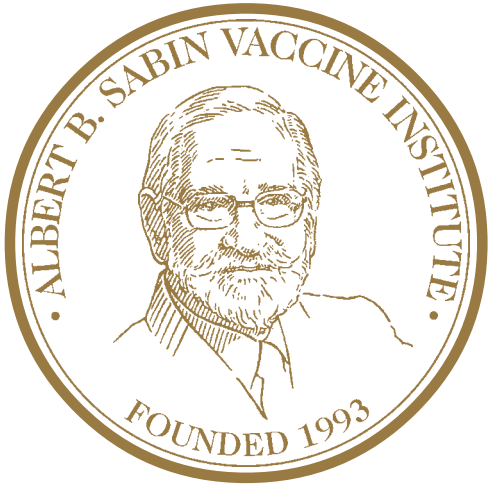
2005 Albert B. Sabin Gold Medal



Address Delivered by Award Recipient

Albert Z. Kapikian, MD

Tributes by Robert M. Chanock, MD
and Roger I. Glass, MD, PhD

&

Memorial Tribute to John R. La Montagne, PhD

May 10, 2005
Baltimore, Maryland

Introduction

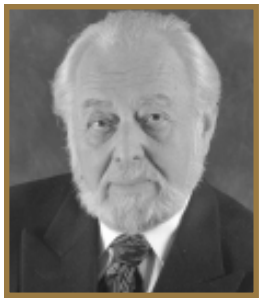
by H.R. Shepherd, DSc
Chairman, The Albert B. Sabin Vaccine Institute

The Sabin Vaccine Institute places high regard on those whose progress in vaccine research and development have afforded the world the benefit of vaccines in our time. The medical miracle of vaccines has achieved some of the greatest and most humanitarian outcomes for children, adolescents, and adults around the globe. This benefit can often be taken for granted as the outcome is health and disease prevention, while it is at the molecular level where exciting events are taking place out of sight, and so often out of mind. This award aims to draw attention to the research that brings vaccines from the theoretical to the practical for our world. We shine a spotlight through the Sabin Gold Medal on the brightest and most dedicated vaccine researchers.

The 2005 Sabin Gold Medal, the 13th such award, goes to Albert Z. Kapikian, MD, who made great strides in viral diseases research and discovery of vaccines for viral disease prevention. His career of more than 47 years, with groundbreaking medical research contributions, is distinguished by the development of the first licensed rotavirus vaccine. Albert Kapikian's contribution to mankind through the field of vaccines is truly extraordinary as it takes a great vision and dedication to achieve such progress for humanity.

The Sabin Gold Medal Advisory Committee, chaired by Maj. Gen. Philip K. Russell, MD (USA Ret.), made its selection after canvassing 300 members of the scientific community. With them, and on behalf of the Board of Trustees of the Institute, I congratulate Dr. Kapikian.

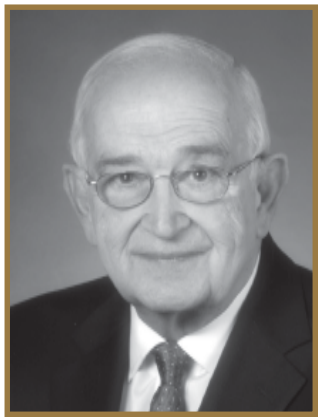
Reproduced in this booklet are the fitting tributes to Dr. Kapikian made by Robert Chanock, MD, and Roger Glass, MD, as well as Dr. Kapikian's personal reflections. The fraternity among these researchers is evident in the stories they tell and the mutual esteem in which each is held. This year we also recognized a sorely missed colleague, the late John R. La Montagne, PhD, whose tribute was part of this year's presentation.



The remarks here make for enjoyable and highly informative reading, so I hope you will be appropriately entertained and informed by this booklet of speeches offered as a commemorative of the 2005 Sabin Gold Medal event.

H.R. Shepherd, DSc

Albert Z. Kapikian, MD
2005 Albert B. Sabin Gold Medal Recipient



The career of Albert Z. Kapikian, MD—physician, medical pioneer and viral diseases researcher—has spanned more than 47 years, and yielded numerous groundbreaking medical research contributions. He is distinguished as the developer of the first licensed rotavirus (RV) vaccine.

In the 1950s Kapikian began studying the epidemiology and causes of various viral diseases. He is renowned for pioneering studies using electron microscopy to discover and characterize viruses causing major diseases in humans. In 1972, Kapikian identified the Norwalk virus, the first virus associated with acute epidemic gastroenteritis, gaining recognition as "the father of human gastroenteritis virus research." In 1973, he and two colleagues identified the virus that causes hepatitis A. He became the first in the United States to detect and visualize human RV, discovered by others in Australia.

At the National Institute of Allergy and Infectious Diseases, Kapikian led a nearly 25-year effort to develop an oral RV vaccine. The team's neo-Jennerian RV vaccine strategy involved mating outer proteins from different human RV strains with a monkey RV and combining the resulting hybrid viruses into one vaccine. From a single-strain vaccine in 1984, the vaccine was thus made to be protective against the four most important clinical strains of RV. In 1998, this vaccine became the first US-licensed RV vaccine.

Kapikian graduated from Cornell University Medical College in 1956 and in 1957 joined the National Institutes of Health as a commissioned officer of the US Public Health Service. In 1967 he was appointed head of the Epidemiology Section of the Laboratory of Infectious Diseases, a position he holds today as a member of the Civil Service. He has received numerous honors and is the author of many scholarly papers.

Tribute to Albert Z. Kapikian, MD

by Robert M. Chanock, MD
Chief, Laboratory of Infectious Disease, NIAID, NIH
1995 Sabin Gold Medal Recipient

Throughout his career Dr. Albert Kapikian has made important scientific contributions that are truly unique. As a rule, his contributions have been those of a pioneer who broke new ground allowing others to follow. For example, in a well controlled, prospective longitudinal study, he and Dr. Neal Blacklow demonstrated that defective adenovirus-associated viruses (AAV), initially detected in adenovirus infected tissue cultures, do infect humans but do not cause disease. This became an important consideration in selecting AAV as one of the preferred viral vectors for gene therapy.

The modern era of gastroenteritis virology can be traced precisely to the initial studies in his Section in the Laboratory of Infectious Diseases (LID) in the early 1970s. During these studies the filterable etiologic agent of the large Norwalk, Ohio, outbreak of non-bacterial diarrhea was transmitted successfully to adult volunteers. However, despite the availability of a known infectious stool filtrate, an etiologic agent could not be isolated or identified by the then newly developed tissue culture techniques. Nonetheless, in 1972 Dr. Kapikian used immune electron microscopy (IEM) to discover a 27nm virus-like particle in an infectious stool filtrate and then succeeded in demonstrating its etiological association with gastroenteric illness. He was also able to detect specific serologic responses to the Norwalk virus that made it possible to perform the earliest epidemiological studies of this virus. Indeed, this was the first time IEM had been used to detect, identify and partially characterize a previously unrecognized viral pathogen and define its natural history. Under Dr. Kapikian's leadership other small (27nm) Norwalk-like virus particles were discovered, identified and associated with other outbreaks of acute nonbacterial gastroenteritis. These viruses were later shown to be the first human caliciviruses. More recently, Norwalk virus, and relatives of this virus, were shown by CDC to cause more

than 90% of acute, nonbacterial gastroenteritis outbreaks ("intestinal flu"), a condition that is the second leading cause for seeking medical attention in the United States. Indeed, these viruses are the leading cause of acute gastroenteritis of any form.

