

Experts Say Global Vaccine Policy for Pandemic Influenza Is Needed

Sabin Vaccine Institute's Annual Vaccine Policy Colloquium Hammers Home Need for Vaccine Plan

Health experts convened by the Sabin Vaccine Institute at Cold Spring Harbor, New York, in October took steps to formulate recommendations for vaccine policy planning in the event of a pandemic flu outbreak. The group sounded a warning that an influenza pandemic, which many experts consider overdue, would overshadow routine annual influenza epidemics. The looming event could be a calamity striking down millions across the globe.

Amid the discussion during the two-day colloquium, at least two practical recommendations surfaced. On the international cooperation front, the numbers of influenza disease surveillance sites should be expanded. In terms of public health prevention, increased global vaccine manufacturing capacity is needed.



Colloquium co-chairs Lewis Miller, left, and David Heymann, MD.

The colloquium, an annual meeting on vaccine policy, took place as H5N1 avian flu surveillance is on high alert and within fresh recollection of the 2003 outbreak of sudden acute respiratory syndrome, or SARS, that so quickly traversed the globe from Asia to North America. This year's colloquium was titled *Pandemic Disease Threats: Can We Develop a Global Vaccine Policy?*

The 35 meeting participants represented the World Health Organization, Pan American Health Organization, UNICEF, U.S. Department of Health and Human Services, National Institutes of Health, Centers for Disease Control and Prevention, and international organizations from Brazil, Canada, India, Korea, the Netherlands, Singapore, Taiwan, and the United Kingdom. Representatives from several influenza vaccine manufacturers attended.

"Certainly the threat of pandemic influenza is one of the preoccupations of the scientific community and (the World Health Organization) at present," said David L. Heymann, MD, executive director, Communicable Diseases, World Health Organization (WHO), who co-chaired the colloquium. "Public health is all about windows of opportunity," he said.

"When these windows open, as is now the case for influenza, maximum efforts must be made to address the problem at hand and also increase resources in public health in general."

A global flu outbreak—flu pandemic—strikes approximately three or four times in a century, when humans come into contact with a new strain of influenza virus for which they have little or no prior immunity. The pandemic flu of 1918 killed 40 million people, which constituted more deaths than all casualties of World War I. John M. Barry, author of *The Great Influenza: The Epic Story of the Deadliest Plague in History*, related anecdotes and statistics from his book



Meeting co-chairs Dr. Albert Osterhaus, left, and Dr. David Heymann.

on the 1918 pandemic at the opening of the colloquium. A global vaccine strategy with advanced planning and government and industry commitments is imperative to avoid a similar outcome from the next pandemic.

Fresh ideas generated at the meeting include broadening the base of vaccine production by in-



Dr. Louis Cooper, Columbia University, and Michael Osterholm, University of Minnesota, discuss pandemic outbreak scenarios.

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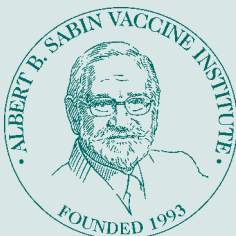
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VIEW

POINT

Influenza and Our National Vaccine Shortage: Looking to the Legacy of Dr. Vannevar Bush

—by Frank Cilluffo and Peter J. Hotez, MD, PhD

THIS COMMENTARY FIRST APPEARED IN *THE ASBURY PARK PRESS* ON OCT. 15, 2004

The shortage of influenza vaccine for the 2004-05 flu season portends a potentially serious health crisis for the United States. Influenza is the single greatest cause of death from infectious disease in the U.S., far exceeding deaths from HIV-AIDS, West Nile fever, and other infectious causes. During the 1990s, an average of 36,000 deaths from influenza occurred annually, with as many as 200,000 annual hospitalizations during a severe season.

Effective and appropriate use of an influenza vaccine could prevent up to 50% or more of the deaths caused by influenza. However, manufacture of the vaccine is a complicated process and business. Because of the changing antigenic properties of the influenza virus it is necessary to produce new vaccines annually. As a result, only a small window of time is available for the two major manufacturers of influenza vaccine, Aventis Pasteur and Chiron, to produce sufficient vaccine in time for flu season. The manufacturing process relies on an old method of growing the virus in embryonated hens' eggs. This method was used to produce the first influenza vaccines in the 1940s and has not been significantly modified in the last 50 years. Unfortunately, it is not uncommon for environmental bacteria and fungi to colonize the eggs resulting in unintentional contamination during manufacture.

If this winter's flu season is severe, it is possible that hundreds if not thousands of Americans will die because they were not vaccinated. Sadly, the latest problem with our influenza vaccine shortage could possibly have been prevented if funds were available to support the development of a new-generation influenza vaccine. Bacterial contamination such as the type that occurred at Chiron's plant in the U.K. is not unexpected. Although newer methods to produce influenza vaccine using mammalian cell substrates would reduce the likelihood of contamination, this requires the construction of new plants, which are prohibitively expensive for most vaccine manufacturers.

We could have, and should have, had new-generation influenza vaccines in our nation's stockpile for more than a decade. One reason for the delay is that research, development, manufacture and clinical testing for new vaccines occur at a snail's pace relative to other pharmaceutical products. The major vaccine producers in North America and Europe have not had the incentive or the right business model to develop new products. Vaccines traditionally provide a return on investment that pales in scale and scope compared to blockbuster drugs. In some cases, vaccines must be sold for pennies a dose. As a result, while the rest of the pharmaceutical industry is thriving, the leading vaccine manufacturing divisions of larger companies are barely hanging on. This simple fact likely explains why we have only four major pediatric vaccine manufacturers left to serve North America (Merck, Wyeth, GlaxoSmithKline and Aventis Pasteur) and this number might easily dwindle to three, or even two, in the coming years. Today, our nation's vaccine supply is extremely fragile and there is no redundancy in the system, so that often we have a sole source supplier for a single vaccine. In recent years, this has resulted in acute shortages of vaccines for diphtheria-pertussis-tetanus, measles-mumps-rubella, chickenpox, and pneumococcal meningitis. Though stockpiles are now being built for the more common childhood vaccines, any shortage of significant duration could result in national shortages even for those products.

