SABIN VACCINE INSTITUTE

Sabin Vaccine REPORT

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The newsletter of the Albert B. Sabin Vaccine Institute —*dedicated to disease prevention* **www.sabin.org**

Nation's Physicians Sign SVI Open Letter on Vaccine Safety

Misinformation Threatens Children's Health Warn Top Doctors

Leading physicians joined the Sabin Vaccine Institute and a virtual "who's who" of the medical, academic and advocacy community to recognize National Infant Immunization Week this past April with the release of an Open Letter emphasizing the critical role of vaccines in protecting public health.

The Open Letter on Vaccines was announced at a press briefing at the Children's National Medical Center in Washington, D.C. Peter Holbrook, MD, chief medical officer, welcomed the media and visitors to the hospital and ceremoniously signed a poster-sized replica of the signatories list.

One of the strongest endorsements for the statement came from Louis Z. Cooper, MD, president of the American Academy of Pediatrics, who also was on hand. "The single most important thing parents can do to protect their children against infectious diseases is to immunize them," he said. "Parents need to know that immunizations are the greatest weapons we have against deadly, preventable illnesses."

Concern over confusing media coverage, widespread Internet misinformation, and the risk of falling immunization rates prompted more than 100 of the nation's top physicians and public health experts to sign the open letter publicizing their strong, unwavering support for vaccines.

A Tennessee mother, Suzanne Walther, delivered a message to parents during the announcement of the Open Letter. She chose not to vaccinate her daughter after reading misinformation about vaccines. Her daughter subsequently developed a form of meningitis that would have been prevented by immunization.

"I don't want my child to be the one in 3 million" who has a reaction to a vaccine. "But I also don't want mine to be the one in 10 that dies if they get the disease; I'd rather take my chances with the one in 3 million than the one in 10," remarked Ms. Walther.

Sabin Scientific Advisory Council Chair Peter Hotez, MD, PhD, who is chairman of Microbiology and Tropical Medicine at GW Medical Center, urged parents who had concerns about immunizing their child to talk to their pediatrician or to seek information from credible websites like those sponsored by the Sabin Vaccine Institute, Centers for Disease Control and Prevention, American Academy of Pediatrics, or the National Network for Immunization Information.

Physicians and health experts around the country are encouraged to sign the letter by visiting *www.sabin.org*. The Sabin Vaccine Institute has set a goal of adding hundreds of signatures to demonstrate the overwhelming support for vaccines within the medical and public health community.

The Open Letter on Vaccines and the signatories to date can be found on pages 8 and 9 of this newsletter.

Peter Holbrook, MD, left, chief medical officer at Children's National Medical Center in Washington, D.C., joins Louis Cooper, MD, president of the American Academy of Pediatrics, and Peter Hotez, MD, PhD, of George Washington University and the Sabin Vaccine Institute, as a signatory of the Open Letter on Vaccines.

Inside

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VIEW POINT

Communicating the Value of Vaccines

Reliable Information is the Critical Component

Vaccines are some of the greatest miracles of modern science. They set up a powerful immune response in the body against diseases that otherwise could imperil one's health or that of an entire community. Vaccines available today protect against preventable and once-common childhood diseases, like measles, mumps, chicken pox, and polio, and from frightening biological agents, including smallpox and anthrax. But be assured, for everyone's protection, long before any vaccine is recommended for broad use, it undergoes rigorous testing for safety and effectiveness. Although there are extremely rare instances of serious adverse reactions to vaccines, they have a demonstrated record of safety and are held to the highest standard.

Public health experts have had an uphill battle lately convincing the population here and abroad about the safety and effectiveness of vaccines. For the past year, inspired by a scientifically questionable study, MMR vaccination rates in England plummeted. A recent report in the British journal, *Clinical Evidence,* did much to put to rest the specter of a link between the measles, mumps, and rubella vaccine (MMR) and autism. Hopefully, the publication of the comprehensive government-sponsored study exonerating the MMR vaccine will change the actions of many Britons who had deferred vaccinating their children, and will prevent similar fears here in the United States.

In recent years, a movement of opposition to vaccines has propagated frightening and unfounded claims associating vaccines and harmful effects. As a result, many parents seeking factual and helpful information about immunizations have been misled. In their concern for the well-being of their children or themselves, many people have turned to the Internet, where anti-vaccination sites abound. It takes the dogged efforts of the scientific, regulatory, and academic communities to correct the misinformation and offer scientifically founded data as a reassuring alternative.

A study published this June in the *Journal of the American Medical Association* pointed a penetrating light on the lack of scientific rigor of those who would challenge the safety of vaccines. The study reviewing 22 anti-vaccination Web sites revealed that most of them focused on concerns about governmental abuses, alternatives to vaccination, and vaccine safety and effectiveness. The study concluded that the concerns expressed on these Web sites about vaccine safety were largely unsupported by peer-reviewed scientific literature.

A coincident survey reported in the *Archives of Disease in Children* should make all of us think twice before we blindly accept what we read on the Web. It indicated that 43% of the links found by Internet search engines point to sites that oppose the vaccination of children. This is sobering data, considering that some estimates are that 55% of adults with Internet access use it to seek health information one time or another.

It would be a tragedy to forget the real pain and suffering caused by the diseases that are now preventable as a result of vaccines. In the case of measles alone, immunization has cut the incidence of the disease by 99.9%—elsewhere around the globe, measles kills 950,000 people each year in countries without comprehensive immunization. Parents should speak to their child's pediatrician to get good information about the risks and benefits of vaccines, or carefully select the Web sites where they gather their information. Our children should never suffer the consequences of preventable diseases.

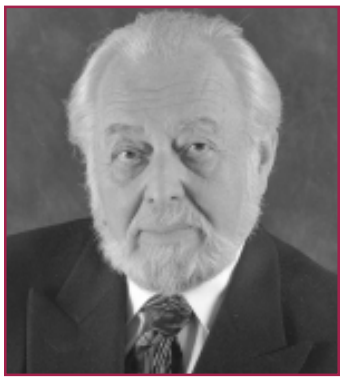
One thing is for certain—vaccines have saved millions of lives and continue to be the world's most humane and cost-effective medical intervention against preventable infectious diseases. We only hope that vaccine science is able to achieve even greater things in years to come in the war on AIDS, cancer, malaria, tuberculosis, and hookworm infection throughout the world.

—by H.R. Shepherd

H.R. Shepherd is Chairman of the Sabin Vaccine Institute.

Taking a Long, Hard Look at the Vaccine Supply Question

A Message from the Chairman



H.R. Shepherd, Chairman

The Sabin Vaccine Institute is taking on the issue of vaccine supply as a matter that concerns individual, domestic, and global well-being. That vaccines have been devised to combat many of the world's worst diseases is not sufficient security, particularly if the supply of vaccines is jeopardized by insufficient production or overly burdensome regulations. In October 2002, the Institute will hold its 9th Annual Vaccine Policy Colloquium at Cold Spring Harbor Laboratory in New York, where an assembly of scientific and public health experts from industry, government and international organizations will bring their unique perspectives to this year's theme: vaccine supply.