His success in discovering and characterizing the human caliciviruses as major agents of acute gastroenteritis provided the impetus for seeking other previously undetected human viral pathogens using the same strategy. During a study employing IEM, he succeeded in visualizing and identifying the virus responsible for hepatitis A. Also, during the course of this study, he, together with Drs. Feinstone and Purcell, identified a previously unrecognized condition that they designated post-transfusion non-A, non-B hepatitis, that is now known as hepatitis C.

Following this pioneering research he turned his attention to the newly described human rotaviruses which he and others showed to be the major cause of severe diarrheal disease in infants and young children. During these studies he characterized the clinical and epidemiological features of these viruses, identified the viral protective antigens and the viral genes that play a major role in virulence, and together with Karen Midthun, Robert Chanock, Yasutaka Hoshino, R.G. Wyatt, and H. Greenberg, developed a viral genetic system for transferring genes from one rotavirus to another. The latter system proved to be critical to success in developing attenuated rotavirus mutants for use in a live attenuated virus vaccine. In his long-term effort to prevent serious rotavirus disease he employed the oldest known strategy for development of a live virus vaccine. This approach utilizes an animal virus that is attenuated for humans but is nonetheless able to prevent disease caused by an antigenically related pathogenic human virus. This strategy was used more than 200 years ago by Jenner who employed an animal poxvirus (cowpox) to immunize humans against one of their most dread diseases, smallpox. As he pursued the development of a safe, effective rotavirus vaccine, he added the cutting edge technologies of immune electron microscopy, virus genetics and molecular virology to the vaccine strategy of Jenner.

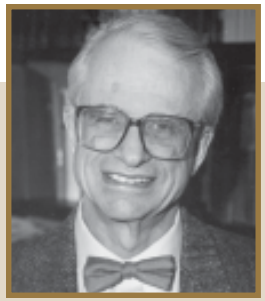
Dr. Kapikian used the simian rhesus rotavirus (RRV) as the animal virus surrogate for immunization against the most important human rotaviruses. Initially, he demonstrated that RRV was attenuated

for fully susceptible infants. Then, this virus was used in gene transfer studies serving as a donor of attenuating genes. This modified strategy was employed to construct reassortant viruses bearing 10 RRV genes and a single human rotavirus gene that coded for the major protective antigen (VP7) of human rotavirus serotype 1, 2 or 4. This was not necessary for the serotype 3 virus component of the quadrivalent vaccine because RRV is itself a serotype 3 virus. Following completion of the pre-clinical development of the quadrivalent rotavirus vaccine, he designed, organized, initiated, supervised and analyzed large clinical trials of the vaccine during which his understanding and consummate mastery of epidemiology and clinical investigation were clearly evident. The quadrivalent live RRV vaccine was shown to be safe and highly effective in preventing severe rotavirus diarrheal disease, providing protective efficacy ranging from 80 to 91%. Of special interest was the significant protection that the vaccine provided against dehydrating disease as well as disease severe enough to require hospitalization.

During 1996-8 Dr. Kapikian's 20 year commitment to research on rotavirus epidemiology, immunology, genetics, molecular virology and vaccine development culminated in the validation of a live attenuated rotavirus vaccine. This was the first and only rotavirus vaccine to be approved by the US FDA Vaccine Advisory Committee as well as the Advisory Committee on Immunization Practices of the US Centers for Disease Control and Prevention (CDC) and the Department of Health and Human Services (HHS).

Unfortunately, subsequently, the CDC recommended that the vaccine not be used in the United States because they perceived an association of the vaccine with development of intussusception. Exhaustive analysis of the recipients of approximately one million doses of the vaccine performed by Lone Simonsen, David Morens, Albert Kapikian, John La Montagne, Brian Murphy, as well as Robert Chanock could not confirm the earlier analysis that led to withdrawal of the vaccine. Pharmaceutical establishments in developing countries representing more than one half of the world's population have voted in this controversy by lining up to license the second generation version of a genetically derived vaccine constructed by the original strategy

Dr. Kapikian's development of the first fully validated, safe, effective rotavirus vaccine is a major achievement in preventive medicine and public health, because human rotaviruses are responsible for 40% to 50% of severe diarrheal disease in infants and young worldwide. In developing countries these viruses are estimated to cause approximately 600 thousand fatal diarrheal episodes each year. In a phase 3 clinical trial in Venezuela, Dr. Kapikian's quadrivalent rhesus rotavirus vaccine was shown to be highly effective, indicating that it should have a major impact on public health by preventing fatal diarrheal disease in developing countries. Although mortality due to rotavirus disease is low in developed countries, the economic burden is quite high. Rotavirus infection is estimated to be responsible for up to 70,000 hospitalizations in the United States yearly and the total economic burden, including lost work time and physician visits, is estimated to be over one billion dollars per year.



Robert M. Chanock, MD, is Chief of the Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health. He was the first to identify and characterize respiratory syncytial virus (RSV), which each year contributes to the deaths of one million infants and children worldwide. Dr. Chanock began his career in Dr. Albert Sabin's laboratory at the University of Cincinnati.

Congratulatory Remarks on the Occasion of the 2005 Sabin Gold Medal Presentation to Albert Z. Kapikian, MD

Roger I. Glass, MD, PhD
Chief, Viral Gastroenteritis Section
Centers for Disease Control

It is an honor for me and for all of us to be here tonight to celebrate Dr. Kapikian's receiving the Sabin Award for Vaccinology. Al, you are joining the incredible ranks of leaders in the field who have previously received this wonderful recognition. Your work is really a continuation of the legacy of Albert Sabin—to make live, oral vaccines that mimic the protection afforded by natural infection. So we really have the light of one Albert shining on another Albert.