The current shortage in influenza vaccine is a wake-up call that something is very wrong with the way we develop, manufacture, and procure our nation's vaccines. To begin seeking answers we might look to similarities between our current vaccine crisis and the state of the defense industry at the beginning of World War II. During the War years and in the years that followed Dr. Vannevar Bush led a charge that reshaped the defense industry and laid the

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What the American Public Should Know About the Influenza Vaccine Crisis

Message from the President

Influenza kills approximately 36,000 people in the United States in an “average year.” In 1957, the Asian flu killed about 70,000 Americans and about 34,000 died from complications from the Hong Kong flu in 1968. The consequences of influenza are abundantly clear—the mode of prevention by vaccination is understood as well.

The announcement this fall that a manufacturing problem would result again this year in a national influenza vaccine shortage should serve as a wake-up call to the American public and our elected officials. In the U.S., only twice in the past six years has the influenza vaccine supply been both sufficient and delivered in a timely manner. The sad truth is that influenza vaccine supply disruptions and inadequacies are now the norm and not the exception. Steps must be taken to establish confidence in the production, supply and administration of influenza vaccines on a national scale every year.

It is unfortunate that the wealthiest, most powerful and most influential country in the world cannot solve the problem of assuring the protection of its citizenry against a disease that is usually preventable through vaccination. If influenza disease were declared a threat to our national security, would the response of our government leaders be different? Does this problem inspire confidence that we could react in a meaningful way to the threat of a new influenza disease strain that might result in a pandemic outbreak?

Here are some key facts that the American public should know about the production of influenza vaccine:

1. The production of influenza vaccine is complicated because it is essentially a new vaccine every year and there are no guarantees concerning the yield or amount of vaccine that will be produced by the manufacturer.
2. The turn around time between the identification of the circulating strains to be included in the trivalent vaccine and actual vaccine production is less than six months.
3. There are only two major companies now producing influenza vaccine for the U.S. market compared to four manufacturers only five years ago.
4. Influenza vaccine production requires the use of thousands of embryonated eggs, a technology that dates back over 50 years.

The problem extends far beyond the 40 to 50% national shortage we will experience this year. When there are shortages, the government has almost no control over the dispersment of the vaccine. National guidelines for influenza vaccine use are strictly voluntary. Though concerted efforts are made by industry to direct the available vaccine to healthcare providers and organizations that serve those most at risk, the reality is that supermarkets often receive the vaccine before primary care providers. Also, advance-sell contracts, preferred by industry, can legally obligate the pre-commitment of perhaps 30% or more of the vaccine. Less well known is that a few mid-level distributors set price based on the knowledge that the demand exceeds the supply, leading to significant and widely varying prices for the vaccine. Even worse, influenza vaccine in times of shortages can be treated as a commodity with two, three, or four wholesalers

transferring it to each other before it is sold to the public. Of course, with each transfer costs are added.

The tragedy is that the problem, while long talked about and known to be solvable, has never been acted upon.

1. The United States must attract other influenza vaccine manufacturers to this market, both domestic and international companies. To do so we must address those problems that are significant to industry including two recurrent U.S. problems: regulatory issues and frivolous litigation.
2. Government must offer incentives that are sufficient to motivate industry to participate.
3. The federal government must dedicate additional resources, including more money and personnel, to the year-to-year management of the influenza vaccine supply and to the stockpiling of antiviral drugs. This might include federal sponsorship of scientists working more directly with industry.
4. Communication links between regulators, industry and public health authorities must be improved, especially when manufacturing problems have the potential to disrupt vaccine supply.
5. The U.S. government must be given authority to direct vaccine supply during periods of national crisis.
6. Consideration should be given to the federal purchase of all influenza vaccine or at least to the purchase of a guaranteed amount.
7. Stockpiling influenza vaccine, including surplus kept in manufacturing storage from the previous year, should be considered. The stockpiled vaccine might be of use even if there is not an exact strain match because it could modify the illness, reduce infectivity, and the period of infection.
8. More long-term strategies include the need for new technologies for more efficient and timely production of vaccine in the necessary quantities.

The influenza vaccine manufacturing problems facing the United States are fundamentally economic. Involved is a commodity vaccine that is undervalued and represents a relatively low profit for manufacturers. Adding to the problem is the fact that market demand is uncertain, there are high regulatory burdens and associated costs, and manufacturers bear substantial risks. The combined effects have been to drive several firms out of the market. Government intervention is needed to save domestic vaccine manufacturing and to diversify the manufacturing base.



Dean D. Mason

Dean D. Mason

President and Chief Executive Officer

Hookworm Disease Weighs Heavily on the Developing World Poor

New England Journal of Medicine *Article Illuminates Latest Findings on Bloodthirsty Parasite*

An article published in the August 19, 2004 *New England Journal of Medicine* calls attention to the enormous impact of parasitic hookworm infection on the developing world poor. The authors of "Current Concepts: Hookworm Infection" have studied the parasite over many years and describe the disturbing effects of mild infection as well as the devastating disease state that results from heavy hookworm infection.

According to Peter J. Hotez, MD, PhD, the article's lead author, hookworm is one of the most common infections in humans with an estimated 740 million cases in areas of rural poverty in the tropics and subtropics. In China alone, approximately 190 million people are infected. Measured against other diseases, hookworm outranks African trypanosomiasis, dengue, Chagas disease, schistosomiasis, and leprosy in its impact on individuals and society.

Hookworm infection plagues vast areas of Asia, Africa, and Latin America and was once prevalent in the United States. Here it was surmounted by sanitation improvements that accompanied 20th century economic development. Ultimately, poverty reduction and economic development has done the most to eliminate hookworm in industrialized nations, but for those living in poor endemic areas around the world, such socioeconomic reforms are a distant prospect.

