Supply of Vaccines Tops Agenda at 2002 Sabin Vaccine Policy Colloquium

Ninth Sabin Colloquium Dubs Vaccines “Weapons of Mass Protection”

Vaccine supply issues took center stage at the Sabin Vaccine Institute’s Ninth Annual Colloquium convened at Banbury Center, Cold Spring Harbor Laboratory, New York, October 23 to 25. Public health experts, domestic and international health economists, industry representatives and immunization advocates participated in the three-day colloquium titled, “Global Vaccine Shortage: The Threat to Children and What to Do About It,” that urged action to address current shortages of key vaccines and to improve the stability of future supplies.

This year’s focus on vaccine supply issues was determined by broad concern for the security of the vaccine supply along with recent supply problems. During the past year, the United States could not meet demand for five vaccines that prevent eight childhood diseases. For the past two years, there were shortages of the flu vaccine and until recently there was a shortage of the tetanus vaccine. In developing countries, the reduced number of qualified manufacturers has led to serious risks of vaccine shortages for four basic vaccines that prevent six childhood diseases including measles and whooping cough.

Underscoring the importance of the vaccine supply issue, Sabin Vaccine Institute Chairman H.R. Shepherd commented, “Vaccines are a critical line of defence against infectious diseases. Stops and starts in the supply of any vaccine can have dire consequences.” Dr. Shepherd was on hand to welcome the colloquium participants and deliver their charge.

Two keynote addresses set the stage for the meeting: Kevin Reilly, past president of Wyeth Vaccines, framed the domestic vaccine supply situation, while Carol Bellamy, executive director of UNICEF and chair of the Global Alliance for Vaccines and Immunization (GAVI), commented on vaccine shortages in the developing world. (See sidebars on page 7.)

“Vaccine security—the sustained, uninterrupted supply of affordable vaccines—is at risk,” said Carol Bellamy. “While there is a growing divide between vaccines given to children in developing and developed countries, shortages affect both. A key factor is that there are fewer manufacturers, especially of basic vaccines where profitability is lower.”

The colloquium focused on four strategies to resolve the current vaccine supply problem in the U.S. and in developing countries:

- Achieving a fair rate of return on investment for manufacturers;
- Making vaccines/prevention of disease a national and international priority;
- Achieving a fair rate of return on investment for manufacturers;
- Making vaccines/prevention of disease a national and international priority;

Colloquium participants considered key issues that impact vaccine supply during roundtable discussions. From left, Karen Midthun, Jan Heinrich, Jose Ignacio Santos, Natalie Smith, and Julie Fischer share perspectives in exercise aimed at uncovering pathways to solutions to vaccine supply problems.

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Vaccines Offer Security on the Home Front

A Message from the Chairman

H. R. Shepherd, Chairman

Vaccines, tracing back to Edward Jenner’s time, still command attention because of their enormous contribution to public health. Popular media and scientific press find ample material for their publications and broadcasts focusing on the benefits of vaccines, their future potential, as well as any controversies surrounding specific vaccines, vaccine legislation or vaccine policy.

New attention is being paid to the everpresent threat of infectious diseases, particularly post 9/11. As a result of increased awareness of biological weapons, we recognize that one disease thought to be eradicated might be an extant threat—smallpox.

Fortunately, our nation’s experts, including SVI founding president and board member Philip Russell, arrived at a clear vaccine policy based on the best available scientific data. The nation has been assured that ample supplies of smallpox vaccine are stockpiled and that new initiatives will bring an improved vaccine into use in the foreseeable future that will provide protection for immunosuppressed segments of our population.

The outstanding success of immunization efforts, however, has created a national mindset of complacency about diseases staved off by immunization. Smallpox is but one of the dangerous infectious diseases for which modern science has found an effective vaccine. Our collective memory may have to stretch back to recall the suffering resulting from polio, diptheria, or congenital rubella syndrome, just a few of the conditions prevented by vaccines. Such an exercise of remembrance would benefit each of us.

We can be encouraged by news of vaccines for the future too. An announcement last month reported an effective vaccine to fight human papillomavirus, and more promising vaccines to treat diseases are in various stages of preliminary and clinical trials.