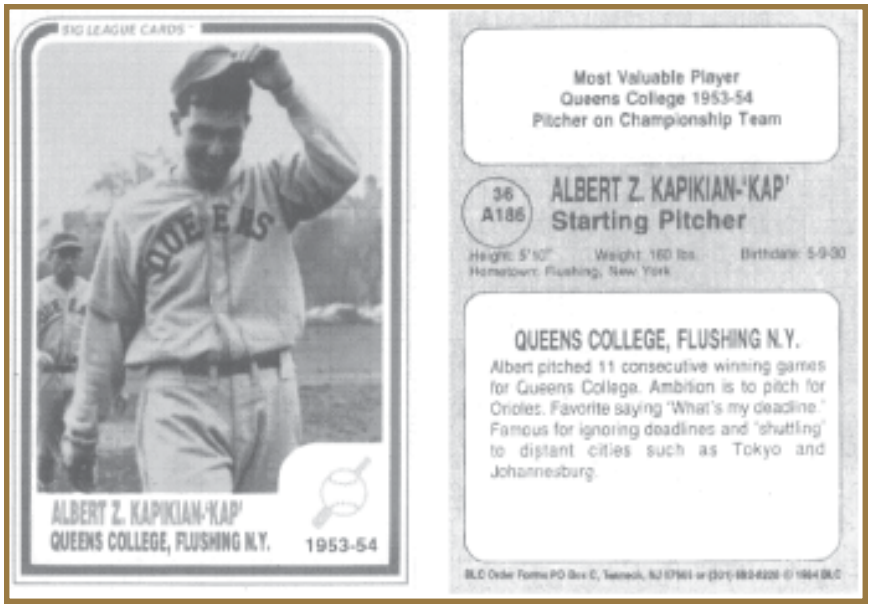
I did not want to speak alone tonight so I called around to many of your former students and colleagues and asked them for suggestions, stories and ideas. From these stories came several themes in common—dedication to science, professional integrity, leadership, tenacity, vision, humor, warm personal qualities, compassion and perhaps most of all, love and passion to improve the health of the world's children through a rotavirus vaccine. But Al has many loves.

Al grew up in Brooklyn of Armenian parents. His first love was his family and his brother. His next love was baseball. He was an early aficionado of the New York game "stepball," a form of baseball for those who lived in row houses and didn't have a full fledged playing field. By college, his street savvy was parlayed into an 11-0 winning season as the pitcher for Queens College in New York, an event celebrated in the early 1980s when John La Montagne produced an official baseball card featuring Al on the mound in his college gear. He went on to medical school at Cornell and ended up at NIH pursuing a career in epidemiology and laboratory research.

As a young man, his next love was—need I say—a young woman in the art department at NIH. The combination of art and science seemed to flourish then as it has for nearly 40 years. Cathy, that beautiful young starving artist, has become a renowned artist of religious tapestries and is still by his side, with their three sons.

After a few years in the Laboratory of Infectious Diseases where all the respiratory viruses—rhinoviruses, RSV, influenza, adenoviruses—had been researched or discovered, Bob Chanock relegated Al to the next great unknown, the enteric viruses. Al took the family to England where he learned electron microscopy with June Almeida and the electron microscope became his next love. He would sit in the dark of the EM lab for hours trying to make absolutely certain that what he was seeing was real and novel. And this love between Al and his microscope bore many fruits. When he turned his microscope on fecal specimens from an outbreak in Norwalk, Ohio, he discovered the Norwalk virus, the first virus definitively linked to gastroenteritis. And he went on with Steve Finestone to use the same methods to discover hepatitis A virus.

When rotavirus was discovered by Ruth Bishop in Australia in 1973, Al went back to his EM to look again at fecal specimens from infants with diarrhea. He immediately confirmed the presence and importance of these viruses. Al's lab took off on a research agenda that was explosive—developing a simple diagnostic—the Enzyme linked immuno-absorbant assay (ELISA) with Bob Yoken essential to assess the epidemiology and burden of the disease, growing the virus with Richard Wyatt essential to make a vaccine,



developing methods for reassorting the virus by Harry Greenberg and Karen Midthun now used in preparing the rhesus and bovine vaccines, working on the immune response to disease with Kim Green, characterizing viruses and neutralization assays with Taka Hoshino, and conducting clinical trials with Irene Perez Schael and Jorge Flores. The efforts of this group together led to the successful development and testing and ultimately licensure in 1998 of the first rotavirus vaccine, RotaShield.

In 1979, Al joined the Steering Committee of the WHO Diarrheal Disease Control Program with Ruth Bishop and Tom Flewett. The group laid out a long-term plan to make rotavirus vaccine development a priority for WHO and prepared an agenda to achieve this goal. Ever since, WHO and the international decision making groups in health have recognized rotavirus disease as a high priority and considered vaccine development as an achievable and worthy goal.

After nearly 20 years of hard work, great science, and many frustrations, this enduring hard hitter finally scored big when the Rhesus Tetravalent Rotavirus Vaccine was finally licensed by Wyeth Lederle as Rotashield and was immediately recommended by the Advisory Committee on Immunization Practices of CDC for the universal immunization of all children in the United States. This was a major victory for Al and the vaccine world. A newspaper editorial at the time wondered who was more worthy of great public acclaim—Monica Lewinsky, Kenneth Starr or Albert Kapikian for their contribution to humanity—and of course, the rhetorical answer was Kapikian who provided the first vaccine for a disease that was killing a half million children each year. In 1999, Al, Ruth Bishop and I together received the Pasteur Award of the Children's Vaccine Initiative. The honor was fleeting.

In July, 1999, when a few rare cases of intussusception were identified following receipt of the vaccine, the universal recommendation was placed on hold. After much epidemiologic research, the vaccine was felt to be associated with a small but significant risk of intussusception and the company withdrew the vaccine from the market. Despite the fact that a half million deaths

per year might have been prevented by this vaccine, this decision changed the face of rotavirus vaccines for years to come.

While the other major vaccine manufacturers, Merck and GlaxoSmithKline, each proceeded to develop alternative live oral vaccines, Al struck out on another front. He took another candidate vaccine, the UK bovine reassortant vaccine, believed to be less reactogenic than the rhesus vaccine, and found it to be equally effective in a single trial conducted by Prof. Timo Vesikari in Finland. NIH is now proceeding to license this vaccine to emerging manufacturers in India, China and Brazil, countries with established local producers who could make this vaccine in bulk and at much less expense. India and China are the countries where rotavirus causes the most deaths and they are countries that also only depend upon vaccines made by their own manufacturers. This could really help speed introduction of the vaccine to the developing world. In February, 2005, Dr. Isaias Raw, head of the Butantan Foundation in Sao Paulo, was the first to license from NIH the new Kapikian vaccine, a bovine-human reassortant product. Dr. Kapikian along with Ciro de Quadros of the Sabin Institute and myself all received awards for technology transfer from the Governor of Sao Paulo, Brazil in a ceremony at the Brazilian institution.

So despite the many ups and downs in this long career, the highs of licensing a new vaccine and the low of seeing it withdrawn for reasons still felt to be in question, the future seems rosy and Dr. Kapikian is still in the forefront of the field and one step ahead of us all.

Al, you have been the head of a great laboratory and mentor to a generation of students and researchers, the visionary of a research effort that has fueled interest and success with rotavirus vaccines, a scientist who has been a role model for creativity, integrity, and adherence to the highest professional standards, a crusader in believing that we can prevent the scourge of rotavirus diarrhea in the developing world through the use of vaccines, a trooper in sticking with these vaccines when the world only spoke of their adverse events, and a victor in now seeing your new vaccines licensed to companies who could well make

them affordable for children in the poorest countries of the developing world. We all salute you tonight as do the generations of future children who can look forward to a life spared of severe diarrhea that is rotavirus.