The term "hookworm disease" refers to the iron deficiency anemia that results from moderate and heavy infections. Worms fasten onto the inner layers of the small intestine and cause blood loss. According to the authors, each hookworm can grow to one centimeter and cause up to 0.2 cc of blood loss per day, and chronic intestinal blood loss results from heavy infections. Because women and young children have the lowest iron stores, they are the ones most vulnerable to chronic hookworm blood loss. Hookworm infection adversely af-

fects childhood memory, reasoning ability and reading comprehension.

The current method of hookworm removal is a single dose treatment with anti-helminthic drugs. However, in highly endemic areas, hookworm infection often reoccurs within just a few months. This, compounded by growing concerns about emerging drug resistance, has prompted efforts to identify new tools for hookworm control, including a vaccine.

Hookworm is one of the most common infections in humans with an estimated 740 million cases in areas of rural poverty in the tropics and subtropics.— Hotez

The authors of the article are Dr. Hotez, Jeffrey M. Bethony, PhD and Maria Elena Bottazzi, PhD, from The George Washington University, Washington, DC; Simon Brooker, PhD, London School of Hygiene and Tropical Medicine, London; Alex Loukas, PhD, Institute of Medical Research, Brisbane, Australia; and Shuhua Xiao, MD, Chinese Center for Disease Control and Prevention, Shanghai, China.

Hookworm Vaccine Initiative Names New Program Manager

Stoever Steps into Role for Clinical Trials of Hookworm Vaccine

The Human Hookworm Vaccine Initiative (HHVI) welcomed Kari Stoever, CCRP, as program manager in November 2004. Stoever, whose offices are at the SVI's Bethesda, Maryland site, will play a key role in managing vaccine clinical trials soon to begin at HHVI.

Stoever was most recently a clinical research coordinator, study monitor, and protocol development team member for Anthrax Vaccine Clinical Studies at the U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Maryland. There, she coordinated clinical research studies, including development of clinical study protocols, and was a voting member on the Human Use Committee, Institutional Review Board. She has experience as principal point of contact for regulatory affairs, quality assurance and clinical monitoring issues, reviews, audits and reports.

With extensive experience as a study coordinator and institution contact, Stoever has worked on studies in oph-



Kari Stoever, CCRP

thalmology, oncology, and infectious diseases.

Stoever previously served as clinical research manager for the Retina Group of Washington, where she developed and implemented a clinical trial program and managed seven clinical studies for the practice. She was a consultant for Berlex Laboratories and man-

aged the quality assurance program of Midwest Cancer Research Group. There, she served as a site coordinator for a multi-hospital hematology and oncology research program and was clinical trials coordinator for phase II and phase III pharmaceutical studies.

Stoever currently is enrolled in The George Washington University School of Medicine and Health Sciences Clinical Research Program. She has been certified as a clinical research professional with the Society of Clinical Research Associates (SOCRA) since 2001 and is a member of the Drug Information Association (DIA) and Regulatory Affairs Professionals (RAPs).

SVI to Team with Brazilians on Human Hookworm Vaccine Trials

Agreement Signed in Rio de Janeiro Clears Hurdle on Vaccine Production

Brazil is the fifth largest country in the world by area and population. This land of famed beauty and diversity is also home to hookworm. SVI Human Hookworm Vaccine Initiative representatives traveled to Brazil in September to sign a memorandum of understanding for prospective hookworm vaccine production in Brazil that could alleviate the distress that hookworm disease causes among a segment of the population there.

SVI sponsors the research funded by the Bill & Melinda Gates Foundation on a newly developed vaccine to prevent human hookworm disease. The memorandum of understanding with federal and state vaccine production facilities in Brazil is for clinical development of the vaccine, including clinical trials and vaccine manufacture.

Representatives from both the Sabin Institute and The George Washington University (GW) were greeted by Brazilian officials hopeful that the new vaccine will prevent an ages-old disease endemic in Brazil that is caused by the devastating intestinal parasite. Fieldwork research on the hookworm vaccine is underway already and Brazilian officials offered visits to research and production plants affiliated with the government of Brazil.

Elated with the success of the trip, lead scientist Peter J. Hotez, MD, PhD, said, “This is the best and most substantive

international collaboration I’ve ever had in 20 years of work in tropical medicine.” Hotez is professor and chair of the Department of Microbiology and Tropical Medicine at the GW Medical Center and senior fellow at the Sabin Institute. He has spent more than 20 years studying hookworm disease and devising a vaccine to prevent infection. His team met with Brazilian scientists at the Oswaldo Cruz Foundation, a research arm of the Brazilian Ministry of Health, and with researchers at the Butantan Institute, both of which operate vaccine-manufacturing plants. Officials from each group signed the memorandum of understanding.

According to Hotez, Brazil is like only a few countries in the world having both high endemic incidence of hookworm and pockets of extreme poverty, along with a high technology capacity and ability to develop biological products. “These features would also describe such middle income countries as China, Mexico, India and South Africa,” he said. “Brazil is one of the few countries with the technical capacity and intrinsic interest in the problem because hookworm is a public health threat in their nation.”

The trip was arranged in order to garner the support of the Brazilian government for their commitment to produce the hookworm vaccine, says Dean Mason, president of the Sabin Vaccine In-



Dean Mason, SVI president, signs memorandum of understanding on behalf of the Sabin Vaccine Institute.

stitute. He and Hotez participated in the visit along with Ciro de Quadros, MD, MPH, director of Sabin’s International Programs, Maria Elena Bottazzi, PhD, project manager and GW assistant professor of microbiology and tropical medicine, and Jeffrey Bethony, PhD, project clinical director.

“What is remarkable is the openness and cooperation of the government of Brazil at the highest levels,” said Mason, who signed the agreement on behalf of the Sabin Institute. “This is a country where they are willing to get the vaccine to the needy. The whole idea, if the vaccine field trials prove successful, is to make the hookworm vaccine available for those afflicted and the poorest of the poor. No one is looking to make a commercial profit, but instead we are doing this for the best of reasons ... necessity.”