The protective public benefit of currently licensed vaccines is enormous and has contributed significantly to the advancement of contemporary society. The Sabin Vaccine Report attempts to provide the public with information on health gains achieved in our time with the help of vaccines. We perceive this dissemination of information to be especially time critical, as there needs to be an increased realization and appreciation of the complexities of vaccine development and production.

The Sabin Vaccine Institute is encouraged in the role played by our colloquia to provide an avenue for all sectors to come to a consensus of how to better serve national and global public health needs. Contributing to collaboration among the partners who enable vaccine and immunization programs is a critical role and the Institute is pleased to be a part of this process.

With all good wishes for a peaceful, healthy and productive year ahead.

Chairman
Sabin Vaccine Institute
We Must Keep All Vaccines off the “Endangered” List

Securing Vaccine Supply is Global Health Priority

U.S. policy makers, physicians, and the general public are now debating how vaccines can be used most effectively to thwart the evil intent of bioterrorists. Such debate focuses largely on the theoretical, however, and the nation must not lose sight of a real need that is much more pressing: the need to ensure that every child is immunized against diseases that are serious, confirmed threats today.

The past several years have been marked by gaps in vaccine supply that have left children vulnerable to debilitating and life threatening infections. Diseases that have become rare in developed countries such as the United States due to our past successes in vaccination, continue to proliferate globally and are easily imported by jet travel. The one exception to this threat is smallpox, which has been eliminated globally (for now, at least).

At an October meeting organized by the Sabin Vaccine Institute, held to focus on resolving vaccine shortages, experts from diverse sectors — academic, scientific, public health policy, nonprofit and industry — agreed on one underlying tenet: unless there is a greater appreciation of the value of vaccines for the individual and for society, they will continue to be underfunded, underused, and more likely to suffer production shortfalls. Vaccines have been the reliable foundation of public health. Consequently, they tend to be taken for granted and are undervalued.

Do vaccines make a significant difference in preventing disease, disability and death? Without doubt. But public perception has placed a higher value on one week’s supply of an anti-cholesterol drug or an anti-impotence pill than on one shot of measles-mumps-rubella vaccine that prevents congenital malformations and possible death in the infant of a pregnant woman. As a result of our unwillingness to give vaccines their social and economic due, the number of vaccine manufacturers has decreased, and shortages of some necessary vaccines have increased.

Vaccines’ perceived value unquestionably lies at the root of the supply question. Vaccine supply will be undermined until parents recognize immunization as an essential part of preventive healthcare. Vaccine supply will not be secure until pediatricians and primary care practitioners take every opportunity to ensure their patients are immunized with the complete recommended schedule of vaccines. Vaccine supply will remain a low priority until legislators are motivated by the welfare of their constituents to encourage vaccine production and additional investments in research and development.

Vaccines offer their greatest reward to the most vulnerable among us — children. Childhood vaccines form the bedrock of global and domestic public health strategy and have unquestionably demonstrated their value and effectiveness over decades. Smallpox killed more people in the twentieth century than did all wars of the same period, and its eradication through a mass vaccination campaign was an outstanding accomplishment. Measles still kills 800,000 children each year in countries where the vaccine is not universally administered. The value of vaccines is clear and incontrovertible.

Children are not the only beneficiaries of vaccines. Preventive vaccines for hepatitis B, pneumococcal infection, and flu offer both children and adults protective immunity. It is a calamity that at least 38,000 American adults die from complications of these infectious diseases every year.

While supplies of flu vaccine are plentiful this year, they have not been in recent years, and there is no guarantee they will remain plentiful in the future. In fact, there is no guarantee that any existing vaccine will remain in strong supply. Without concerted collaboration among government, industry and consumer groups, the availability of vaccines remains vulnerable to market economics and production difficulties. It is incumbent on all stakeholders to address the realities of vaccine economics and manufacturing complexities, both nationally and internationally. It is vital for the public health community to persist in its efforts to communicate the value of vaccines and to remind the public of the lurking dangers of preventable diseases.

Let us not forget that vaccines unquestionably are the most humane and cost-effective medical intervention against preventable infectious diseases. Can civilized society allow such wondrous tools in the battle against disease to languish, or even be lost, because we haven’t taken care to nurture them?

Lance K. Gordon, PhD
Chief Executive Officer, VaxGen, Inc.