In closing, since you are such an avid baseball enthusiast, I thought it only proper to end by dedicating a baseball poem to you as a tribute to your efforts. The poem is titled "Albert at the Bat," a takeoff of a poem written in 1888 by Ernest Thayer on the occasion of Casey striding to the plate at Mudville.

See poem on next page.

Roger Glass, MD, PhD, is Chief of the Viral Gastroenteritis Section of CDC's National Center for Infectious Diseases. Dr. Glass has been a consultant and advisor to many groups interested in new vaccines and is the scientific advisor to the Rotavirus Vaccine Program and the Children's Vaccine Program at PATH (Program for Appropriate Technology in Health), the World Health Organization's Program on New Vaccines, Fondation Mérieux, and UNICEF, and he was recently elected to the Institute of Medicine of the National Academy of Science.

Albert at the Bat

Adapted from Ernest Lawrence Thayer, 1888
by Roger Glass, 2005

The outlook wasn't brilliant for the kids with runs that day
The first vaccine struck out when CDC recalled the play.
WHO was in a quandary and FDA called Foul
And back into the batter's box came a man known as simply "Al".

A straggling few got up to go in deep despair, the rest
Clung to that hope that springs eternal in the human breast
They thought if only Kapikian could take another whack
We'd put up even money with Albert at the Bat!

There was ease in Albert's manner as he stepped into his lab
There was pride in Albert's bearing as he took another stab.
For his public health grand slam he needed only to focus
His efforts on a vaccine to beat that terrible rotavirus.
Ten thousand eyes were on him as he rubbed his hands in poop.
Five thousand tongues applauded as he wiped them on his suit.
Then while the pitcher ground the virus ball into his hip
Defiance flashed in Albert's eye, a smile curled Albert's lip!

And now the pitch came once again and Albert's look was stark,
He eyed the ball and swung sending the ball out of the park
It sailed beyond the ball field , it would bring him joy and fame,
For Albert, mighty Albert was running the bases again!

He ran to Finland, China, India and landed in Brazil
If his vaccine were successful no child should go ill.
He turned the bases slowly and his fans and spirits soared
And hope rose for children round the world who let out a mighty roar.

And somewhere in this favored land the sun is shinning bright,
The band is playing somewhere and somewhere hearts are light,
And somewhere children are laughing and today Sabin doth proclaim
That there is great joy in Baltimore, Al Kapikian has won the game!

Remarks Upon Acceptance of the 2005 Albert B. Sabin Gold Medal

by Albert Z. Kapikian, MD

I am truly honored to receive the Albert B. Sabin Gold Medal and thank the committee for their selection. The award carries with it not only the name of one of the great pioneers of virology and vaccinology, but it also carries with it the responsibility to strive to continue Dr. Sabin's legacy of excellence.

I've entitled my presentation tonight simply "A Privileged Odyssey" because indeed my 47-year career at NIH has been a privilege. I recall the words of my first mentor Dr. Bell who told me soon after my arrival at NIH that "in this job we're paid to do a hobby." How right he was and indeed how privileged I've been! Besides the intellectual rewards from scientific explorations, one of the privileges I've enjoyed greatly has been the ability to forge friendships in our everyday activities with unique colleagues.

A little biographic information is usually called for in this setting. As senior medical students, we were given a one-month elective period. I chose to spend part of it at the Memorial Hospital Walk-in Clinic and the rest writing a review paper on a new group of viruses, the adenoidal-pharyngeal-conjunctival viruses (which were the forerunners of the adenoviruses). These viruses had been discovered in 1953 at the NIH by Rowe and Huebner. However, there was a stumbling block for me. As I began reading the papers about these new viruses, the term "monolayer tube cultures" kept recurring and I did not know what they were. Tissue culture virology was in its infancy and thus we were not exposed to this in our microbiology course. My preceptor Dr. Ed Kilbourne in the Department of Public Health, a department led by Dr. Walsh McDermott who incidentally was my idol as a student, suggested that I write to Dr. Robert Huebner, the chief of the lab at NIH where the discovery was made, to see if I could arrange a visit. I was invited by Dr. Huebner, drove from New York to NIH and to my surprise was greeted by Dr. Huebner himself.

He proceeded to take me to his lab to show me what a monolayer cell culture tube was. He also asked me to send him a copy

of the review article, which I did. The following year, I received a phone call from Dr. Huebner inviting me to visit NIH to look at a position dealing with mouse studies in a new program of cancer research. I visited but turned down this position. I accepted a second offer from Dr. Huebner a few weeks later to join the epidemiology section to study predominantly human respiratory viruses in various epidemiologic settings in Dr. Bell's Epidemiology Section, and I've been there ever since.

The three individuals who had the greatest influence on my career at NIH have been Dr. Joseph Bell, who was the epidemiologist's epidemiologist and who taught by example; Dr. Huebner, who was always an inspiration and who had more ideas in 5 minutes than anyone I've ever known; and Bob Chanock, whose creativity, enthusiasm, and leadership have kept the LID in a prominent position for over 30 years.

When I arrived at NIH in 1957, the lab in Building 7 was a beehive of activity because it was the golden age of virology with regard to the discovery of new viruses, which was made largely possible by the tissue culture era ushered in by the discovery of the growth of polio virus in nonneural cells by Enders, Weller and Robbins. Many viruses were discovered at NIH and other labs.

A meeting at the New York Academy of Sciences, the year before my arrival at NIH, titled "Viruses in Search of Disease" summarized the story in this publication of the proceedings. Scores of viruses were being discovered and many of them could not be associated with any disease and thus were called "orphan viruses." Dr. Huebner was the conference chairman and he wrote the final paper entitled "The Virologist's Dilemma" in which he described the criteria for associating a virus with a disease.

Why do I tell you this background? I'd like to share with you a letter that Dr. Sabin wrote to Dr. Huebner in October 1982 regarding this scenario. Dr. Sabin wrote the letter in recognition of a tribute which was to be held on Oct 18, 1982 honoring Dr. Huebner's retirement to NIH scientific emeritus status. In addition, the letter tells us so much about both Dr. Sabin and Dr. Huebner.

Letter follows...

October, 1982

Dear Bob,

It will be a special pleasure for me to join your many friends on October 18 to recall the highlights of your exciting life and the important contributions you have made to our understanding of the maladies that bring misery to human existence.

To me, it matters not that I cannot find some special reason or purpose for my existence among the myriads of creatures on this planet. It is enough to be able to witness the awe-inspiring grandeur and order in nature, to enjoy the magnificent beauty that the best minds of the human species have added to the raw grandeur of nature, and to be a member of that great army that struggles in a multiplicity of ways to reduce the pain and misery that unfortunately is also a part of human existence.

Dear Bob, for many decades you and I have been members of this great army. The search for understanding the mysteries of human diseases and of the agents that caused them has enriched our lives. The moments when our paths crossed were illuminated by a special light.