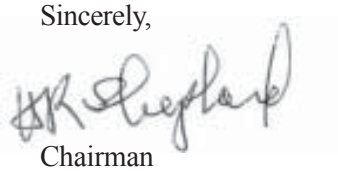
There have been significant shortages of childhood vaccines around the world—in the United States alone, 8 of 11 vaccines have been in short supply during the latter months of 2001 and into the first half of 2002—and demand for adult immunizations also has exceeded supply, raising concern on a global scale about the ability of the system to handle potential disease threats. Why have these situations developed? We can make the following observations about the present system:

- There is *insufficient collaboration and communication* among federal agencies and among companies, further burdened by a complex, lengthy, and unpredictable regulatory approval process.
- *Vaccine manufacturing and production is a complex process* with stringent quality control.
- *Manufacturers sometimes abruptly leave the marketplace* when the return on investment of a vaccine is no longer considered profitable. Meanwhile, though the number of vaccine manufacturers has declined, the number of vaccines has increased.
- *Financial incentives do not exist* for manufacturers to market medically necessary but unprofitable vaccines.
- *Current vaccine production capacity does not meet long-term needs*, to say nothing of surge capacity in the event of a bioterror incident. Government programs fail to ensure an adequate long-term stockpile of necessary vaccines.
- *Low reimbursement* has driven many physicians out of the delivery system; consequently, immunization is uneven and uncoordinated.
- *Divergence of vaccine products* between the U.S. and developing countries destroys economies of scale, negatively impacting issues of tiered pricing and profitability in developing country markets and lessening availability of routine vaccines.

These problems are occurring on a global scale, and are further compounded by the urgent need to immunize the poorest populations of the world and to develop "orphan vaccines" for diseases that are not common to developed nations. Furthermore, the events of fall 2001 highlighted the shortage of vaccines for defense against biological warfare agents such as smallpox and anthrax.

We have identified the issues and, in October, will certainly examine them in depth. A forward-thinking process fundamental to our meeting at Cold Spring Harbor is necessary to solve these issues. I welcome your feedback as we make preparations for our colloquium. Also, I would ask that you continue to provide us with your thoughts on issues you would like to see the Sabin Vaccine Institute cover in its various forums—either in publication or in a meeting we may convene. Thank you for your ongoing support.

Sincerely,



Chairman
Sabin Vaccine Institute

Would you like to read the *Sabin Vaccine Report* online? Our newsletter is available in a PDF format at *www.sabin.org*.

Notable Quote—

Benjamin Franklin's Advice on Immunization:

"In 1736 I lost one of my sons, a fine boy of four years old, by the small-pox, taken in the common way. I long regretted bitterly, and still regret that I had not given it to him by inoculation. This I mention for the sake of parents who omit that operation, on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that, therefore, the safer should be chosen."

Benjamin Franklin: *Writings, The Autobiography,* ed. J.A.L. Lemay, The Library of America, 1987, p. 1402.

Hotez Leads Review of Chinese Parasitology Grant

June Trip Follows Four Years of Discovery on Hookworm, Malaria, and Trichinosis

Hookworm, malaria, and trichinosis are each diseases that originate from parasitic infections. A unique grant from the Chinese Medical Board (CMB) of New York has for the past four years supported researchers at institutions in China and the United States in collaboration on investigations into how to prevent each of these serious diseases. Their investigations, including work that also is supported by the Sabin Vaccine Institute, have led to promising discoveries that may ultimately lead to vaccines

Peter Hotez, MD, PhD, Sabin Scientific Advisory Council chairman and chairman of Microbiology and Tropical Medicine at The George Washington University, met this past June in China with colleagues working on vaccine development funded by the CMB Parasitology Grant. The meeting was conducted in Beijing, at the Peking Union Medical College, School of Basic Medical Sciences. Hotez is a parasitologist and infectious disease pediatrician specializing in developing vaccines for helminth infections. He leads the Sabin-supported Hookworm Vaccine Initiative, which also receives funding from an $18 million Bill and Melinda Gates Foundation grant.

On a tour of Beijing are participants in the Parasite Grant review of the Chinese Medical Board of New York. From left, Zhu Xin Ping, Wang Heng, Cohava Gelber, Peter Hotez, and Xiao Shu Hua.

Approximately 20 Chinese scientists who participated in CMB Parasitology Grant-sponsored research convened for the one-day meeting to review scientific progress obtained over the period from 1998 to 2001 and to discuss future directions for research activities. Hotez led the review with Cohava Gelber, PhD, MBA, a molecular immunologist specializing in development of new vaccine platform technologies and senior vice president of Pharmaceutical Discovery Corporation of Elmsford, New York.

NEWS FROM THE BENCH

An impressive body of scientific data has been compiled as a consequence of the funding, including the discoveries of new important vaccine antigens for malaria, trichinellosis and hookworm. In the last eighteen months, new efforts were made to re-engineer these antigens for appropriate vaccine delivery. The group discussed strategies for translating the major discoveries into papers for peer-reviewed international scientific journals, and it anticipates the publication of a number of manuscripts submitted to top tier journals including *Nature Biotechnology*, *Infection and Immunity*, and *TheJournal of Biological Chemistry*.

Peking Union Medical College, Beijing, is the site of research on **malaria** molecular biology and vaccine development under the Parasite Grant. The investigators reported progress in three major areas: development of a hepatitis B core antigen platform technology; discovery of a new gene family from *Plasmodium sp.* that exhibits homology to intracellular trafficking proteins known as dynamins; and application of proteomics to the discovery a new family of surface proteins known as malaria surface reactive antigens. The proteomic approach is now been submitted for international patents. "It is exciting work," says Hotez, who believes it will merit journal publication. The method might also offer promise for the development of other microbial vaccines, according to Hotez.

Beijing's Capital University of Medical Sciences is the site of research for a vaccine to prevent **trichinosis**, a parasitic nematode infection passed to humans by exposure to raw or undercooked meat. Emphasis by the investigative group focuses on an antigen known as Ts87. Some of this work was done in collaboration with Zhan Bin, MD, of the Institute of Parasitic Diseases in Shanghai and Dr. Hotez at The George Washington University.

The Institute of Parasitic Diseases, Shanghai, reported on the status of their progress in **hookworm** research. Professor Xiao Shuhua is the lead investigator on this project while Zhan Bin works in the United States on the hookworm vaccine project sponsored by the Sabin Vaccine Institute. Xiao also heads an NIH-sponsored Tropical Medicine Research Center project to examine the genetic diversity of hookworm. With help from CMB funding, Xiao's group has now developed a model of vaccine immunity, explored leishmanization as a platform technology, and made progress in the area of gene discovery.

According to Hotez, the reviewers agreed that the productivity of the research sponsored by the CMB Parasitology Grant has been extremely high. The outcome of this research could have major impact both throughout China and globally, and serves as a model of international scientific cooperation.