The hookworm vaccine developed by Hotez will soon undergo clinical trials, so a team of a dozen workers led by Bethony is now assembling baseline data. The team is based in Belo Horizonte, Brazil, near the rural area impacted by hookworm disease. In just more than a year, that data and data from safety and tolerability trials in the United States will serve as required groundwork for a wider clinical trial to ascertain the efficacy and safety of the new vaccine.



Brazilian officials welcome SVI and GW representatives at Castelo Mourisco, headquarters of the Oswaldo Cruz Foundation in Rio de Janeiro, Brazil.

Cancer Vaccine Consortium Joins Forces with International Partner Cancer Society

Report from the Fourth Meeting of the Cancer Vaccine Consortium

Participants at the Fourth Semi-Annual Meeting of the Cancer Vaccine Consortium were told to “memorize the moment” because in years to come, the meeting may be known as the birthplace of several important steps in the development of cancer vaccines.

Although not formally announced, several meetings between the leadership of

the Consortium and the International Society for Biological Therapy of Cancer took place, and a joint initiative was agreed to in principle. Members of the iSBTc are joining forces with the CVC to create a Cancer Vaccine Clinical Trials Working Group (CVCTWG). The working group aims to write a scientific paper describing the “state of the art” of clinical development of cancer vaccines and combination immunotherapies. There is active liaison with the FDA, and hopes are high that the publication could contribute to a future FDA guidance document.

Chairpersons of the CVCTWG include Dr. Axel Hoos from Antigenics, Dr. Geoffrey Nichol from Medarex, Dr. Giorgio Parmiani from the Istituto dei Tumori in Milan, Italy, and Dr. Mario Sznol from Yale University. The group has divided the work into four workstreams. Each workstream is co-chaired by a member of the CVC and the iSBTc and includes broader representation from the CVC, iSBTc, industry, academia, and regulatory agencies. Drs. Hoos and Nichol were in attendance at the CVC meeting and co-chaired the morning’s activities, which included a

breakout session to kick off each of the workstreams.

The project has an ambitious work schedule. It will include many teleconference calls, a spring meeting of workstream leaders to prepare a preliminary document for wider circulation, ultimately culminating in an important workshop at the iSBTc meeting in Alexandria, Virginia, in November of 2005. Many experts will have the opportunity to contribute to this comprehensive work.

Keynote speakers at this year’s CVC meeting November 7-8 in San Francisco included Dr. Drew Pardoll (Johns Hopkins Medical School) whose talk on “Regulatory Barriers for Cancer Vaccine Development” engendered good-humored debate with the second speaker, Dr. Steven Hirschfeld from the FDA. His presentation, “Clinical Trial Endpoints for Biologics Developments in Oncology,” drew much interest from the audience. Also of keen interest was the third speaker’s subject. Dr. Holden Maecker (BD Biosciences) talked about “Standardization of Cellular Immune Monitoring Assays and What They Can Tell Us.” All attendees received a complete meeting presentation package.

Correction of Fact in the History of Polio Vaccines

The path of scientific discovery, including vaccine discovery, is often complex and evolves from the contributions of many. Such has been the case with the discovery of vaccines to prevent poliomyelitis. In the Summer 2004 issue of *The Sabin Vaccine Report* we published a letter celebrating the 50th anniversary of the launching of a mass vaccination trial with a polio vaccine developed by Jonas Salk, MD. The letter referred in error to the 1954 landmark mass vaccination campaign with the Salk vaccine as the “first-ever polio vaccination.” In fact, earlier vaccination trials had occurred.

The Salk vaccine was later replaced on the immunization schedule by the oral polio vaccine developed by Albert B. Sabin, MD. Neither the vaccine developed by Salk nor that developed by Sabin was used in the “first-ever polio vaccination.” A polio vaccine developed by Hilary Koprowski, MD was administered in a trial four years earlier to 20 subjects and was reported in March 1952 at a meeting of the National Foundation for Infantile Paralysis in Hershey, Pennsylvania. There were at least two previous vaccine candidates tested in the 1930s that were not proven safe and effective and were abandoned. The editor thanks Dr. Koprowski for taking time to inform the readers of *The Sabin Vaccine Report* of his groundbreaking discovery. We regret the error.

Your gift is no small drop.

Your donation goes a long way in support of the Sabin Vaccine Institute.

As a partner with us, your donation promotes disease prevention through immunization, effective vaccine policy, and vaccine research and development. We hope you will consider a tax-deductible contribution to the Sabin Vaccine Institute. Readers may enclose a check in the envelope (no

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Photo: Marcel Crozel/WHO

Thank you!

11th Annual Vaccine Policy Colloquium on Pandemic Influenza Vaccine

Sabin Vaccine Institute—"New, Important and Credible Participant" in Worldwide Influenza Partnership

Continued from page 1

cluding developing country manufacturers in the discussions—two developing country manufacturers of quality assured vaccine were present at the meeting. According to Heymann, they are now committed to explore the possibility of technology transfer between companies to increase influenza vaccine production and to promote discussions with other developing country manufacturers. "The pandemic influenza meeting could be a launch point for a new way of working on influenza vaccines internationally if particular recommendations are followed up," Heymann said.

"This meeting can serve as a catalyst among participants from around the globe," said organizer Dean Mason, president of the Sabin Vaccine Institute. "Though a number of countries and regional organizations have drafted plans to address pandemic influenza, there is still much coordination and planning to

be done. This meeting identified some important gaps in the planning." The number of people who would need to be vaccinated greatly exceeds the number of vaccine doses that can be manufactured today. The time it would take to make the vaccine available using existing technologies and planning for the use of antiviral drugs are other areas where contingent planning is needed.