I want to recall here one of the stories you told about 25 years ago at a meeting on the so-called "orphan" viruses, when someone called for a moratorium on the search for new viruses for which there were no known diseases. It was a story about a farmer in a remote part of Scotland whose wife was about to have a baby in the middle of the night. The doctor who was examining his wife in the dark called out: "Angus, come here with the lamp - the baby is coming." The baby came, the doctor congratulated him, and as Angus was walking away with the lamp, the doctor again called from the darkness: "Come back with the lamp, I think there is another on the way."

Angus trudged back with the lamp, another baby was born, the doctor congratulated him again. As Angus once more was walking away with the lamp, the doctor excitedly called him to come back with the lamp because there was still another baby on the way. Angus stopped dead in his tracks and yelled: "I'll na come back with the lamp - it's the light that attracts them."

The moral you drew from this story is that those who believe that one can get rid of problems by turning off the light are poor misguided souls. Bob, it can be said of you that you turned on many lights where darkness prevailed and helped to solve many problems that seemed insoluble before.

If I may use symbolic biblical language I will thank God for having created Bob Huebner – in Bob Huebner's image. With respect and admiration from your friend and colleague,

Albert

This was a familiar scene in the lab showing Bob Chanock and Bob Huebner with a roller drum with monolayer tissue culture tubes.

The goals of the lab were clear : To study the natural history and epidemiology of acute illness and infection; to detect new infectious agents and determine their etiologic role in disease; and to develop methods for disease control with special emphasis on vaccines—I worked on respiratory viruses, mostly rhinoviruses and coronaviruses. Since almost all human coronaviruses did not grow in tissue culture, the electron microscope was a method of choice for their recognition. Dr. Chanock suggested that I go to Tony Waterson's lab in London to learn electron microscopy from one of the most prominent electron microscopists—June Almeida, who pioneered the use of immune electron microscopy (IEM). The arrangements were made quickly by Bob, and I was on my way with my family in March 1970.

I learned the IEM technique—which is the direct observation of antigen—antibody interaction. However, when we added serotype specific antiserum to a preparation of the same material in a companion tube and examined it by electron microscopy, we saw aggregation of virus particles by the specific antibodies which bridged the particles and thus, there was no question now that the suspension contained rhinovirus particles.

In the late 1960s-early 1970s our lab at LID began a new research program on trying to find the cause of viral gastroenteritis. It was assumed that viruses were important agents of this disease but no virus had ever been found to be an important cause. Thanks to Bill Jordan and his colleagues, we knew infectious gastroenteritis, predominantly viral, was the second most common disease experience in the Cleveland Family Study covering a period of about 10 years and 25,000 illnesses.

In addition, the importance of diarrheal diseases on a worldwide scale is shown as diarrheal diseases are consistently ranked as one of the top 10 causes of death from all conditions and one of

the top three from infectious diseases. The greatest toll from diarrheal disease occurred in infants and young children.

It was in this setting that we began to investigate various outbreaks of viral gastroenteritis looking for putative etiologic agents, but without success.

However, one sharp outbreak that occurred in a Norwalk, Ohio elementary school that was studied by Adler and Zickl of CDC proved to be very rewarding. Half of the students and teachers developed gastroenteritis during the outbreak and secondary cases were also observed. No agent, viral or bacterial, could be found as the cause. The CDC provided specimens from this outbreak to NIH where Dolin, Blacklow et al initiated a series of adult volunteer studies. A rectal swab specimen from a secondary case was diluted and after being tested for known agents, this bacteria-free filtrate was given orally to three volunteers—two of the three developed gastroenteritis. A stool filtrate from one of these volunteers induced illness on passage to other volunteers indicating that there was a transmissible nonbacterial agent responsible for these illnesses. However, all attempts to grow and identify the agent using the new tissue cultures and organ cultures were unsuccessful.

An example of IEM is shown here in a study carried out in England on a rhinovirus suspension, In this preparation, the rhinovirus does not have a very distinctive structure by negative stain electron microscopy. It looks like a "dot" and it is not really possible to say whether this "dot" is a virus particle.

I had returned from England and decided to use my newly learned IEM technique on the stool filtrate which was known to be infectious to try to detect virus particles. I thought that the same principle as observed with the rhinovirus IEM study might apply, and thereby enable the identification of a virus particle in the stool filtrate. I reacted the stool filtrate with a volunteer's convalescent phase serum to see if aggregates of virus particles might be identified. After months of negative findings, we found aggregates of 27nm particles coated with antibody in the infectious stool filtrate.

A particularly clear example of the morphology of the Norwalk virus is shown in this aggregate because the filtrate was reacted with a pre-challenge serum containing a low-level of antibody and thus the structure of the particles is not obscured by the antibody. However, the identification of virus-like particles was hardly enough evidence to establish an etiologic association, because they could have been adventitious agents totally unrelated to the illness.

To establish an etiologic relationship, it was important to devise an antibody assay by IEM for this fastidious virus which still cannot be grown in tissue cultures. In this example of a serologic response, the 27nm particle-containing stool filtrate has been incubated with a volunteer's pre-challenge or convalescent-phase serum. It is very clear that the volunteer developed an antibody response because the antibody that is coating the particles that were incubated with the convalescent phase specimen is significantly greater in amount than the antibody coating the particles incubated with the pre-challenge serum. We also found that individuals in the original Norwalk outbreak who had become ill under natural conditions developed antibody responses also to the 27nm particle in the filtrate and from this and other evidence we suggested that this 27nm virus particle was the etiologic agent of the Norwalk outbreak.

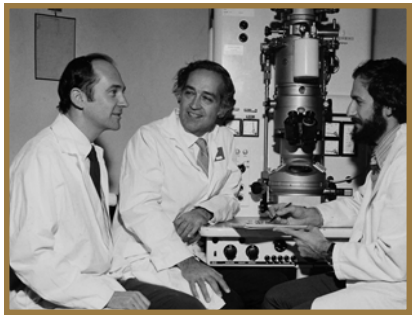
The antibody responses were rated on a 0-4+ scale and a 1+ difference was considered to be a significant response, and most importantly, studies were done under code. The Norwalk and Norwalk-like viruses (now known as noroviruses) are considered to be the major cause of nonbacterial epidemic gastroenteritis in adults and older children being responsible for over 90% of such outbreaks in CDC studies. In addition, noroviruses were found by CDC to be the leading cause of total gastroenteritis in the United States (23 million cases/yr) and the leading cause of food-borne gastroenteritis. Their role in diarrhea of infants and young children is under study.

Following the Norwalk virus studies, Steve Feinstone, Bob Purcell and I began an intensive effort to identify the virus of hepatitis A using IEM techniques similar to those used for the discovery of the 27nm Norwalk virus. Stool and specimens were provided by Dean Gibson (Armed Forces Institute of Pathology) from previous infectious hepatitis (MS-1) adult volunteer studies.

In 1974, we identified a 27nm virus-like particle in stool suspensions by IEM and demonstrated that hepatitis A volunteers developed an antibody response by IEM as did other individuals who developed hepatitis A under natural conditions. From this and other evidence, we suggested that these 27nm particles were the etiologic agents of hepatitis A.