Lewis A. Miller
Corporate Editorial Director, Dowden Health Media
Chairman, Intermedica, Inc.

The authors co-chaired the 9th Annual Sabin Vaccine Institute Colloquium on Vaccine Policy this past October.
PAHO’s 100th anniversary celebration included the Conference on Vaccines, Prevention and Public Health: A Vision for the Future, held November 25-27. The three days of talks followed a forward-looking theme for vaccines, from the present status of polio and measles eradication efforts, to the newest epidemiological information, to the future and quest for vaccines on the horizon.

As part of the sessions, Peter Hotez, MD, PhD, Sabin Scientific Advisory Council chairman and chairman of Microbiology and Tropical Medicine at The George Washington University, provided a presentation on Parasitic Diseases and discussed the value and promise of a vaccine to immunize against hookworm infection. He discussed approaches and progress of his team’s efforts in development of a hookworm vaccine.

A welcome to the conference was delivered by Sir George A. O. Alleyne, director of PAHO. “This celebration is not only about the conquest of the world’s diseases with that most effective of health technologies—vaccines,” he said. “It is also a celebration of the vibrancy of the Pan American spirit and the ideal—a celebration of things done together, for let us not forget that the success of immunization in the Americas is a triumph of partnerships.”

The conference featured presenters whose expertise and scope reflected the pinnacle of research on vaccines. Among the roster of speakers were Ciro de Quadros, MD, former director of the PAHO Division of Vaccines and Immunization, who presented a sweeping perspective of the past 100 years of vaccines and immunization in the Americas as well as a discussion regarding measles and the feasibility of global eradication. Louis Cooper, MD, past president of the American Academy of Pediatrics, presented the status of rubella and congenital rubella syndrome, including compelling cases from his pediatric practice and research. Noted public health expert D.A. Henderson, MD, director of the U.S. Department of Health and Human Services Office of Public Health Preparedness, discussed the heightened awareness of bioterrorism threats and the strategies for renewed smallpox vaccination. Many other vaccine experts provided a collective picture of the dynamic research taking place to carry out vaccine programs and develop new vaccine products.

As one of the culminating events of PAHO’s centenary celebration, the vaccine conference demonstrated the contribution of vaccines to public health efforts in the Americas and around the globe.

New Goals Enliven PAHO’s 100-Year Commitment to Public Health

One of PAHO’s most notable successes in controlling vaccine-preventable disease was the eradication of smallpox from the Americas in 1973, a triumph that led five years later to global eradication of the disease. In 1994, PAHO assisted in the elimination of polio from the Americas. Polio eradication is now a global goal for 2005, and PAHO has set a new target of eliminating measles from the hemisphere.

In November, PAHO’s member countries fully endorsed the Integrated Management of Childhood Illnesses (IMCI) strategy. The Organization is working to reduce by half the more than 200,000 preventable deaths among children under five years. The initiative is called Healthy Children: Goal 2002, based on the IMCI strategy. Acute respiratory infections, diarrheal diseases, and malnutrition are the three leading causes of illness and death in this age group. These diseases and others, such as those caused by vaccine-preventable diseases and malaria, are the primary reasons for medical consultation and hospitalization in the Americas.

“Children are being evaluated for cough, diarrhea, and fever; health workers are verifying the vaccination status of children, and children are being weighed and families given preventive advice and an appointment for the next consultation,” said Christopher Drasbek, PAHO’s regional technical advisor in IMCI. “PAHO is convinced that this strategy should be the principal intervention of primary health care to reduce mortality from infectious diseases in children under five.”
President Bush Announces Smallpox Vaccination Plan

New Threat of Bioterrorism Prompts Policy, Nation to Revisit Inoculations Against Smallpox

President George W. Bush announced a plan on December 13 to better protect the American people against the threat of smallpox attack by hostile groups or governments. The announcement laid out a plan to resume smallpox vaccination, which was declared successfully eradicated by the World Health Organization in 1980. With new bioterrorism threats, the President has deemed it appropriate to begin a tiered administration of the vaccine.

Smallpox Response Teams

Under the plan, the Department of Health and Human Services (HHS) will work with state and local governments to form volunteer Smallpox Response Teams who can provide critical services to their fellow Americans in the event of a smallpox attack.