A further goal of pandemic disease preparedness beyond strengthening the global vaccine manufacturing enterprise would be development of new vaccine technologies to prevent other killer diseases. Each year approximately 15 million people in the world die of infectious diseases and most of these diseases—



Pictured with author John Barry, signing book, are from left, Lewis A. Miller, SVI trustee; David L. Heymann, WHO; Barry; and Dean Mason, SVI president. Barry's book, titled, *The Great Influenza*, chronicles the 1918 pandemic. Photo by M. Chua, CSH Laboratory.

including AIDS, TB, malaria, childhood diarrheal diseases, and pneumonias—are the target for research to develop vaccines or improve coverage and effectiveness of existing products. According to WHO's Heymann, "The meeting will have direct positive impact on WHO's activities in influenza pandemic planning and adds a new, important and credible participant to the worldwide influenza partnership." It also adds to the international coalitions working to better assure that influenza vaccine will be made available to all countries.

The colloquium, held at the Banbury Conference Center, Cold Spring Harbor Laboratory, New York, was co-chaired by Heymann, with Lewis A. Miller, principal of WentzMiller & Associates and Sabin trustee, and Albert Osterhaus, DVM, PhD, head of virology at Erasmus Medical Center in Rotterdam, Netherlands. Also serving on the expert committee for the colloquium was Ciro de Quadros, MD, MPH, director, International Programs, at the Sabin Vaccine Institute. It was the 11th annual vaccine policy colloquium in an ongoing series sponsored by the Bill & Melinda Gates Foundation.

The proceedings of the colloquium is being prepared for publication in January 2004. The document will be published in print and made available online at www.sabin.org.



Colloquium participants gathered at the Banbury Conference Center at Cold Spring Harbor Laboratory are, from left, front row: Helen Garey, Chun Kang, Dean Mason, David Heymann, Lew Miller, Albert Osterhaus, Theresa Tam; 2nd row: Conny Mason, Isaias Raw, James Matthews, Veronica Korn, Sharon Hammer, and Suresh Jadhav; 3rd row: Sarah Landry, John Barry, Michael Osterholm, Lance Gordon, Diane Simpson, Karen Nielsen, Richard Knox, and Louis Cooper; back row: David Salisbury, Mary Ann Chaffee, Shanelle Hall, Otavio Oliva, James LeDuc, Benjamin Schwartz, Mark Miller, Clem Lewin, John Woodall, Klaus Stohr, and Raymond MacDougall.

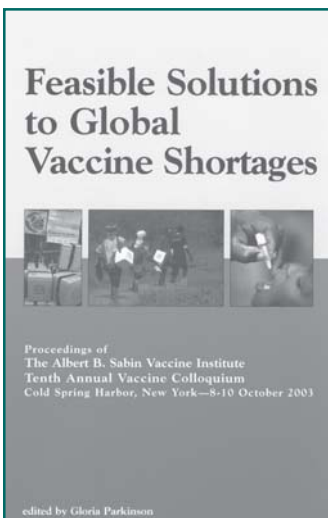
BOOK CORNER

Vaccine Shortages Examined, Prescription Formulated in SVI Release

Public Health Experts Provide Guidance to Vaccine Supply Problem in Meeting Proceedings

Recent highly publicized vaccine shortages have cast a shadow over the otherwise enormous success of vaccines as a tool for disease prevention around the world. Vaccines have been the cornerstone of public health for the past 50 years and shortages have shaken public confidence and exposed real vulnerabilities in the current system of vaccine production. A new publication of the Sabin Vaccine Institute (SVI), *Feasible Solutions to Global Vaccine Shortages*, addresses a set of issues that may hold the key to remedying the threats of vaccine shortages.

A precipitous decline in the number of manufacturers in the 1990s was amplified by sudden regulatory decisions, heightened liability concerns, and a relatively low return on investment for vaccine producers. SVI convened the 10th Annual Vaccine Colloquium at Cold Spring Harbor in the fall of 2003 to bring together key players to address key related issues, namely stockpiling, financing, advocacy, and regulatory harmoni-



zation. Each issue received thorough consideration by the group of global experts representing the medical and public health communities, U.S. and international governments, international agencies, non-governmental organizations, academia, and the manufacturing sector.

“The complexities and pitfalls challenging the stability of vaccine supply are much better understood following the in-depth analysis and guidance shared by this group,” said H.R. Shepherd, chairman of the Sabin Vaccine Institute. Edited by Gloria Parkinson, *Feasible Solutions to Global Vaccine Shortages* is the latest in a series of colloquium proceedings that the Sabin Vaccine Institute has published in order to generate discussion on critical topics related to vaccines.

Review copies of this proceedings publication are available upon request to sabin@sabin.org. A pdf version may be downloaded from www.sabin.org.

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Spanish Edition of Vaccines Available

PAHO Offers Spanish Edition of Centennial Commemorative Volume

In the previous issue of *The Sabin Vaccine Report* we ran a review of a recent publication release from the Pan American Health Organization (PAHO), which has since been published in the Spanish language.

To reiterate a brief description, during 2002, the centennial year of PAHO, a meeting was held to review the accomplishments of vaccines and vaccination programs—both within the Region of the Americas and throughout the world—and challenges for the Future. Over 250 scientists, health care and public health officials participated. From that meeting, has come *Vaccines: Preventing Disease and Protecting Health*. The book, edited by Ciro de Quadros, the major driving force behind many of PAHO’s successful immunization initiatives, represents a comprehensive and easily readable compilation of outstanding articles on a wide variety of immunization is-

sues, ranging from improving the impact of immunization programs using existing vaccines to the frontiers of vaccine research. The text consists of 48 chapters written by 76 authors, most of whom are among the top international authorities in their fields.

Visit the PAHO web page for order information: publications.paho.org or call 301-617-7806.