Vaccine Supply Needs a Shot in the Arm

Harvard Medical School Student Warns Against Taking Vaccines for Granted

The following article was written by Erica Seiguer, a third-year MD, PhD student at Harvard Medical School. Ms. Seiguer formerly served as a research fellow at the Sabin Vaccine Institute. The article is reprinted from *FOCUS, News from Harvard's Medical, Dental, and Public Health Schools.*

Most of us seem to take vaccines for granted. We go about our business protected from some of the most dread diseases of mankind—polio, measles, diphtheria, and even smallpox—without concern for contracting them. By the time our children enter school, they've received between 16 and 20 vaccinations. We feel confident that they won't come home from school with anything more threatening than a minor infection common in childhood. In recent years, however, shortages of critical vaccines have highlighted the fragile nature of the U.S. vaccine supply and distribution system. A variety of factors are thought to have contributed to widely publicized shortages of influenza vaccine in the 2000-2001 flu season, and recent shortages in childhood vaccines preventing diphtheria, tetanus, whooping cough, polio, *Haemophilus influenzae,* chickenpox, measles, mumps, rubella, and invasive pneumococcal disease. The declining number of vaccine manufacturers, low profits in the vaccine area compared with other pharmaceuticals, federal regulations, lack of coordination between public- and private-sector providers, and a growing antivaccine movement have all been cited as indicators of a failing system. As of April 2002, there were shortages of DTaP, IPV, Hib, varicella, MMR, and pneumococcal vaccines, prompting revisions in current vaccine recommendations and rationing of childhood vaccines. Together these vaccines constitute a public health arsenal against major childhood diseases and have raised concerns of outbreaks of diseases not seen in decades. In the wake of recent concern over preparedness for possible biowarfare, the inadequacies of the current system have been brought to the forefront.

Ills of the System. *Declining number of vaccine manufacturers*. The private sector is primarily responsible for research and development, and manufacturing and delivery of vaccines. There are currently only four major vaccine manufacturers in the world, and only two in the U.S. Twenty years ago there were approximately four times as many firms. In 1979, eight American pharmaceutical companies held 70 percent of all licenses for vaccines in this country while foreign companies and institutes held 17 percent, with the remaining 13 percent held by state laboratories and a university. *Lower profits in the vaccine industry in relation to other pharmaceutical operations*. Vaccine revenues make up only a small fraction of the pharmaceutical industry's revenues, an estimated 3.5 percent. While newer vaccines and those in the pipeline may bring greater revenues to the industry, the pharmaceuticals market is much more profitable compared to vaccines and other biologics. *Federal regulation of vaccines*. The vaccine industry is regulated by the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration. CBER evaluates each vaccine candidate and either accepts or rejects applications to license the vaccines. Each vaccine manufacturing plant must be licensed separately, and the FDA regularly inspects facilities to ensure high quality of the product. After licensure, the FDA continues to monitor the vaccine and manufacturing facilities as long as a manufacturer holds a license. In the case of single-source vaccines, a change in FDA requirements or the need to upgrade a plant can, and has, led to shortages. *Lack of coordination between public and private sectors*. Vaccines are purchased and supplied through a complex network of public and private providers. While approximately 52 percent of vaccines for U.S. children are purchased with federal funds, the rest are privately purchased (often by individual physicians or group practices). The 2000-2001 flu vaccine shortage highlighted a worrisome failure to ensure that high-risk individuals were immunized first. According to an audit by the General Accounting Office, there was no formal mechanism in place to ration the available vaccine to those most in need. In this case, according to the GAO's findings, doctors were not able to secure vaccines for at-risk elderly patients, while supermarkets were able to offer free or low-cost flu shots to customers. *The antivaccine movement*. The growth in the antivaccine movement in recent years has had an impact on the vaccine industry, as well as the public health sector. Fears concerning side effects of immunization (for example, autism with the MMR vaccine) as well as some parents' desire not to vaccinate their children and highly publicized concerns about mercury in vaccines have required an aggressive public awareness campaign by the public health community. This campaign has been gaining momentum in the past several years, leading to the creation of several organizations responsible for communicating both the risks and benefits of immunizations.

Cures to Come? Why should we worry about an unstable vaccine supply? Vaccines are critical to the prevention of infectious diseases and are often considered the underpinning of our public health system. The enormous decline in infectious diseases due to vaccines and the reduction in attendant morbidity, mortality, and financial cost is remarkable. Yet due to their often invisible ef-

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The Sabin Report seeks to enrich the current dialog on vaccine research and policy with article and review contributions. Opinions expressed in the articles are those of the authors and do not necessarily represent the position of the Institute.

Exploring New Vaccine Development

Gregory Poland and Colleagues Undertake an Assessment of Vaccine Science

Vaccines are hailed as one of the most important public health achievements of the 20th century.[1] In the next five to 15 years, new vaccines and new vaccine delivery technology will fundamentally change how clinicians prevent and treat disease, with a substantial impact on public health. This review describes recent developments in the basic science underpinning the development of new vaccines and summarizes the potential of these vaccines to treat and prevent a wide range of infectious and non-infectious diseases.[2-5] In addition, research is being carried out on much needed vaccines for the developing world for diseases such as malaria, hookworm, dengue, enterotoxigenic *Escherichia coli*, shigella, and tuberculosis, but these are beyond the scope of this brief review.

Methods. We searched PubMed and Medline databases (1995-2001), as well as our own libraries, for articles of relevance to this brief review.

New Vaccines against infectious diseases

Development of DNA vaccines. One approach generating great interest is that of inducing protective immune responses by injecting engineered DNA sequences from infectious organisms against which protection is desired. If an antigen can be identified it is possible to insert the DNA sequence coding for the protein antigen into a carrier genome (such as several of the poxviruses or alphaviruses). Once delivered into the host, the organism (and hence the inserted DNA) undergoes limited replication, the protein of interest is produced, and the host develops an immune response against the protein.

In a related strategy, so called naked DNA is injected directly into the host to produce an immune response (fig 1). Naked DNA is simply sequences of DNA inserted into bacterial plasmids (simple, extrachromosomal rings of DNA found in bacterial cells) and injected into the host. These have been effective in animal models, but intramuscularly injected DNA in humans has failed to generate vigorous immune responses, although transdermal or intradermal delivery of DNA has been more encouraging. A clinical trial of transdermally delivered microscopic gold beads coated with DNA coding for hepatitis B surface antigen generated protective levels of antibodies to the antigen.[6] This vaccine has also generated CD8 cytotoxic lymphocytes.[6] Although efforts have been successful in animal models of vaccines against several pathogens, progress in humans has been much slower. To date, only DNA vaccines against hepatitis B[6] and malaria[7] have induced immune responses thought to be protective in humans.

Development of therapeutic vaccines. Traditional vaccination is the prevention of a specific infectious disease by delivering an immunogenic antigen derived from the surface of the infectious agent, resulting in immunity against the foreign organism replicating and establishing an infection. A therapeutic vaccine, however, can limit or eradicate an already present and established infectious agent or condition. The development of therapeutic vaccines has depended in part on the ability of DNA vaccination to induce both humoral and cell mediated immune responses by inoculation of plasmid DNA containing sequences for transcription and translation, resulting in the in vivo synthesis of an immunogenic peptide or protein.

Attempts are being made to develop a therapeutic vaccine against HIV that will induce virus-specific cytotoxic T lymphocytes against HIV, with the goal of having activated T cells destroy latently infected cells. Other efforts include developing therapeutic vaccines against *Helicobacter pylori*, mucosal candidiasis, herpes viruses, and human papillomavirus. DNA vaccination for hepatitis B virus has shown great promise. The delivery of viral DNA sequences can induce longlasting humoral and cell mediated immunity in mice infected with hepatitis B virus. [8 9] In transgenic mice, at least, there is a decrease in or clearance of the hepatitis B surface antigen, with evidence of induction of antibodies and proliferation of CD4 T cells.[10] Clearly, the capabilities of the immune system to eliminate an infectious agent even after an infection or disease is established could substantially improve human health.