To ensure that Smallpox Response Teams can mobilize immediately in an emergency, health care workers and other critical personnel will be asked to volunteer to receive the smallpox vaccine.

The federal government is not recommending vaccination for the general public at this time. There may be some members of the general public who insist on being vaccinated now. Public health agencies will work to accommodate them, but that is not the federal recommendation at this time.

Department of Defense and State Department Personnel

The President also announced that the Department of Defense (DOD) will vaccinate certain military and civilian personnel who are or may be deployed in high threat areas. Some United States personnel assigned to certain overseas embassies will also be offered vaccination.

Although there is no reason to believe that smallpox presents an imminent threat, the attacks of September and October, 2001 have heightened concern that terrorists may have access to the virus and attempt to use it against the American public. Immediately after these attacks, HHS began working, in cooperation with state and local governments, to strengthen our preparedness for bioterror attacks by expanding the national stockpile of smallpox vaccine. The United States currently has sufficient quantities of the vaccine to vaccinate every single person in the country in an emergency.

The smallpox vaccine, which was routinely administered to Americans until 1972, is a highly effective protection against the disease when given before or shortly after exposure to the virus. Pre-attack vaccination of Smallpox Response Teams will allow them, in the event of a smallpox attack, to immediately administer the vaccine to others and care for victims.

HHS is working with states to identify health care workers and first responders to serve on Smallpox Response Teams. Pre-attack vaccination of these Smallpox Response Teams will allow them to better protect the American public against smallpox attack.

The federal government is not recommending that members of the general public be vaccinated at this point. Our government has no information that a biological attack is imminent, and there are significant side effects and risks associated with the vaccine.

HHS is in the process of establishing an orderly process to make unlicensed vaccine available to those adult members of the general public without medical contraindications who insist on being vaccinated either in 2003, with an unlicensed vaccine, or in 2004, with a licensed vaccine. (A member of the general public may also be eligible to volunteer for an ongoing clinical trial for next generation vaccines).

Preparing Military and Overseas Personnel

The President also announced that DOD will take steps immediately to reinstitute vaccination of certain military and civilian personnel. Those personnel who are deployed or who may deploy to certain high threat areas will be vaccinated. The State Department will also offer vaccination to certain overseas personnel.

Although the vaccine is effective if administered shortly after exposure, it may not be feasible during an emergency to vaccinate overseas troops and civilian personnel. Pre-attack vaccination is therefore warranted. Vaccination of military personnel was conducted during WWI and WWII and routinely from the 1940s until 1984. Between 1984 and 1990, vaccinations were provided to many recruits entering basic training.

Sources of Smallpox Vaccine Information

The Centers for Disease control and Prevention has made the information provided above available and also recommends the following web pages for further information:

- To read more on the disease, visit [www.bt.cdc.gov/agent/smallpox](http://www.bt.cdc.gov/agent/smallpox)
- To read more on the vaccine, visit [www.bt.cdc.gov/agent/smallpox/vaccination/facts.asp](http://www.bt.cdc.gov/agent/smallpox/vaccination/facts.asp)
- To read more on medical conditions that make pre-vaccination unadvisable, visit [www.bt.cdc.gov/agent/smallpox/vaccination/contraindications-public.asp](http://www.bt.cdc.gov/agent/smallpox/vaccination/contraindications-public.asp)
- Persons interested in participating in an ongoing clinical trial can obtain additional information at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
Ninth Sabin Colloquium Explores Pathways to Secure Vaccine Supply

Vaccine Supply Issue Commands Front-and-Center Status at Three-Day Meeting

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- Harmonizing the regulatory process to arrive at global standards for safety, efficacy and good manufacturing practices;
- Securing adequate vaccine capacity.

“The world is a far safer place for us and our children because of the advent and advances made on the vaccine front,” said Lance Gordon, CEO of VaxGen and colloquium co-chair. “It is imperative to achieve a steady and secure supply of existing vaccines as we press forward to achieve vaccine breakthroughs of the future.”

The Sabin Vaccine Institute received funding support for the colloquium from the Bill and Melinda Gates Foundation. Support was also received from UNICEF, a major funding source for vaccination programs worldwide.