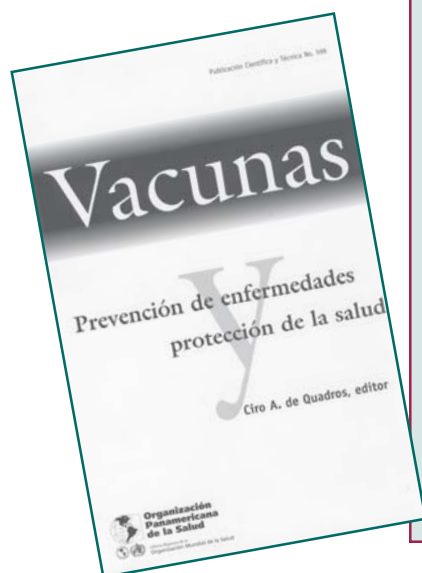
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Rotavirus Vaccine: A Major Tool for Child Survival

A Public Health Commentary by **Ciro A. de Quadros, MD, MPH,** *and* **Jon Kim Andrus, MD**

The following Op Ed appeared in Latin American daily newspapers, including La Prensa in Managua, Nicaragua; O Globo in Rio de Janeiro, Brazil; La Tribuna in Tegucigalpa, Honduras; and Ultima Hora in Asuncion, Paraguay.

Over the course of the last century, the Americas have repeatedly led the world in tackling killer diseases. It was the first region to free itself from smallpox and then polio—two killers of global dominion. Once again, this region has the opportunity to pave the way in a vital public health effort: increasing child survival through targeting rotavirus, the most common cause of severe diarrhea in infants and toddlers. Every year this virus claims the lives of more than 500,000 children worldwide.

Severe rotavirus kills by inducing acute diarrhea and vomiting that can quickly dehydrate a small child. In such a dire emergency, children may need fluids delivered intravenously if they are to survive. So, although nearly every child in the world will become infected by rotavirus within their first years of life, children in poor countries that lack adequate medical care suffer 85 percent of rotavirus deaths. For these children, a preventive vaccine against rotavirus would offer the best protection against this ubiquitous disease.

Until now, no such vaccines have been available to the world's children. This, however, is about to change, and Latin American countries are at the center of this transformation.

This past July, 350 public health experts, scientists, clinicians and representatives of governments, the vaccine industry and the multilateral, bilateral and NGO community met in Mexico City to assess the current state

of knowledge about rotavirus and efforts to combat it. The symposium marked a turning point in the fight against rotavirus. It spotlighted recent efforts across Latin America, Africa and Asia to assess the burden of rotavirus disease and produced new estimates of global mortality, finding that rotavirus accounts for 39 percent of all diarrheal deaths, up from the previous estimate of 22 percent.

The symposium also noted the emergence of two vaccines, one developed by Merck & Co., the other by GlaxoSmithKline, and preliminary data presented at the meeting indicate that both will be safe and effective. Each has been tested in more than 60,000 infants and children. The GlaxoSmithKline trials were based in Latin America, and carried out in cooperation with Ministries of Health and scientific investigators from many of the region's leading hospitals and research universities. In fact, just days after the symposium, Mexican health authorities announced plans to offer this vaccine on Mexico's immunization schedule next spring.

What is striking, however, is not only the scientific triumph of developing safe, effective vaccines against one of the largest killer diseases of childhood, but also the deep commitment evidenced by the public health community and collaborating agencies to ensure that these, and any future vaccines against rotavirus, are made available to all children who need them.

Until now, vaccines have become available first in developed industrialized countries, which are able to pay a premium price for the new products that typically cost up to \$800 million to develop. New vaccines such as those for hepatitis B and *Haemophilus influenzae* type b have taken 10 to 15 years to "trickle down" to developing countries. In this regard, the new rotavirus vaccines represent a turnaround of business as usual. Vaccine accessibility is an equity issue, and partnerships between the public and private

sectors are essential to ensuring full access to life-saving vaccines.

Health officials from 16 Latin American countries emphasized this point of view when they delivered a declaration underscoring support for immunization, with the highest political priority, as a public good for the region. The representatives called upon the Pan American Health Organization and its Revolving Fund for Vaccine Procurement to work with collaborating agencies, national and global health organizations, and with vaccine manufacturers, "to facilitate the introduction of vaccines against rotavirus at prices accessible to all countries of the region as soon as they become available." The Pan American Health Organization is committed to making this happen in a way that ensures vaccines are affordable to all children, particularly those who need them most. This provides another opportunity to reduce inequities in health services.

In Latin America, rotavirus accounts for an estimated 75,000 hospitalizations annually, and the deaths of more than 15,000 children. Country-by-country, the burden varies. In Mexico, 2,000 children die of diarrhea each year, and a vaccine could cut those deaths by 40 percent. Each episode of diarrhea costs families an average of US\$100, which represents 85 percent of the monthly income for families living on minimum wage. In a single outbreak earlier this year in Guatemala, more than 6,500 children were treated for rotavirus at hospitals, and at least 50 children died.

For all of these children, new vaccines offer hope that rotavirus disease will no longer be a rite of passage and test of survival.

Ciro A. de Quadros, MD, MPH, is the Director, International Programs at the Sabin Vaccine Institute. Jon Kim Andrus, MD, is Chief of the Immunization Unit at the Pan American Health Organization.



Benjamin, a one-year-old Chilean boy, almost died of rotavirus, an infection that kills 500,000 children every year worldwide. (Photo: Victor Hugo Durán)

Ciro de Quadros Elected to Institute of Medicine Membership

Also Elected Are SVI Trustee Osterholm, SVI Scientific Advisor Hoffman

The Institute of Medicine (IOM) of the National Academies announced in October the election of 65 new members, including Sabin Vaccine Institute (SVI) Director of International Programs **Ciro de Quadros, MD, MPH**. New members bringing the roster to 1,416 also included SVI trustee **Michael T. Osterholm, PhD** and SVI Scientific Advisory Council member **Stephen L. Hoffman, MD**.