Other important examples of therapeutic vaccine development include the development of vaccines against certain cancers,[11] which is discussed later.

Fig 1. Principle of DNA vaccination. An immunogenic gene is inserted into an expression plasmid (A), which is inserted into cultured cells (B). The cells are screened for expression of the gene protein and then cultured. The plasmid DNA is then extracted from the cells and purified before being used to immunise a host (C)

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This article is by **Gregory A Poland**, *chief* [a], **Dennis Murray**, *senior research fellow* [b], **Ruben Bonilla-Guerrero**, *senior research fellow* [a].
It is reprinted with permission of the authors and the British Medical Journal. It first appeared in the journal on June 1, 2002, 324:1315-1319.

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Advances in current vaccines

The bacterium *Streptococcus pneumoniae* and influenza viruses account for considerable morbidity and mortality worldwide. Now approved in several Western countries, *S pneumoniae* conjugate vaccines should help reduce the number of cases of invasive *S pneumoniae* disease (bacteraemia, meningitis, and sepsis) in infants and young children. A live, attenuated influenza virus vaccine is nearing approval in the United States. This vaccine, administered as an intranasal spray, should stimulate both systemic and mucosal immunity, while decreasing reliance on the use of parenteral injections (see box for a list of potential vaccines).

Streptococcus pneumoniae. Multivalent polysaccharide vaccines for *S pneumoniae* have been available in the United States since 1977, but they produce a poor or inconsistent immune response in children, especially those less than 2 years old. Polysaccharide vaccines induce antibodies primarily by mechanisms independent of the T cells and are not long lasting and do not induce an immune memory response. For these reasons, a protein carrier conjugated to a polysaccharide antigen of *S pneumoniae* has now been developed, which causes the immune response to be T cell dependent, allowing infants and children to respond better to the vaccine. The US licensed heptavalent *S pneumoniae* conjugated polysaccharide vaccine contains the seven serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F) most commonly associated with invasive disease among infants and young children. The new vaccine is also expected to have the benefit of reducing nasopharyngeal carriage of these seven *S pneumoniae* serotypes.

Influenza virus. The only influenza vaccines currently licensed in the United States are parenteral inactivated influenza virus vaccines prepared in chick embryos. Because of changes in the influenza viruses circulating each year (antigenic drift), protection of high risk individuals requires annual vaccination.

A live attenuated influenza virus vaccine being proposed for US approval contains recombinant cold-adapted strains of influenza A and B and is given by intranasal spray. Several studies have examined the use of live attenuated influenza vaccines in children and adults.[12-14] In seronegative children more than 15 months old antibody responses to the influenza A and B components after a single dose of vaccine indicated an overall efficacy of 93%.[12] Use of a live attenuated trivalent vaccine in adults significantly reduced the occurrence of illness, visits to healthcare providers, and days of work lost.[14]

New vaccines against non-infectious diseases

When correctly targeted, an immune response can be used to eliminate cells with aberrant behaviour (dysplasia) or aberrant genomic function (malignancy) or to reduce the amount of inflammation affecting a specific organ (such as in diabetes).[15 16] This raises the possibility of developing vaccines against diseases not known to be related to infectious agents. Two of the most exciting and promising areas in this regard are vaccines against cancer and autoimmune diseases.

Cancer. The identification of specific tumour antigens (tumour associated antigens) that are present only in cancer cells—such as those found in leukaemia, breast cancer, melanoma, prostate cancer, and colon cancer—provide immune targets for which immunogenic vaccines may conceivably be designed. For example, the expression of protein GPI-B7-1 transferred onto membranes from a murine thymoma tumour cell protects mice against this kind of tumour.[17] In humans it is possible to stimulate T cell responses using isolated membranes surgically removed from human tumour tissues that express major histocompatibility complex (MHC) class II molecules, suggesting the possibility of establishing an immune response that could specifically target and eliminate tumour cells.[18]

Other efforts include therapeutic vaccines against melanoma, colorectal cancer, leukaemia, and other cancers.[19 20] The ability of DNA vaccines to deliver precise and specific nucleotide sequences representing target genes—such as the ALVAC gp100 gene for melanoma and the ALVAC CEA-B7.1 gene for colorectal cancer—and specific protein fragments such as the HER2/Neu peptide found in breast cancer cells[21 22] have been studied as a potential means with which to induce an immune response.[19 23]

Autoimmune diseases. Diseases related to pathological immune activation, such as autoimmune diseases and allergies, might be treatable or preventable with vaccines. Efforts are being made to develop vaccines against rheumatoid arthritis, multiple sclerosis, myasthenia gravis, food allergies, and especially type 1 diabetes because of its associated substantial morbidity and mortality.

In the case of type 1 diabetes, lymphocytes infiltrate the pancreatic islets

Summary points

- New prophylactic and therapeutic vaccines will prevent and potentially cure disease by providing people with the necessary immunological tools
- Advances in current vaccines such as conjugated pneumococcal vaccines for adults, nasal spray vaccines for influenza, and adult acellular pertussis vaccines will provide an efficient way to produce longlasting protective immunity
- Development of vaccines against non-infectious diseases (such as cancer, diabetes, and Alzheimer's disease) and nicotine and cocaine dependence will provide alternative treatments
- Vaccines against biological weapons will be possible by advances in DNA vaccines
- New vaccine delivery technology will provide easier delivery routes (such as transcutaneous, depot, nasal, and oral delivery) without compromising efficacy

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Open Statement on Vaccines

We, the undersigned, support immunization as the safest, most effective way to control and eradicate infectious diseases. Infectious diseases were once prevalent in the United States, inflicting widespread suffering and death on young and old, rich and poor alike. Deadly diseases such as smallpox, polio, diphtheria and measles have, for the most part, become distant memories. Most of the credit goes to vaccines, medical miracles that many take for granted.

Vaccination eradicated smallpox but the other diseases still exist. Without immunization, they quickly can return and cause widespread harm, as the examples below demonstrate. Although there are extremely rare instances of serious adverse reactions to vaccines, vaccines have a demonstrated record of safety and are held to the highest standard. Vaccines are rigorously tested for safety and effectiveness before licensure by the Food and Drug Administration, and their safety and purity are continuously monitored.

Childhood and adult infectious diseases pose a real threat to personal and public health. Those who are not vaccinated leave not only themselves, but others, vulnerable to dangerous diseases. Vaccines are the most effective option for preventing and stopping the spread of infectious diseases.

Vaccines Save Lives

- Immunization has cut measles incidence in the U.S. by 99.9%. Vaccination still is important—measles kills 950,000 people each year in countries without comprehensive immunization.
- Immunization wiped out smallpox in 1979. Before smallpox was eradicated, it killed over 300 million people in the 20th Century—more than all wars combined.
- Vaccination eradicated paralytic polio from the Western Hemisphere. Before a vaccine was available, polio affected as many as 57,000 Americans per year with paralytic disease.
- Without routine vaccination, infectious diseases can quickly return and cause widespread harm. In Russia, diphtheria cases jumped from 900 in 1989 to 50,000 in 1994 after a drop in vaccination rates.
- Immunization has nearly eliminated a major cause of childhood meningitis, *Haemophilus influenzae* type b, everywhere the vaccine is used. Before the vaccine became available, 20,000 cases of the disease were reported and nearly 600 died each year in the United States.