Because there was now a way to measure antibodies to hepatitis A virus by IEM, Steve Feinstone, Bob Purcell and I examined serum specimens from patients who had transfusion-associated hepatitis that was negative for hepatitis B antigen. We found that none of the 22 patients had developed antibodies to the newly identified hepatitis A virus and thus suggested that another agent was responsible for the hepatitis since neither hepatitis A nor hepatitis B viruses appeared to be causally related. Later, of course, hepatitis C was discovered by others and has emerged as an important new hepatitis virus.

In 1973, about one year after the discovery of the Norwalk virus, Ruth Bishop et al. reported the identification of virus particles in epithelial cells of duodenal mucosa from children with acute nonbacterial gastroenteritis, marking the discovery of the 70nm rotaviruses. These particles were found in the stools also a short time later in various locations.



Steve Feinstone, Kapikian, and Bob Purcell shown with the Siemens Elmiskop 1A electron microscope.

We began clinical studies at Children's Hospital in DC using electron microscopy as our primary method of virus detection to determine the importance of the Norwalk virus. However, 13 of the first 21 stool specimens we examined were rotavirus positive. This study was continued in collaboration with Karl Brandt, and rotavirus was found to be the major cause of diarrhea requiring hospitalization as about one-third of the infants and young children admitted had rotavirus gastroenteritis over a period of about six years of study.

Rotaviruses are quite egalitarian viruses, causing about 45% of severe diarrheal illnesses in both developed and developing

countries. It also shows that rotaviruses are clearly the single most important agents of severe diarrhea when compared to all other known viruses and bacteria. It is interesting to note that the noroviruses, members of the calicivirus family, appear to be the second most important viral cause accounting for about 8% of the severe diarrheal illnesses.

Rotaviruses are responsible for about 400,000-600,000 deaths/year in infants and young children under five years of age, predominantly in developing countries. The greatest toll of deaths is in Asia and sub-Saharan Africa. In the United States rotaviruses cause deaths infrequently but are responsible for 60-70,000 hospitalizations and 500,000 outpatient visits each year in the <5 year age group. Rotaviruses are consistently shown to be the single most important cause of severe diarrhea in developed and developing countries, being responsible for 30-50% of all such illnesses in the under two-year age group. It became clear that a vaccine was needed to prevent the severe diarrheal illnesses caused by the four epidemiologically important serotypes VP7 1, 2, 3, and 4.

We developed a live rotavirus vaccine comprised of 4 G (VP7) serotypes: rhesus rotavirus (RRV) itself represented serotype G3; and three human RV-RRV reassortants, which were made by Karen Midthun et al. in our lab, with each of the reassortants containing 10 RRV genes and one human RV gene encoding G serotype 1, 2, or 4 ("Jennerian" and "modified Jennerian approaches).

In 1998, this quadrivalent vaccine, which was named RotaShield, was licensed by the FDA to Wyeth-Ayerst Labs after demonstration of its safety and efficacy. The vaccine was recommended by the Advisory Committee on Immunization Practices for routine administration to infants at two, four, and six months of age.

Reassortant rotaviruses were isolated from tissue culture monolayers coinfected with RRV and a poorly cultivatable human rotavirus with serotype 1, 2, or 4 specificity. The desired reassortant was selected by exposing the progeny of the coinfected cultures to a set of monoclonal antibodies directed to the VP7 outer capsid neutralization protein of RRV. This led to the selection of reassortant strains that possessed a single VP7 gene from human rotavirus 1, 2, or

4, and 10 genes from RRV. RRV itself provided coverage for VP7 serotype 3.

The final product, RotaShield, was a lyophilized vaccine reconstituted with a buffer diluent which was squeezed from the dispette into the vial containing the vaccine. The reconstituted vaccine was withdrawn into the dispette and the vaccine was administered orally via the dispette.

After over one million doses of the vaccine had been given to over 600,000 infants, the CDC summarized in the July 16, 1999 MMWR the events involving 15 cases of intussusception that had been reported to the Vaccine Adverse Event Reporting System, following RotaShield administration.

Although about 2000 total cases of intussusception occurred annually in the United States in infants under one year of age, almost 40 a week, it was disturbing that 13 (87%) of the 15 cases clustered after the first dose and 12(80%) of the 15 cases had onset within one week of any dose. Therefore, use of the vaccine was suspended pending further studies.

What is the status of RotaShield? The vaccine was withdrawn in October 1999, as CDC reported a link with intussusception from three studies, with odds ratios of up to 1.8, which translates to an attributable risk of 1:2500, and projected an excess of up to 1600 cases in a national program of vaccination.

There continues to be controversy on the attributable risk of the vaccine as NIH-AHRQ (Agency for Healthcare Research and Quality) studies led by Lone Simonsen examining hospital discharges for intussusception in 14 RotaShield high-use states (~250,000 vaccinees) found a 3% decrease in intussusception admissions in <1 year olds during the period of RotaShield's use when compared to the previous year when RotaShield had not been used. There was clearly no "epidemic" of intussusception.

In October 1999 at the ACIP meeting when the vaccine recommendation was withdrawn, CDC projected that there would be up to 1600 excess cases of intussusception from the case-control study. However, when this study was published, following various adjustments, CDC reported that there would be 361 excess cases of intussuception in a national program. The NIH-AHRQ study observed

a decrease of eight cases (3%) of intussusception in <1 year olds during the RotaShield use period compared to the same period in the previous year in this age group when the vaccine was not available, in a population in which ~250,000 infants had received one or more doses of RotaShield. Thus, there were no excess cases of intussusception in the <1 year age group in this study and there was actually a projected negative attributable risk in a national immunization program.

Was it possible that there was a compensatory decrease in intussusception beyond the immediate three week postvaccination interval that might explain these dicrepant results regarding the attributable risk of the vaccine? There was indeed a highly increased risk of intussusception after the first dose in the first two weeks in the CDC case-control study. However, in a later published analysis, CDC reported an odds ratio of 0.3 (i.e. ~70% fewer cases of intussusception in vaccinees than in controls) in the period beyond 21 days after vaccination. CDC attributed this to socioeconomic factors.

However, in an NIH analysis by Simonsen of CDC's case-control database, the odds ratio for weeks 1-12 post RotaShield confirmed an initial temporal increase in intussusception followed by a temporal decrease (odds ratio 0.3) in intussusception beginning at three weeks post RotaShield. Socioeconomic factors could not be confirmed.

Did this compensatory decrease account for no excess cases in the NIH-AHRQ hospital admission study? Was RotaShield a trigger that was compensated for later after vaccination? Simonsen's expanded analysis of CDC's case-control study showed the initial temporal increase in intussusception followed by the compensatory decrease resulting in no apparent increase in intussusception.

What is the current status of RotaShield? NIH recently licensed RotaShield to BIOVIRx, Inc which plans global commercialization using identical manufacturing technology as Wyeth Labs had previously.

