaled back and hospitals sold from positions of weakness, so I know that Jack did an extraordinary job to forge a combination of strength and excellence with Mount Sinai and NYU.”

The awards dinner is a benefit for the Sabin Vaccine Institute. Co-chairs of the event are E. John Rosenwald, vice chairman of Bear Stearns, and David Low, managing director of JPMorgan Chase. The 2000 event raised nearly \$600,000 to support the Institute’s research and education programs, and this year’s dinner already has surpassed that benchmark. Tickets are available by contacting the Sabin Vaccine Institute at (914) 244-0910.

New Staff Member Has Personal Link to Sabin Vaccine Institute Mission

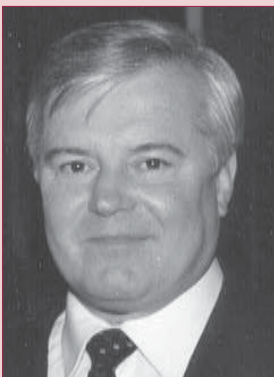
The new executive assistant to the chairman, David Bedell, has a close family connection to the Sabin Vaccine Institute’s mission. His father, George Bedell, contracted polio in 1954, before the Salk and Sabin vaccines became available. During the polio epidemics that struck North American cities in the 1940s and early 50s, George Bedell was in Mexico and Korea, somewhat removed from the industrialized epicenters and the media scares surrounding the “summer plague.” However, he came down with polio at the age of 27 while traveling in rural Mexico. He was diagnosed and admitted to the polio ward at the American British Cowdray Hospital in Mexico City, where he received therapy that led to a full recovery, but only after three months confined to bed and wheelchair. His recovery coincided with his wedding to David’s mother—he depended on his best man to support him as he walked to the altar of the hospital chapel.

David Bedell recalls: “As a child, I remember my father showing me the wasted flesh between his left thumb and forefinger and letting me compare the unequal grip of his two hands. Although he had, in general,

the full strength of an average adult, certain specific actions were difficult for him, and I always knew I could outrun him. He enjoyed hiking and biking, but only in his dreams could he run or jump hurdles as he had on his high school track team. For him, the lasting effects of polio were only minor inconveniences, not really disabilities. He was far luckier than some of his contemporaries who ended up in iron lungs or bed-ridden for life.”

In recent years, George Bedell has felt the effects of post-polio syndrome, where his muscles, especially for walking or climbing stairs, tire easily. David Bedell, like others of his generation, was given the Sabin oral vaccine as a child, and he took a booster dose before a trip to China in 1992. He knows that polio still exists “only a plane ride away,” and he looks forward to the final eradication of the disease.

David Bedell comes to the Institute after many years of teaching English, first in China and then with international students in the United States. He has also worked with various nonprofit organizations on issues related to the environment, public health, and social justice.



E. Andrews Grinstead, III

In February, the Institute lost our valued colleague, E. Andrews Grinstead, III. Andy

was a founding member of the Albert B. Sabin Institute’s Board of Trustees. He will be missed for the guidance and insight he so generously provided to the Institute since its beginnings, but most of all he will be missed for his friendship and kindness. Andy was chairman of the board and chief executive officer of Hybridon, Inc. Prior to joining Hybridon,

Eugene Andrews Grinstead, III August 10, 1945-February 28, 2001

he served in various operational and executive positions at Eli Lilly, Drexel

Burnham Lambert, Kidder Peabody, and Paine Webber. Andy was a member of the President’s Circle of the National Academy of Science and the Institute of Medicine and served on numerous boards.

—by H. R. Shepherd

H.R. Shepherd is co-founder and chairman of the Albert B. Sabin Vaccine Institute.

BOOK REVIEW

Continued from page 14

extreme lethality, are the least likely to pose a threat to mankind. Why? Because they are spread by human-to-human contact and they are so virulent that they quickly burn themselves out. The truly dangerous viruses are not these, but rather those that are carried by vectors where the spread is not arrested by the immobilization and death of the host or by those that are carried silently within infected people and spread over long periods of time before symptoms appear—such as in the case of HIV infection.