For more information about vaccines and immunization, we recommend that you talk to your physician, nurse or local health agency. This message is brought to you by the Albert B. Sabin Vaccine Institute, Inc., a public 501(c)(3) charitable organization, www.sabin.org.

As of June 30, 2002, the following medical and public health leaders have signed the Open Statement on Vaccines.

Mohammad Akhter, MD, MPH
Executive Director
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Richard D. Andersen, MD
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Dean, School of Public Health
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Georges Benjamin, MD
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Howard S. Britt, MD
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Betty Bumpers
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Joseph A. Califano, Jr.
President, National Center on Addiction and Substance Abuse

John Clymer
President, Partnership for Prevention

Louis Z. Cooper, MD
President, American Academy of Pediatrics

Richard F. Corlin, MD
President, American Medical Association

Stephen Crane, PhD
Executive Vice President and CEO
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Janet L. Cranshaw, MD
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James Curran, MD, MPH
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John David, MD
Professor, School of Public Health
Harvard University

Ciro de Quadros, MD, MPH
Director, Division of Vaccines & Immunization, Pan American Health Organization

Vincent Devita, Jr., MD
Director, Cancer Center, Yale University

Molly Droge, MD
General Pediatrician, Dallas Texas

Kathryn Edwards, MD
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Ann M. Endy
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New Ulm Medical Center

For an updated list of signatories in this ongoing campaign please visit *www.sabin.org*. There you will find your state's immunization requirements and other helpful information about vaccines and their effectiveness in preventing and stopping the spread of infectious diseases.

Exploring New Vaccine Development

—by Gregory Poland (continued from page 7)

and selectively destroy the insulin secreting β cells. One strategy for vaccine development is to reduce the pathological lymphocytic infiltration by tolerisation. [15 16 24] Tolerisation involves the administration of small amounts of the same antigens that are the target of the aberrant immune response, which, in the absence of cytokine costimulation, fuels the activation of T cells, which reduce inflammation.

In disorders such as Alzheimer's disease, it may be possible to target the β amyloid protein that is responsible for the neurodegenerative plaques observed in this disorder. In murine models vaccines have been shown to reduce and prevent plaque formation, with some improvement in cognitive function.[25] Other examples of potential vaccine development include vaccines to prevent cocaine and nicotine addiction. With the use of immunopharmacotherapy, antibodies can be designed to neutralise a drug rather than target the receptors in the brain. Efforts are also being made to develop vaccines against atherosclerosis and to prevent conception.[26-28]

Vaccines against biological weapons of mass destruction

Interest has increased in biological weapons of mass destruction as terrorists look for methods with which to inflict harm on the greatest number of people, with the lowest possible cost and technology needs, while creating mass panic. While vaccines have been licensed against smallpox, plague, anthrax, and others, only limited amounts of anthrax vaccine are being produced in the United States for specific risk groups. Limited and ageing stockpiles of smallpox and plague vaccine are available but are insufficient for large numbers of people.

Because of the ability of biological weapons to infect and kill large numbers of people, and the risk of person-to-person transmission, vaccines are likely to be the only practical means of protection. [29 30] Second generation vaccines against anthrax, smallpox, and plague are being developed, and vaccines against other agents of bioterrorism such as the haemorrhagic fever viruses and others are also in development. However, major obstacles in producing such vaccines for public use include the need for a financially viable market, the impossibility of conducting human efficacy trials, the intangible risk:benefit ratio at the public health level, and governments' reluctance to face the reality of bioterrorism.

New vaccine delivery technology

Virtually all recommended immunisations require parenteral administration, and many require a series of injections. To be effective, vaccines for some diseases will need to enhance mucosal immunity as well as systemic immunity. For these reasons, new vaccine delivery methods, specifically alternatives to injections, are being sought. Topically applied (transcutaneous) vaccines, transgenic edible plants that contain genes for human vaccine antigens, and controlled delivery depot systems with vaccine antigens encapsulated in biodegradable polymers are possibilities currently under study. Such new delivery methods could decrease reliance on repeated injections, the need for trained healthcare workers, and perhaps the need for a stringent cold chain for vaccine storage.

Transcutaneous immunisation. Animal studies have shown the production of both systemic and mucosal antibodies after topical vaccine application. Agents such as cholera toxin and the heat labile enterotoxin of *Escherichia coli*, in combination with a vaccine antigen such as tetanus toxoid, act as an adjuvant and produce protective antibodies after being applied to the skin of animals.[31] Non-toxic mutants or subunits of cholera toxin and *E coli* enterotoxin would be needed, however, for any application on to human mucosal surfaces. Various other adjuvants besides cholera toxin and *E coli* enterotoxin (including bacterial ADP-ribosylating exotoxins, interleukin -1b fragment, interleukin 2, and tumour necrosis factor -a) have also been shown to produce an immune response after topical application.[32]

Transgenic edible plants to deliver vaccines. The development of plants capable of expressing vaccine antigens is a novel and promising strategy (fig 2). Such genetically engineered plants would produce vaccine antigens in their edible parts and would, like subunit vaccine preparations, contain no genes capable of replicating a whole infectious organism.[33] Because food plants can be regenerated rapidly, it may be possible that crops containing vaccine antigens could be produced indefinitely and on a local basis. Potato and tomato plants have synthesised antigens from Norwalk virus, enterotoxigenic *E coli*, *Vibrio cholerae*, and hepatitis B virus. A recently completed human study has shown that a recombinant bacterial antigen, subunit B of heat labile enterotoxin, produced in a potato and eaten resulted in production of both serum antibodies (IgG and IgA) and mucosal antibodies (sIgA) to the antigen.[34] Other plants, such as bananas, and other vaccine antigens, including tetanus and diphtheria toxoids, may be included in future studies.

Controlled delivery depot systems. The use of controlled delivery of vaccine antigen, or depot vaccine technology, reduces the number of parenteral injections while potentially mimicking natural infection. Various vaccine antigens have been encapsulated in microspheres composed of biodegradable polymers such as poly (lactic/glycolic) acid (PLGA), which can be targeted to various cells in the immune system or can form a depot at the injection site, allowing slow release of the antigen over time.[35] The release profile of vaccine antigen depends on the particle size of the delivery vehicle, and a

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combination of large and small microspheres can create a pattern that mimics the antigen concentration profile in conventional immunisation, combining both primary and booster injections. A recent study in animals found that encapsulated tetanus toxoid or *Haemophilus influenzae* type b polysaccharide elicited high antibody levels that persisted for months.[36]

Conclusions. The future of vaccinology provides tremendous promise for controlling diseases. Vaccines will be delivered orally, by nasal spray, or transcutaneously by a minimally trained layperson and in a manner that does not require expensive equipment. However, despite rapid advances in the development of new vaccines, concerns about vaccine safety and a rise in anti-vaccine sentiment adversely affect immunisation coverage, the willingness of manufacturers to develop new vaccines, and the willingness of individuals and healthcare workers to use them. [37] [38] As advanced vaccines and vaccine technologies become available, massive public education efforts will be required to alleviate these concerns. This is particularly true for DNA vaccines, combination vaccines, vectored vaccines, and vaccines administered in a parenteral depot fashion. The more distant potential for person-specific vaccines based on individual genotyping (vaccines against a specific malignancy in a specific individual) will also raise serious concerns. None the less, the prospect of both preventing and treating many serious diseases by the use of vaccines portends an exciting era in public health and vaccinology.