According to IOM President Harvey V. Fineberg, membership is highly selective and recognizes people who have made major contributions to the advancement of the medical sciences, health care, and public health. "Election is consid-



Michael T. Osterholm, PhD

ered one of the highest honors in the fields of medicine and health," he said. Current active members elect new members from candidates nominated for their professional achievement and commitment to service. Members commit volunteer time as members of IOM committees, which engage in a broad range of studies on health policy issues.

The Institute of Medicine is a national resource for independent, scientifically informed analysis and recommendations on issues related to human health. Recent studies included the titles *Immunization Safety Review: Vaccines and Autism*, a report that closed the question of any such link; and *Financing Vaccines in the 21st Century: Assuring Access and Availability*, which proposes new strategies for assuring access to vaccines and sustaining the supply of vaccines.

"I am honored that the IOM membership elected me to join their distinguished ranks," said de Quadros, who joined the Sabin Vaccine Institute in early 2003 to direct several international advocacy projects. Beforehand, he was director of the Division of Vaccines and Immunization of the Pan American Health Organization in Washington, DC. He completed medical studies in Brazil in 1966 and received a Master of Public Health degree from the National School of Public Health in Rio de Janeiro in 1968. He is among the pioneers in developing strategies of surveillance and containment for smallpox eradication. He also directed the successful efforts of polio eradication from the Western Hemisphere and efforts to eradicate measles from the region.

Michael T. Osterholm is director of the Center for Infectious Disease Research and Policy at the University of Minnesota, Minneapolis; **Stephen L. Hoffman** is chief executive and scientific officer of Sanaria Inc., Rockville, Maryland.



Stephen L. Hoffman, MD

For more information on the Institute of Medicine see www.iom.edu.

SVI Chairman **H.R. Shepherd** is a longstanding member of the National Academies Presidents' Circle, heading its Library Outreach Program.

Weizmann Institute Recognizes Science's Select

H.R. Shepherd Honored During Weizmann Institute's New York Event

The American Committee for the Weizmann Institute of Science, New York Region, hosted its gala dinner, *In Celebration of Science*, November 4, 2004 at the Mandarin Oriental Hotel in New York City. The focus of the honors were leading "Women of Vision" among a select group of others celebrated for their scientific contributions to humanity. Also honored at the event were a group of "Distinguished Guests from the Scientific Community" including **H.R. Shepherd, DSc**, chairman of the Albert B. Sabin Vaccine Institute.

"This event celebrated an exceptional group of talented scientists," Shepherd said. "The Weizmann Institute is unparalleled in the research and discovery it promotes, so I am honored to have played a part in the celebration." The Weizmann Institute, located in Rehovot, Israel, is a top-ranking multidisciplinary research institution, noted for its wide-ranging exploration of the sciences and technology.

The "book of honors" distributed at the dinner mentioned Shepherd's distinguished career as a chemist in the aero-

sol cosmetics and medical technology industry. He is recognized as the developer of the metered-dose inhaler used broadly by asthmatics and others requiring respiratory treatment.

For the past 11 years, Shepherd has served as founding chairman of the Sabin Vaccine Institute and established a reputation of excellence for the Institute within the scientific community worldwide promoting vaccines and immunization.



Stephen L. Hoffman, MD

Pediatrician and Vaccine Executive Join Sabin Board of Trustees

Louis Cooper, MD and Kevin Reilly Elected at October Board Meeting

The Board of Trustees of the Albert B. Sabin Vaccine Institute announced the election of two new board members during its September 2004 meeting in New York City. Members of the board provide guidance and valued expertise on all of the Institute's programs. The election of Louis Z. Cooper, MD and Kevin Reilly to the SVI Board adds a depth of experience in vaccine research, immunization advocacy, and vaccine manufacturing and economics.

Dr. Louis Cooper is a retired professor of pediatrics at the College of Physicians and Surgeons of Columbia University and a past president of the American Academy of Pediatrics (2001-2002) and Chairman of the Board of Directors of its Center for Child Health Research.

Since 1964, Cooper has been extensively involved in vaccine research. At Bellevue Hospital in New York, he created the Rubella Project, a vaccine research program, which evolved into a multidisciplinary team dedicated to defining and resolving the rubella problem. This project enabled Cooper to translate scientific information into public policy, legislation and program building in health, education, and social services.

Dr. Cooper served as chairman of the Department of Pediatrics at St. Luke's-Roosevelt Hospital Center for 25 years, becoming chair emeritus in 1998. He has served on numerous advisory bodies at the federal, state, and city level, including chairmanships of the Medical Society of the State of New York Committee on Medicaid and the Public Policy Committee (PPC) of the Pediatric Infectious Disease Society. He is also a member of the corresponding PPC of the Infectious Diseases Society of America. He recently chaired a Blue Ribbon Panel on Vaccine Safety for the Centers for Disease Control.



Louis Z. Cooper, MD

Cooper was the founding co-chairman of the Campaign for Healthy Children, which is best known for designing, advocating, and facilitating implementation of the Child Health Plus Program, New York's effort to guarantee health insurance for every child in the state. Dr. Cooper is a graduate of Yale University and received his medical degree from Yale University School of Medicine.

Kevin Reilly has more than 20 years experience in pharmaceutical management and was president of Wyeth Vaccines and Nutrition, a division of Wyeth, for five years. Prior to joining the vaccine division, Reilly was president of Wyeth Nutrition International and was responsible for management and direction of the business worldwide. During his rise through Wyeth, Reilly held the positions of group vice president and area vice president for the Pacific Rim Group, an area that encompasses the Philippines, Australia, New Zealand, India and Pakistan.



Kevin Reilly

He began his career at Connaught Laboratories, Ltd. as a senior vice president in charge of Canadian and export operations.

Reilly earned a bachelor of science degree from the University of Melbourne in 1963 and a master of business administration degree from York University, Toronto in 1973. Mr. Reilly is also a 1981 graduate of the Advanced Management Program at Harvard Business School.