Even in cases such as AIDS, however, evolutionary thinking can offer help. It is Ewald's contention that we can understand why HIV type I suddenly became such a virulent plague, and why HIV type 2 gives rise to a much milder form of the disease. Experiments have shown that pathogens that are quickly spread between animals tend to become more virulent.

A possible reason for this is that rapid passage from host to host selects for the fastest growing strains which are more likely to be more harmful. In areas where HIV type 1 predominate, multi-partner sex leads to exceptionally rapid passage of the virus from person to person, making the resulting disease far more lethal. In areas where HIV type 2 predominates, passage is far slower because of sex practices that favor having fewer sexual partners—which selects for slower growing strains. According to Ewald, anything that slows down infection—for example, the use of condoms—act as a selective pressure favoring the evolution of less virulent strains of the disease.

Needless to say, many of Ewald's ideas are highly speculative because the research necessary to prove them has yet to be done. Nevertheless, his argument is a very powerful and persuasive one, and he successfully highlights both the price paid for not integrating evolutionary perspectives into our understanding and treatment of infectious diseases and the potential benefits from rectifying this omission.

—by *William Muraskin, PhD*

William Muraskin, PhD is a Sabin fellow and professor of urban studies, Queens College, New York.

SABIN CALENDAR

MAY 2001

May 27-31, 2001

7TH CONFERENCE OF THE INTERNATIONAL
SOCIETY OF TRAVEL MEDICINE (CISTM7)
www.istm.org

Innsbruck, Austria

May 29-June 1, 2001

35TH NATIONAL IMMUNIZATION CONFERENCE
www.cdc.gov/nip/NIC

Atlanta, Georgia

May 31, 2001

4TH ALBERT SABIN VACCINE INSTITUTE
AWARDS CELEBRATION

Honoring:

Jean-Jacques Bertrand, Aventis-Pasteur
Chairman and CEO

Albert B. Sabin Humanitarian Award
and

John W. Rowe, M.D., Aetna Inc. Chair-
man and CEO

Lifetime Achievement Award

www.sabin.org

The Pierre Hotel, New York, New York

JUNE 2001

June 8-10, 2001

NEW AND REEMERGING INFECTIOUS
DISEASES: A CLINICAL COURSE
Nat'l. Foundation for Infectious Diseases
www.nfid.org/conferences/june01/

Atlanta, Georgia

June 13-16, 2001

5TH INTERNATIONAL SYMPOSIUM ON
HEMORRHAGIC FEVER
www.fond-merieux.org/eng/colloque/
Hantavirus.html

Veyrier-du-Lac, France

JULY 2001

July 9-11, 2001

2001 AMERICAN IMMUNIZATION REGISTRY
ASSOCIATION CONFERENCE
www.cdc.gov/nip/registry/2001broc.pdf
E-mail: eparra@cdc.gov
Little Rock, Arkansas

AUGUST 2001

August 13-14, 2001

7TH INTERNATIONAL DENGUE COURSE
Instituto Pedro Kouri
Havana, Cuba
lupe@ipk.sld.cu

SEPTEMBER 2001

September 10-12, 2001

BRITISH SOCIETY OF PARASITOLOGY 12TH
MALARIA MEETING
www.abdn.ac.uk/bsp
University of Leeds, UK

September 12-14, 2001

VACCINES FOR ENTERIC DISEASES
Tampere, Finland
jherriot@meetingsmgmt.u-net.com

September 26-29, 2001

WORLD MELIODOSIS CONGRESS
www.e-tiology.com/
Perth, Western Australia

September 30-October 4, 2001

53RD MEETING OF THE GERMAN SOCIETY FOR
HYGIENE & MICROBIOLOGY
www.dghm-2001.de
Aachen, Germany

OCTOBER 2001

October 9-11, 2001

8TH ANNUAL SABIN VACCINE COLLOQUIUM
*Accessing & Evaluating New Technologies for
Vaccines for the Developing World*
Sponsored by Sabin Vaccine Institute
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