Select Recommendations Made by Colloquium Participants

On Communication
- Create greater communication among all stakeholders including private and public sectors.
- Advocate the value of vaccines as an international priority.
- Improve understanding of industry to the public health sector.
- Translate the concern over bioterrorism into an opportunity for advocacy of immunization’s value to a country’s security.

On Capacity
- Determine the feasibility of stockpiles.
- Explore tax incentives in the U.S. and EU to expand manufacturing capacity for developing countries.
- Improve long-term demand forecasting.
- Track supply versus demand and improve planning at the country level.
- Create incentives for industry to continue long-term and innovative vaccine development through grant programs.

On Regulatory Issues
- Develop a strategy to manage the uncertainty of liability exposure.
- Promote predictability and stability through greater transparency in the timelines, costs and licensure in a development of a vaccine.
- Globalize vaccine markets by focusing on regulatory harmonization.
- Look at the pros and cons of standardization of vaccine products.

On Financing
- Translate value of vaccines into political terms to ensure long-term funds.
- Set up GAVI and UNICEF as a revolving fund to ensure long-term funding.
- Improve capacity and infrastructure of developing countries to purchase vaccines through a series of incentives/aid from the U.S.
- Identify mechanisms between Ministries of Health and Donors to ensure long-term financial reliability.
- Create a public and private sector discussion on procurement, factoring the role of competition, the importance of international forecasts, and supply.
Carol Bellamy, executive director of the United Nations Children’s Fund (UNICEF) and chair of the Global Alliance for Vaccines and Immunization, delivered opening keynote remarks at the October colloquium. UNICEF is the single largest buyer of vaccines for children, purchasing 40% of the global volume of vaccines, worth $261 million.

“Twenty years ago, children in both developed and developing countries received the same basic vaccines and their availability was more than adequate,” she explained. “Today, capacity is a growing source of worry. While a number of new vaccines have been developed, there are fewer vaccine manufacturers. There is also a growing divide between vaccines given to children in developing and developed countries. Children in developing countries still receive the same basic vaccines that children around the world used to get, but those in industrialized countries are now receiving a new, considerably more expensive battery of vaccines.”

Ms. Bellamy described disconcerting changes over the past decade in the global vaccine market. With the introduction of new vaccine products, less profitable older ones become progressively devalued. In this environment, vaccine producers have exited the market, leaving just four World Health Organization-approved manufacturers of basic pediatric vaccines. Also, tiered pricing is less viable when developed countries buy different vaccines than poor countries. Further, the shift to a single-dose preference among high-income country buyers and the required removal of the preservative thimerosal has placed greater demand for capacity in the manufacturing infrastructure.

She noted that domestic and international manufacturers and buyers face common issues regarding the need for long-term planning and commitments, as well as better communication between regulatory bodies, manufacturers and buyers. The long lead times involved in vaccine production and capacity increases make forward planning especially critical.

Touching upon the thematic issues to be addressed by the participants at the colloquium, Ms. Bellamy pointed to remedies to the vaccine market in appropriate returns for suppliers; open, collaborative relationships; and credible and predictable demand.

UNICEF’s principal strategy for ensuring a sustained, uninterrupted supply of affordable vaccines recognizes the need for enhanced accuracy in long-term forecasting of demand; working closely with governments to arrange for firm multi-year funding commitments, and solid future vaccine-supply contracts with multiple manufacturers.

The challenges remaining include overcoming inaccurate forecasting despite underdeveloped health delivery and public health systems, ensuring functional public-private partnership for immunization, and mobilizing producers to make decisions that are driven not only by short-term market gains, but also by long-term concerns for human security.

Ms. Bellamy presented a clear and compelling picture of the challenges facing secure global vaccine supplies.

Kevin Reilly is past president of Wyeth Vaccines & Nutrition and his career in the industry spans 35 years, with exposure to both the North American and international markets during that time. He provided a second keynote talk drawing from experiences in running a vaccine business. His remarks looked at economic issues, problems created by the interaction between demand and supply, and the driving forces on the supply side.

He described that people are genuinely committed to the value of immunization and vaccines, including the business people running the vaccine operations. Their level of dedication is very high, and as a result vaccines and immunization in the 20th century have made an enormous contribution to public health. Another aspect of the vaccine manufacturing picture is economics, inclusive of
Danish Team Explores MMR Data, Finds No Link with Autism

Article Appearing in November Issue of New England Journal of Medicine Reassures Pediatricians and Parents

Findings of an eight-year study of half a million children in Denmark provided added evidence of the safety of the measles, mumps, and rubella vaccine (MMR). The study was reported in the November 7 issue of The New England Journal of Medicine.