In announcing the election of the two new board members, SVI Chairman H.R. Shepherd said, "Lou Cooper has been an advocate with us since the beginning of the Institute. He is respected across the country and globally as a champion for immunization and children's health." Of Mr. Reilly, Shep-

herd acknowledged the insights into the challenges and economics of the vaccine manufacturing that Reilly has provided as an industry partner representative. "The value of having expertise from the private sector is immeasurable. We look forward to expanding the programs of the Institute and drawing from the strength of leadership represented on our board of trustees."

CDC's Uyeki and SVI's Mason Present New Canaan Lecture

The Sabin Vaccine Institute participated in the first Davidoff-Sabin Health Science Lecture held at the New Canaan Library in New Canaan, Connecticut on December 9, 2004. Guest speaker for the lecture was Tim Uyeki, MD, MPH, Medical Epidemiologist, Influenza Branch, Centers for Disease Control and Prevention, Atlanta, who along with SVI President and CEO Dean Mason provided insight on influenza.

The free public lecture was titled *Influenza Vaccine—Missing the Point: Vaccine Shortages and the Larger Threat*. The lecture provided an opportunity for the community to become better informed about the impact of influenza and the importance of a secure vaccine supply.



Dr. Tim Uyeki

National Vaccine Shortage

Continued from page 2

groundwork for our present-day industrial-academic-military complex. In his capacity as director of a newly created Office of Scientific Research and Development, Dr. Bush coordinated the activities of some 6,000 leading American scientists and engaged the defense industry, the U.S. military, and major research universities in an unprecedented dialogue and partnership, aided by federal support. Our national military strengths are partly a result of his vision and legacy.

Vaccines, whether for influenza, major childhood illnesses, biodefense, or global health, have effectively become orphan drugs. If we realistically expect a new generation of vaccines, we have to look at alternative business models to ensure their development and testing. We need to develop novel private-public partnerships between the remaining vaccine manufacturers, research universities, the Department of Health and Human Services, and the U.S. military. In so doing, we would create a critical vehicle to marshal and mobilize the best and brightest American biomedical scientists into vaccine development. We need to develop new business models for ensuring a steady pipeline for our nation's vaccine supply. We need also to attract vaccine manufacturers from other countries to the U.S. market, support/subsidize research and development, streamline our regulatory system, better protect against frivolous litigation and encourage competition among vaccine makers, giving consumers more choice.

Some estimates suggest that vaccines saved almost 200 million lives in the 20th century – more lives saved than all lives lost in wars over the same period. Almost all of these were produced by the vaccine industry. In this sense, our remaining vaccine manufacturers should be thought of as national and international treasures. Because vaccines are our greatest resources for disease prevention, their manufacture and distribution are deserving of thoughtful support and leadership.

Peter Hotez, MD, PhD is co-chair of the SVI Scientific Advisory Council and is chair of Microbiology and Tropical Medicine, The George Washington University (GW). Frank Cilluffo is vice president for Homeland Security at GW.

SABIN CALENDAR

JANUARY-JUNE 2005

- January 24 - 25** *Washington, DC*
2nd Workshop on Strengthening the Supply of Vaccines in the U.S.
www.hhs.gov/nvpo
- February 8 - 9** *Washington, DC*
National Vaccine Advisory Committee Meeting www.hhs.gov/nvpo
- February 10 - 11** *Atlanta, Georgia*
Advisory Committee on Immunization Practices (ACIP) www.cdc.gov/nip/acip
- February 17 - 22** *Santa Fe, New Mexico*
Antibody-Based Therapeutics for Cancer
www.keystonesymposia.org/Meetings
- February 24 - 26** *Hershey, Pennsylvania*
8th Annual Meeting of the Regional Cancer Center Consortium for the Biological Therapy of Cancer
www.cancerbiologicaltherapy.org/symp.html
- March 17 - 18** *London, United Kingdom*
DNA Vaccines Forum
www.marcusevans.com/events/CFEventinfo.asp?EventID=9175
- March 18 - 20** *Madrid, Spain*
Frontiers in Neonatal & Infant Immunity www.themacraegroup.com
- March 18 - 22** *San Antonio, Texas*
American Academy of Allergy, Asthma and Immunology
www.aaaai.org/members/annual_meeting
- March 19 - 24** *Keystone, Colorado*
Basic Aspects of Tumor Immunology
www.keystonesymposia.org/Meetings
- March 21 - 24** *Washington, DC*
39th National Immunization Conference
www.cdc.gov/nip/NIC
- April 2 - 5** *Copenhagen, Denmark*
15th European Congress of Clinical Microbiology and Infectious Diseases
www.akm.ch/eccmid2005
- April 9 - 15** *Banff, Alberta*
HIV Vaccines: Current Challenges and Future Prospects (X8)
www.keystonesymposia.org/Meetings
- April 16 - 20** *Anaheim, California*
96th Annual Meeting of the American Association for Cancer Research
www.aacr.org
- April 19 - 20** *Montreal, Canada*
World Vaccine Congress Montreal 2005
www.lifescienceworld.com/2005/wvcm_CA
- April 24 - 30** *U.S. Nationwide*
National Infant Immunization Week
www.cdc.gov/nip/events/niiw
- May 9 - 11** *Baltimore, Maryland*
8th Conference on Vaccine Research
www.nfid.org/conferences
- May 10** *Baltimore, Maryland*
Albert B. Sabin Gold Medal Ceremony
www.sabin.org/awards_gold.htm
- May 23 - 25** *Amsterdam, The Netherlands*
Phacilitate Vaccine Forum Spring 2005
www.phacilitate.co.uk
- June 7 - 8** *Washington, DC*
National Vaccine Advisory Committee Meeting www.hhs.gov/nvpo
- June 15 - 18** *Lisbon, Portugal*
12th International Congress on Infectious Diseases (12th ICID)
www.isid.org
- June 21 - 24** *Cold Spring Harbor, New York*
7th Annual Sabin Colloquium on Cancer Vaccines and Immunotherapy
www.sabin.org/programs_walkers_cay.htm



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