A key factor to its implementation will be a revised age of vaccination in order to avoid the peak period of vulnerability to naturally-occurring intussusception (4-9 months of age). This last point will be discussed further.

The age distribution of naturally-occurring intussuception in a Southern California health maintenance organization peaked between

4-9 months of age over an almost seven-year period in 78 infants under one year of age, with a relative refractory period for developing intussusception during the first three months of age.

In a review of 400 hospitalized cases of intussusception in the London Hospital over an 18-year period, 1903-1920, about 70% or 279 cases occurred in infants under one year of age indicating that this was a condition of infants predominantly.

The distribution of intussusception cases by month of age in the 279 infants under one year of age in the London Hospital study showed that the two month and older age group experienced over 99% of the cases, indicating that the 0-<2 month age group was relatively refractory to developing intussusception.

What is the relevance of this information to the RotaShield saga? Simonsen examined the age distribution of the 43 cases who developed intussusception which had onset during the two weeks after the first dose in the CDC case-control study and found that over 81% of the cases were three months of age or older whereas only 19% were <3 months of age.

Further analysis by Simonsen showed that the three month or older age group that developed 81% of the cases had received only 38% of all first doses according to the CDC National Immunization Survey. Thus, they developed a disproportionately greater number of cases relative to the lower percentage of first doses of vaccine they had received. In addition, no cases of intussusception were detected in the <60 day old age group even though this age group had received 16% (~70,000) of ~433,000 first doses.

It thus appears that "catch-up" vaccination of older infants (1st dose given after the ideally recommended age of two months) during the age period of high vulnerability to intussusception contributed disproportionately to the number of cases. Therefore, the vaccination age had a striking effect on the absolute risk of intussusception.

The non-availability of RotaShield has fueled intense discussion in both scientific and lay publications because of risk/benefit considerations particularly in the developing countries, where over 600,000 infants die each year from rotavirus diarrhea.

For example, Charles Weijer, a physician-ethicist at Dalhousie University has written in the British Medical Journal in 2000 regarding the withdrawal of RotaShield: "…If the next vaccine takes three to five years to get to the stage where tetravalent rhesus rotavirus vaccine is now, the choice to wait must be weighed against the cost of waiting: 1.4 to 3.2 million preventable deaths. Some have falsely assumed that inaction is a morally neutral state. But if one is culpable for vaccine related deaths, then one is also culpable for deaths caused by withholding the vaccine.

Is there a moral difference between a treatment that may cause a sick child to die and a vaccine that may cause a healthy child to die? Because public health doctors treat unhealthy populations rather than unhealthy patients, the risk of death or serious disability must be lower with vaccines than with clinical treatments. The risks of tetravalent rhesus rotavirus vaccine seem comparable to the risks associated with measles, mumps, and rubella vaccine. The moral yardstick for the public health physician is ultimately the same as for clinicians: do the benefits of vaccination exceed the risks? In a developing country in which a child's risk of death from rotavirus diarrhea is 1 in 200 or greater the answer may well be "yes."

News stories about this dilemma also appeared, such as: *The Lancet* in 2000 entitled "Lifesaving vaccine caught in an ethical minefield"; in *Science* in 2001 entitled "Rethinking a vaccine's risk" with the sub-heading "Worried about rare but severe side effects, 2 years ago Wyeth pulled from the market a new vaccine that prevents a major cause of diarrhea. Now the medical community is questioning that risk-benefit calculation"; in *Science* in 2004 regarding new rotavirus vaccines on the horizon, entitled "Rotavirus vaccines' second chance" with the sub-heading "Two new vaccines against a major cause of deadly childhood diarrhea are nearing the market. Will the entire effort crash and burn as spectacularly as it did 5 years ago?"; in *Lancet Infectious Diseases* in 2004 entitled "New vaccines to fight killer rotavirus" with the opening sentence "The withdrawal of the world's first rotavirus vaccine, RotaShield, in 1999—within one year of its approval—was a devastating blow to all those involved in the fight against the deadly virus."

I was surprised to find an editorial in the *NY Times* on January 29, 2005 entitled "The vaccine balance" regarding the introduction of a rotavirus vaccine by GlaxoSmithKline in Mexico. In the fifth paragraph the editorial states: "Glaxo may also have come to Mexico because of the fate of Wyeth's RotaShield vaccine, which was pulled from the American market because it was found to cause intussusception, an intestinal obstruction, at a rate of one case for each 10,000 vaccinated children. A later study by the National Institutes of Health, however, argued that RotaShield was not responsible, but the damage had been done. Once the vaccine was deemed unsafe in the United States, it was politically impossible for Wyeth to sell it even in countries where it might have caused a handful of deaths while saving 100,000 lives." The final sentence of the editorial states "America should not be setting the standards for diseases that cause light winds at home, but hurricanes abroad."

We also pursued a second generation bovine rotavirus-based rotavirus vaccine in parallel with our studies with RotaShield and its precursors because (1) the rhesus rotavirus-based vaccines were associated with a transient and characteristically low grade fever in up to one-third of vaccinees; (2) bovine rotavirus-based vaccines were characteristically non-reactogenic; and (3) human-bovine (UK) rotavirus reassortants had already also been made by Midthun et al in our laboratory for each of the four serotypes.

We initiated clinical studies with the bovine rotavirus-based reassortants. In 1991, we carried out safety and immunogenicity trials with individual human-bovine rotavirus reassortants at Johns Hopkins University (JHU) sequentially in adults, children and infants. Reassorants with G1, 2, 3, or 4 specificity were safe and immunogenic.

In 1995, we initiated similar sequential studies at JHU with the four reassortants combined (BV-TV) and showed it was safe and immunogenic. These studies at JHU were led by Mary Lou Clements-Mann, who with her husband, Jonathan Mann, died in the Swiss Air flight on September 2,1998. She and her husband made seminal contributions to science and each had genuine empathy for the well-being of humanity, and both are sorely missed.

We carried out a collaborative trial of the RotaShield precursor vaccine (RRV-TV) and the BV-TV vaccine in ~500 infants and young children in Finland under the leadership of Timo Vesikari. The goal

was to evaluate the reactogenicity, immunogenicity, and protective efficacy of each vaccine given in a two dose schedule.

The number of febrile episodes was significantly greater in RRV-TV vaccinees than in controls, whereas for the BV-TV vaccinees the number of febrile episodes was not significantly different between vaccinees and controls. Importantly, BV-TV and RRV-TV each induced over 85% protection against severe rotavirus diarrhea.

Another important question is whether or not a 4 serotype rotavirus vaccine will provide adequate protection for the epidemiologically important serotypes in developing countries. In a recent review of the distribution of rotavirus serotypes worldwide by Santos and Hoshino, it appeared that in addition to the conventional serotypes in the vaccines, serotype VP7(G):9 was emerging in several areas of the world and serotype VP7(G):8 was emerging in regions of Africa.