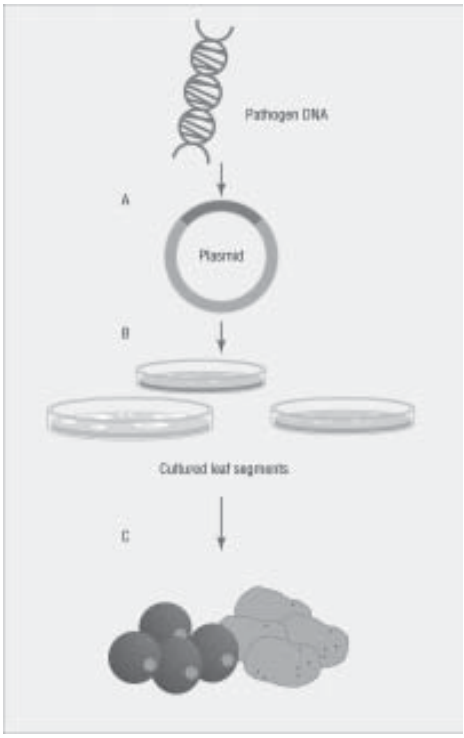

Fig 2. *Principle of delivering vaccines in edible plants. A gene from a human pathogen is inserted into a bacterium that infects plants (A). The bacterium then infects cultured leaf segments of the selected food plant (B), which sprout into whole plants containing the human pathogen gene (C). Once the plant is eaten, it triggers an immune response to the pathogen*

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Additional educational resources

- Centers for Disease Control and Prevention, *www.cdc.gov*
- World Health Organization, w*ww.who.int/home-page*
- Merck Vaccines, *www.merckvaccines.com*
- National Vaccine Information Center, *www.909shot.com*
- DNAvaccine.com, www.dnavaccine.com/) a global platform for vaccine research
- Food and Drug Administration, *www.fda.gov/default.htm*
- National Foundation for Infectious Diseases, *www.nfid.org*
- American Society for Microbiology, *www.asm.org*
- Infectious Diseases Society of America, *www.idsociety.org*

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Developer of Rubella Vaccine, Stanley A. Plotkin, Receives Sabin Gold Medal

Honoree Acclaimed as "Maverick" in Vaccine Development

Stanley A. Plotkin, MD, best known for developing the rubella, or German measles, vaccine, received the Sabin Gold Medal on May 7, 2001 in Baltimore during the 5th Annual Conference on Vaccine Research of the National Foundation for Infectious Diseases. He is the tenth recipient of the Medal, presented annually to a scientist recognized for exemplary leadership in the field of vaccinology and disease prevention.

"Plotkin joins a highly distinguished group who would in any endeavor be considered peers, but in the field of vaccine development and application must also be described as mavericks," Michael Katz, MD, senior vice president for research, March of Dimes Birth Defects Foundation, affirmed to an audience of over 300 scientists present at the ceremony.

"Stanley Plotkin is an extraordinary figure in the field of vaccinology," said H.R. Shepherd, chairman of the Sabin Vaccine Institute, "He epitomizes dedication to conquering disease with vaccines and immunization, the same passion by which Albert Sabin lived."

Those gathered for the 2002 Sabin Gold Medal Ceremony included, from left, Maurice Hilleman, PhD, DSc (1997 Honoree); Myron Levine, MD, DTPH (1998 Honoree); Stanley Plotkin, MD (2002 Honoree); Peter Hotez, MD, PhD, Ciro de Quadros, MD, MPH (2000 Honoree); and Philip Russell, MD (1999 Honoree).

Dr. Plotkin is a medical and scientific advisor to Aventis Pasteur, and emeritus professor at the University of Pennsylvania, where he served as associate chairman of the Department of Pediatrics. He is known as the "founding father" of the Pediatric Infectious Diseases Society. Dr. Plotkin developed the rubella vaccine now in use, and has worked extensively on a range of other vaccines. He continues to devote efforts to the development of a cytomegalovirus vaccine and has collaborated on a rabies vaccine and two rotavirus vaccines. These accomplishments have resulted in nearly 600 original publications and four editions of the *Vaccines*, of which he is co-editor.

The End of Polio: A Global Effort to End a Disease

Photography Publisher Aperture Opens Exhibit of Sebastião Salgado Photos

Photography publisher, Aperture, hosted an exhibition this summer titled, "The End Of Polio: A Global Effort to End a Disease." The exhibit featured the work of photojournalist Sebastião Salgado, and was held at Aperture's Burden Gallery in New York. Following a showing in Berlin through September 25, it will return by the year end to the Washington, D.C. area and will visit California and Texas in 2003.

In Somalia, armed guards accompany health workers during the March 2001 round of National Immunization Days aimed at vaccinating all children under the age of five. To reach children in conflict zones, international partners have negotiated complex logistical arrangements, including temporary cease-fires between warring factions called 'Days of Tranquillity'. These efforts must continue, as many of the remaining 10 polio-endemic countries are affected by conflict.

"The story told in these images is very moving," said Heloisa Sabin, widow of Albert B. Sabin, developer of the oral polio vaccine. "This exhibit educates those who might not remember how devastating the polio epidemic was and how great has been the dedication of health care workers and the volunteers of WHO, Rotary International, UNICEF, and CDC." Mrs. Sabin is co-founder of the Sabin Vaccine Institute and a trustee of the Institute.

The photographic exhibition is the first depicting the epic story behind the largest public health initiative in history—the bid to eradicate polio globally by 2005. Salgado's images tell the polio eradication story by both depicting the ravages of the disease on children to the heroic efforts to deliver vaccine in conflict-ridden countries.

To document the campaign, United Nations Children's Fund (UNICEF) Special Representative Salgado worked with the four Global Polio Eradication Initiative lead agencies: the World Health Organization (WHO), Rotary International, the U.S. Centers for Disease Control and Prevention (CDC) and UNICEF. In 2001, Salgado journeyed to the Democratic Republic of Congo, India, Pakistan, Somalia and southern Sudan to witness and document efforts to eradicate polio from some of the most challenging and remote places on earth. "The End of Polio" breaks with traditional photography exhibition formats in that Salgado's imagery goes beyond promoting public awareness. It points to a solution and encourages participation by demonstrating that the eradication of polio is within grasp.

SVI Convenes Scientific Meeting on Bioterrorism

Facing the Challenge: Disease Prevention in a Time of Crisis

The Sabin Vaccine Institute presented a one-day scientific colloquium May 30 on the theme, *Facing the Challenge: Disease Prevention in a Time of Crisis*, held at the New York Academy of Sciences in New York City. Prominent guest speakers examined the nation's vulnerability and public health response to bioterrorism and the role of vaccines in the nation's defense.