Many studies suggesting a link between MMR vaccination and autism were based on case-series, cross-sectional studies rather than a population-based cohort design. Danish epidemiologists, however, designed a follow-up study of all children born in Denmark between 1991 and 1998. A unique administrative system in that country provided the researchers with extensive civil registries including birth and hospital records. Through the use of personal identification numbers, they were able to trace those children born during this time who were vaccinated against MMR and those who remained unvaccinated. The Danish team then looked at the cohort for incidences of autism between the two groups.

Three strong arguments against a link between MMR vaccination and autism emerged from the study. First, the risk of autism was similar between the two groups, second there were no temporal clusters of autism after immunization and third, neither autistic disorders nor any other related disorders were associated with MMR.

Lead author of the Danish research team responsible for this work, Dr. Kreesten Madsen, provided the following interview with the Sabin Vaccine Report to further comment on the study and its implications.

SVR For those of our readers who are trying to appreciate this issue, can you help us define a few things? For instance, “autism”?

KM The condition we call “autism” is actually a group of developmental disabilities called the autism spectrum disorders (ASDs) that are caused by abnormalities in the brain. ASDs include autistic disorder, pervasive developmental disorder - not otherwise specified (PDD-NOS), and Asperger’s disorder. These three conditions all have some of the same symptoms and share unusual social development as a common feature; but they differ in terms of when the symptoms start, how fast they appear, how severe they are, and their exact nature. ASDs begin during childhood and last throughout a person’s life; however, some individuals may participate in typical community activities as adults.

SVR Do we yet know the causes of autism?

KM No one knows exactly what causes ASDs, but scientists think that both genetic and environmental factors may play a role. Family studies have shed the most light on the genetic contribution to autism. Studies of twins have shown that in identical twins there is about a 3% concordance rate. The risk of autism in siblings ranges from 2 to 6 percent. And in families with autism, there are often other developmental problems as well, such as language delays or learning disabilities. The inheritance pattern is complex and suggests that a number of genes are involved. Autism also tends to occur more frequently than expected in individuals with certain other medical conditions, such as Fragile X syndrome, tuberous sclerosis, congenital rubella syndrome and untreated phenylketonuria (PKU). Some harmful substances taken in pregnancy also have been associated with an increased risk for autism, specifically the prescription drug, thalidomide. We do know that parents do not cause ASDs in their children. In the US, the Children’s Health Act of 2000 directed CDC to establish regional centers of excellence for ASD and other developmental disabilities.

SVR When does autism begin and what are the first signs of autism?

KM Children with ASDs develop differently from other children, but it is often difficult to see signs of an ASD dur-
ing the first year of a child’s life. Children without disabilities develop at about the same rate across areas of development such as motor, language, cognitive, and social skills. Children with ASDs develop at different rates in different areas of growth. They may have large delays in language, social, and cognitive skills, while their motor skills may be about the same as other children their age. Most children with autism have delayed development from birth, such as delays in developing language skills or an inability to interact with other people, but maybe a third of children with autism seem to regress, that is develop normally then lose skills.

SVR Is autism on the rise?

KM Few researchers have been able to look at autism trends over time because they haven’t been able to monitor the number of people with autism in a specific area on an ongoing basis. But, in Europe, including Denmark, and elsewhere outside the US, the more recent prevalence rates suggest a higher rate of autism than previously thought. We don’t know how much of these higher rates are due to a real increase in autism or due to other factors related to identifying children with autism. We do not know if ASDs are becoming more common in the United States. We do not know that more children are being identified as having an ASD.

SVR Now can you describe the MMR vaccine?

KM The MMR is a combination vaccine that protects children from getting measles, mumps and rubella. The Danish vaccination program recommends that the first dose is given between 12 and 15 months of age because vaccination before 12 months does not generate sufficient immunity to protect against infection. Delaying vaccination unnecessarily leaves children at risk for these vaccine preventable diseases.

SVR What record of safety does the MMR vaccine have?