For this reason, we believe that the rotavirus vaccine should be designed for use in developing countries by the addition of these serotypes to the tetravalent rotavirus vaccine, thus formulating a hexavalent vaccine. Coverage of the VP7 serotypes will eliminate the need to protect against the various VP4 specificities recognized for various VP7serotypes. Reassortants for each of these strains have been prepared by Taka Hoshino in our lab.

I believe that the risk of intussusception clouds the future of all rotavirus vaccines. Therefore, we are proposing a strategy of vaccine delivery derived from lessons learned from RotaShield that has the potential to eliminate the risk of intussusception.

We are proposing a revised schedule for administration of the hexavalent vaccine: The first oral dose given at 0-4 weeks of age; the second oral dose given at 4-8 weeks of age with a minimum of 3 weeks between the 1st and 2nd doses; and no "catch-up" vaccination beyond 8 weeks of age. In this way, the period of maximum vulnerability for developing intussusception (4-9 months) under natural conditions would be avoided.

What are the prospects for the manufacture and development of a bovine rotavirus-based vaccine? License applications have been received by the NIH Office of Technology Transfer from one company in the United States, two institutes and one company in China, four

companies in India and one foundation-institute in Brazil (Butantan). The license was granted to Butantan on Feb 23, 2005. The Butantan Institute produces 81% (i.e. 188 million doses) of all the vaccines made in Brazil.

Just as it takes a lot of people to make a beautiful rainbow, it takes many people to carry out the work I have described. I have only been able to mention a few of them but I express my deep thanks to all of the collaborators.

I would like also to acknowledge my family members who have also contributed to the beautiful rainbow and who are here tonight—my wife Catherine, our three sons Albert, Tom, and Gregg, Tom's fiancée Lisa, and my brother Carl, sister-in-law Stella, and niece Carla.

Thank you.

Catherine and Albert Kapikian

Memorial Tribute to John R. La Montagne, PhD

(1943-2004)

John R. La Montagne, PhD, was recognized with a special memorial tribute during the 2005 Sabin Gold Medal Presentation Ceremony. Regina Rabinovitch, MD, MPH, director, Infectious Diseases, Bill & Melinda Gates Foundation, provided a photographic montage and commentary that eloquently depicted the professional contributions and personal friendships that her colleague accumulated during his life. She also presented the a special posthumous recognition gift from the Sabin Vaccine Institute to Mary Elaine Elliot La Montagne.

Albert Kapikian, in his evening's remarks said: I am particularly saddened by the untimely loss of John La Montagne who was one of my closest friends at NIH. John and I shared many common interests, both scientific and non-scientific, the latter being our passion for baseball. Before John's death we had discussed and looked forward to attending a baseball game in DC to see the proposed new Washington team. In addition, a while ago, John had sent me some information about a new membership of his. He had become a charter member of the Cal Ripken Sr. Foundation, a membership that cost the significant amount of $26.32 or, for you baseball afficionados 2632 cents, which signifies the number of games that Cal Jr. had played consecutively to beat Lou Gehrig's record of 2130 consecutive games. John encouraged me to join also and I did by sending in my $26.32 and

also became a charter member. John was a unique human being—courageous, with impeccable integrity, loyal, fun to be with and a man of great humility. He was admired by all and is sorely missed.

La Montagne served as deputy director of the National Institute of Allergy and Infectious Diseases (NIAID) from 1998 until his sudden death this past November. He was a presenter of the Sabin Gold Medal at last year's ceremony. During his 30-year career at NIH, he was a noted scientist and an influential leader in the field of infectious diseases. His contributions to domestic and global efforts to fight emerging and re-emerging infectious diseases included biodefense.

John R. La Montagne received his PhD from Tulane University in 1971. In 1976, he came to NIH as the Influenza Program officer at NIAID. He became the program officer for the Viral Vaccines Program in 1983, and the Influenza and Viral Respiratory Diseases program officer in 1984. Beginning in 1986, La Montagne assumed the role of director of the AIDS Program. In 1987 he was appointed director of the Microbiology and Infectious Diseases Program, which became a division in 1988. He was appointed deputy director of the NIAID in February 1998.

He received numerous awards for his scientific accomplishments, including the Public Health Service Special Recognition Award for leadership in childhood vaccine research programs, the Surgeon General's Certificate of Appreciation, and the Secretary's Award for Distinguished Service for design and implementation of critically important biodefense strategies.

Regina Rabinovich, MD, MPH, right, delivered a moving memorial tribute to her former colleague John La Montagne followed by the presentation of etched crystal gift from the Sabin Vaccine Institute to Mary Elaine Elliot La Montagne.

THE ALBERT B. SABIN GOLD MEDAL

The Albert B. Sabin Vaccine Institute annually recognizes and honors those who have made extraordinary contributions to the field of vaccinology by awarding the Albert B. Sabin Gold Medal.

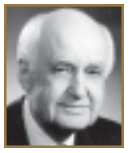
PAST HONOREES

1994~Donald A. Henderson, MD, MPH · 1995~Robert M. Chanock, MD
1996~Joseph L. Melnick, PhD *(d. 2001)* · 1997~Maurice R. Hilleman, PhD, DSc *(d. 2005)*


1994


1995


1996


1997

1998~Myron M. Levine, MD, DTPH & 1998~Allen C. Steere, MD
1999~Maj. Gen. Philip K. Russell, MD (USA Ret.) · 2000~Ciro A. de Quadros, MD, MPH


1998


1998


1999


2000

2001~John B. Robbins, MD · 2002~Stanley A. Plotkin, MD
2003~Samuel L. Katz, MD · 2004~William S. Jordan, Jr., MD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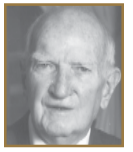
2002


2003


2004

ALBERT B. SABIN VACCINE INSTITUTE

The twofold mission of the Albert B. Sabin Vaccine Institute (SVI) is to realize the enormous potential of vaccines to control and to eradicate disease by developing new vaccines and better delivery systems, and to promote increased use of currently available vaccines. The vision of the SVI is to save lives by stimulating development of new vaccines and increasing immunization rates globally. The Institute promotes cutting-edge vaccine research and innovations, identifies new research opportunities, advocates sound public policy toward vaccines and immunization, and educates the public and media about the benefits of vaccines. Founded in 1993, SVI builds bridges between leaders in science, academia, industry, and government to create solutions to worldwide health threats. In pursuing the legacy of renowned vaccinologist and statesman Dr. Albert B. Sabin, the Institute facilitates the exchange of ideas for solutions to emerging and ancient diseases, from hookworm to cancer. By helping to unlock the vast potential of vaccines, SVI is working to ensure that the diseases that threaten the world today will be only history lessons for future generations.

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The Albert B. Sabin Vaccine Institute gratefully acknowledges support for this event from Antigenics, Inc., Bharat Biotech Intl. Ltd., BIOVIRx, Inc., Chiron Vaccines, GlaxoSmithKline and Merck & Co., Inc. In addition, we thank the hundreds of individuals, foundations and companies who make possible the Institute's ongoing programs to prevent disease, reduce suffering, and save lives through the use of vaccines.