The meeting was funded by GlaxoSmithKline and organized by Peter J. Hotez, MD, PhD, chairman, Department of Microbiology and Tropical Medicine, The George Washington University (GW) Medical Center, and chair of the Sabin Vaccine Institute Scientific Advisory Council, and Allan L. Goldstein, PhD, chair, Department of Biochemistry and Molecular Biology, GW, and Sabin Vaccine Institute trustee.

Scientific Colloquium presenters and organizers gather at the New York Academy of Sciences. Front row, from left, Margaret Hamburg, MD; Peter Hotez, MD, PhD; Tee Guidotti, MD, MPH, Tom Zink, MD; Sam Katz, MD; and Tom Frieden, MD. Back row, from left, Philip Russell, MD; John Robbins, MD; John Woodall, PhD; Allan Goldstein, PhD, and Paul Offit, MD.

Hotez moderated the morning session on "How Vulnerable Are We? Why?" The guest speaker line up included Margaret Hamburg, MD, Nuclear Threat Initiative; John P. Woodall, PhD, Federal University of Rio de Janeiro, Brazil; and Tee L. Guidotti, MD MPH, GW. Thomas Frieden, MD, New York City public health commissioner, provided the luncheon keynote message. In the afternoon, Major General Philip K. Russell, MD (USA Ret.), moderated a session Philadelphia; and John B. Robbins, MD, National Institute of Child Health and Human Development, National Institutes of Health.

Hotez invited the group to address "one of our nation's great challenges, namely, how to rebuild our public health infrastructure to combat new enemies armed with bioweapons." Vaccine shortages were exemplified by the lack of a ready-to-use stockpile of anthrax vaccine and want of an adequate stockpile of smallpox vaccine. He added that "equally troubling is the new realization that our nation's vaccine supply for childhood immunizations, including tetanus, is in danger." The group was called upon to look at the problems facing our national public health infrastructure in a new light.

"Our nation's vaccine supply for childhood immunizations, including tetanus, is in danger . . ."
—Hotez

Patricia Thomas Welcomed by SVI and GW

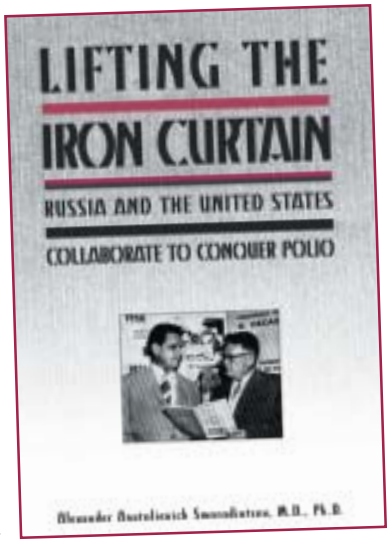
Author of Big Shot: Passion, Politics, and the Struggle for an AIDS Vaccine Discusses Her Book at Special Evening With the Author

Patricia Thomas, author of *Big Shot: Passion, Politics, and the Struggle for an AIDS Vaccine,* is welcomed by Sabin Vaccine Institute Trustee Allan Goldstein, PhD, chair of Biochemistry and Molecular Biology at The George Washington University. Thomas, a Sabin fellow, read passages from her book that chronicles the search for an AIDS vaccine.

Polio Vaccine Trials and a Little-known Chapter in U.S.-Soviet Cold War Diplomacy

Lifting the Iron Curtain Chronicles Vaccine Scientists' Collaboration During Icy Period Between U.S. and Soviets

A Russian virologist writes of an historic period of bilateral collaboration at the height of the Cold War in a new release from the Sabin Vaccine Institute, *Lifting the Iron Curtain*. Alexander Anatolievich Smorodintsev, MD, PhD, was a member of his father's research team and eye-witness to the fortunate partnership between his father, Anatoli Smorodintsev, MD, Mikhail Petrovich Chumakov, MD, and the U.S. oral polio vaccine developer Dr. Albert B. Sabin. The scientists from Cold War adversary nations faced off against a common enemy, poliomyelitis, which at the time threatened the youth of both countries with grave illness and crippling long-term effects.



Very few of us are aware that the live oral polio vaccine that we received as children was developed only with the help of Soviet virologists in the 1950s. The events Smorodintsev describes unfold over a period of three to four years at the very height of US-Soviet Cold War tensions. This unprecedented cooperation between American and Soviet medical scientists roughly coincided with the Sputnik launch and is a remarkable, but little known chapter in the history of modern vaccine science.

The live oral polio vaccine pioneered by the late Dr. Albert B. Sabin in his Cincinnati Children's Hospital laboratory was licensed in the U.S. only *after* it was first tested in thousands of Soviet children. The successful collaboration is a testament to the power of vaccines to break down national, political, and ideological barriers. It is an impressive example of what we sometimes term "vaccine diplomacy."

Smorodintsev's account is a powerful reminder of how vaccines can serve as agents of conflict resolution. It provides a lesson that is still relevant to civil conflicts in Africa and Central Asia, and possibly even to international conflicts among the major superpowers.

Also included in this new book is a reprinting of Saul Benison's "International Medical Cooperation: Dr. Albert Sabin, Live Poliovirus Vaccine, and the Soviets," from the *Bulletin of the History of Medicine*, originally published in 1982 by The Johns Hopkins University Press.

SABIN VACCINE INSTITUTE PUBLICATION

About The Author

Alexander A. Smorodintsev, M.D., Ph.D., was born in 1929 in Leningrad (now St. Petersburg), Russia, son of the late Anatoli A. Smorodintsev. He obtained his medical degree from the Medical University of Leningrad and his Ph.D. in virology, immunology and vaccinology. During the 1950s Dr. Smorodintsev worked closely with Dr. Albert B. Sabin on the development of live attenuated oral polio vaccine (OPV), and his daughter was one of the first children to be immunized with the experimental vaccine. He later served as Chief of the Laboratory at the State Influenza Research Institute and at the Pasteur Institute in St. Petersburg. Between 1968 and 1976, he was an official coordinator of Soviet-American collaborative work on influenza, and from 1976 to 1985 coordinator of Russian-Finnish collaborative studies on human interferon. He has published more then 200 scientific papers and made many contributions to the cultivation, pathogenesis, and vaccinology of respiratory viruses such as measles, mumps, and rubella.

Book Ordering Information

The new release, *Lifting the Iron Curtain,* is available from the Sabin Vaccine Institute for US $15 (add $8 for international orders). Those wanting to purchase the book may send a check or money order to Albert B. Sabin Vaccine Institute, 58 Pine Street, New Canaan, CT 06840, or call (203) 972-7907 for credit card purchases.

Vaccine Supply Needs a Shot in the Arm

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fect of preventing disease, vaccines have tended to be underfunded and underappreciated. This neglect, some claim, is manifested in the decline of the vaccine industry, its consolidation into a handful of firms, and the breakdown of the entire system of development, manufacture, delivery, and monitoring. The recent shortages, results of an unstable supply, concern public health officials, policymakers, physicians, and parents alike. Recent meetings of the National Vaccine Advisory Committee as well as others have discussed several options for shoring up the supply, including rotating stockpiles, national immunization awareness campaigns, and other initiatives aimed at addressing the current shortages and preventing them in the future.

SVI Honors Pharmaceutical CEO and U.S. Diplomat at New York City Benefit Dinner

GlaxoSmithKline's Jean-Pierre Garnier, PhD, and The Honorable Richard C. Holbrooke Recognized for Humanitarianism and Leadership

The Sabin Vaccine Institute presented its two highest non-science awards on May 30 to Jean-Pierre Garnier, PhD, Chairman and Chief Executive Officer of GlaxoSmithKline, and The Honorable Richard C. Holbrooke, Former U.S. Permanent Representative to the United Nations. Garnier received Sabin's Humanitarian Award and Holbrooke received the Institute's Lifetime Achievement Award at a benefit dinner at The Pierre Hotel in New York City.

"We honor two individuals this year both of whom are engaged strategically in the global effort to meet the health needs of populations whose vulnerability to disease is great, but whose resources are extremely limited," said H.R. Shepherd, Chairman of the Sabin Vaccine Institute. "Jean-Pierre Garnier's corporate vision and leadership has been widely recognized and he has been an advocate for humanitarian efforts through which GlaxoSmithKline has engaged in international cooperation and independent disease prevention efforts to combat preventable childhood diseases, the great HIV/AIDS epidemic, and disfigurement of Lymphatic Filariasis. Richard Holbrooke has drawn upon his international profile to elevate disease prevention as an global priority and to redefine the great scourge of HIV/AIDS as a matter of global security. "

Heloisa Sabin, widow of the late Albert B. Sabin, introduced the Humanitarian Award recipient; William Haseltine, PhD, chairman of the board of Directors and CEO of Human Genome Sciences, Inc., introduced the Lifetime Achievement winner. Colleagues of the honorees and corporate and individual supporters of the Sabin Vaccine Institute were represented at the dinner in Garnier and Holbrooke's honor. The awards dinner is an annual benefit for the Sabin Vaccine Institute. Co-chairs of this year's event were Jean Stéphenne, GlaxoSmithKline Biologicals, and Sanford I. Weill, Citigroup, Inc. The Honorable Hillary Rodham Clinton, United States Senate, was Honorary Chair.

Pictured at the 2002 Sabin Vaccine Institute Annual Dinner are, from left, the Honorable Richard C. Holbrooke, GlaxoSmithKline CEO Jean-Pierre Garnier, PhD, and H.R. Shepherd, Chairman of the Sabin Vaccine Institute.

2002 Sabin Vaccine Institute's Lifetime Achievement Award Honoree

Richard C. Holbrooke served as the U.S. Ambassador to the United Nations and member of President Clinton's cabinet from 1999 to 2001. He played a central role in the development of U.S. policy toward the United Nations, the Balkans, Africa, Asia, the Middle East and humanitarian crisis issues such as AIDS. As Assistant Secretary of State for Europe from 1994 to 1996, Holbrooke was chief architect of the momentous 1995 Dayton peace agreement that ended the war in Bosnia. He previously served as U.S. Ambassador to Germany and as Assistant Secretary of State for East Asian and Pacific Affairs. There, he was in charge of U.S. relations with China when Sino-American relations were normalized in 1978. He is president and CEO of the Global Business Council, the business alliance against HIV/AIDS and is currently Vice Chairman of Perseus, a leading private equity firm.

2002 Sabin Vaccine Institute's Humanitarian Award Honoree

Jean-Pierre Garnier is chief executive officer of GlaxoSmithKline. He assumed this role in December 2000 with the merger of SmithKline Beecham and Glaxo Wellcome. Dr. Garnier joined SmithKline Beecham in 1990 as president of its pharmaceutical business in North America and served as chairman, Pharmaceuticals from 1994 until his appointment as chief operating officer in 1995. He was elected to the company's Board of Directors in 1992. He became chief executive officer in April 2000. Prior to SmithKline Beecham, Dr Garnier served as President of Schering-Plough's US business. Dr Garnier serves on the boards of the United Technologies Corporation and the Eisenhower Exchange Fellowships, Inc. In January 1997, Dr Garnier was selected by President Chirac of France to receive the Chevalier de la Légion d'Honneur. In 2001, he was named one of 50 "Stars of Europe" by *BusinessWeek* magazine. Dr Garnier holds a PhD in pharmacology and an MS in pharmaceutical science from the University of Louis Pasteur in France. As a Fulbright Scholar, he earned an MBA at Stanford University, California, in 1974.

Vaccine Development

Gregory Poland Explores the Latest Vaccine Science, *from page 10*

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SABIN CALENDAR

SEPTEMBER 2002

11-12 *Copenhagen, Denmark*
Thorvald Madsen Intl. Vaccine Symposium: Vaccines for the 21st Century-Development and Strategies
E-mail: *norvac2002@dsb.dk*

16 - 27 *Antwerp, Belgium*
Twenty-first European Course in Tropical Epidemiology
Contact: Anne Marie Trooskens
amtrooskens@itg.be

18 - 22 *Hinxton, United Kingdom*
7th Intl. Symposium on Pertussis: Genome, Pathogenesis, and Immunity
www.asmusa.org/mtgsrc/Pertussisg.htm

19 - 22 *Anaheim, California*
6th Annual U.S. Conference on AIDS
Conference Registrar: Paul Woods
pwoods@nmac.org

30 - October 1 *New York, New York*
Cancer Vaccine Collaborative
www.cancerresearch.org/cvc2002

30 - October 2 *Lyon, France*
World Vaccine Congress 2002
Contact: NYAS
E-mail: *sarah.butt@terrapinn.com*

OCTOBER 2002

2 - 5 *Charlotte, North Carolina*
The 76th Annual American School Health Association Conference
Contact: Mary Bamer Ramsier
E-mail: *mbramsi@ashaweb.org*

13 - 15 *Nice, France*
Pros and Cons in Infectious Diseases
E-mail: mediaxa@wanadoo.fr

23 - 25 *Cold Spring Harbor, New York*
9th Anual Sabin Vaccine Colloquium: Gobal Vaccine Shortage: The Threat To Children and What To Do About It
Contact: Veronica Korn
E-mail: *veronica.korn@sabin.org*

23 - 25 *Edinburgh, Scotland, UK*
DNA Vaccines 2002 - The Gene Vaccine Conference
Contact: John Herriot
jherriot@meetingsmgmt.u-net.com

24 - 27 *Chicago, Illinois*
IDSA 2002 - 40th Annual Infectious Diseases Society of America Meeting
Contact: Suzanne Johnson-DeLeon
E-mail: *info@idsociety.org*

28 - 30 *Philadelphia, Pennsylvania*
3rd Annual Immunization Registry Conference
E-mail: *ghl2@cdc.gov*

NOVEMBER 2002

10 - 14 *Denver, Colorado*
Amer. Society of Tropical Medicine& Hygiene 51st Annual Meeting
E-mail: *astmh@astmh.org*

9 - 13 *Philadelphia, Pennsylvania*
American Public Health Association 130th Annual Meeting: Putting the Public Back Into Public Health
www.globalhealth.org

19 - 23 *Santiago, Chile*
3rd World Congress of Pediatric Infectious Diseases
E-mail: *wspid@kenes.com*

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