KM The MMR vaccine has an excellent safety record. It does commonly cause minor reactions, and rarely more serious reactions. Most reactions result from vaccine virus infection, 6-12 days after immunization. The measles vaccine virus infection causes fever, rash and/or conjunctivitis, and affects 5-15% of the children vaccinated. The rubella vaccine may cause similar local reactions on the injection site as mumps and measles. Mild systemic reactions may also occur with the use of rubella vaccine. Those vaccinated sometimes develop a mild case of the disease that includes fever, rash, lymphadenopathy, sore throat and headache. Also rubella may be associated with joint symptoms. However, such adverse reactions are very rare in children receiving MMR vaccine (less than 1%). When combination vaccines (MMR) are used, both mild and severe reactions are similar to those described above.

SVR What are the benefits of the MMR vaccine?

KM Vaccines are the best possible protection against measles, mumps and rubella. In an outbreak, the unvaccinated child runs a much higher risk of disease than those who are already vaccinated. This risk of disease vastly overshadows the small inconvenience and extremely small risks associated with the vaccination. As it takes several days to achieve the protective effect from a vaccination, it may be too late to immunize when the first cases of a disease occur in your environment. Besides, with high vaccination coverage in a popula-

tion, new outbreaks of the disease become more and more unlikely. A coverage rate of 80-90% may in some cases suffice to eradicate the disease. Hence, by vaccinating you are not only protecting your own child, but even adding to the protection of the population at large. I think, that we in this debate have forgotten how serious a disease Measles is. Measles causes pneumonia (1 in 20), encephalitis (1 in 2,000) and death (1 in 3,000 in industrialized countries - as much as 1 in 5 in outbreaks developing countries). I certainly won’t hesitate to vaccinate my children.

SVR What is the logic that is used to draw a hypothetical link between MMR vaccine and autism?

KM In general terms, the hypothesis states that MMR-vaccination leads to a nonspecific intestinal injury that leads to the absorption of certain molecules produced in the gut, which then leads to damage to the brain and causes autism and other serious developmental disorders.

SVR Did you set out to test this hypothesis?

KM A number of scientific studies have looked at the MMR vaccine and autism but none have found evidence to support the idea that MMR vaccine causes autism. However, because of some limitations in these other studies, the seriousness of autism, and the great public concern, we decided to carry out our study. The public concern follows from two sources: first, there have been case reports of patients with inflammatory bowel conditions and regressive developmental disorders, mostly autism, that appeared to begin after MMR vaccination. Because the first signs of autism are often noticed by parents around the same time that the MMR vaccine is given, this may make parents worry that the MMR vaccine caused autism.
ond, it has been suggested that the apparent rise in autism coincides with a rise in MMR vaccine coverage.

**SVR** Have other studies been done on MMR vaccine and autism?

**KM** Some epidemiological studies have tried to evaluate the connection between MMR vaccination and autism. None of the studies support an association.

**SVR** How is your study different/better than the previous studies?

**KM** The Danish study is by far the biggest study performed so far. It included about a half million children and more than 700 autistic children. It thus had sufficient power to examine a possible connection between MMR vaccination and autism. Furthermore, the Danish study used a population-based cohort design. That type of design is superior to the designs that have been used to evaluate the hypothesis so far. In this study all children born in Denmark from January 1991 through December 1998 were included.

**SVR** Why was Denmark a good place to do this study?

**KM** In Denmark it is possible to do very large studies based on the whole population. This is due to the extensive use of administrative registries that contain information on all citizens throughout their lives, including information on health and illness, medical care and life styles. These different registries can also be linked very accurately with the use of a unique personal identification number that is used by all the registries. So, by linking information on thousands, or millions, of people over time makes it possible to do large studies even of relatively rare health conditions such as autism. Another reason why Denmark was a good place for this study was that the vaccination coverage in Denmark has been rising in recent years but our study still had an unvaccinated group of almost 100,000 children. This made it possible to compare vaccinated and unvaccinated children, which was not possible in previous studies in which very few children were unvaccinated.

**SVR** Could there still be some children who could be harmed by the vaccine?

**KM** In general the Danish study has shown that MMR vaccination does not increase the risk of autism. However, it has been speculated whether a small vulnerable subgroup could exist. In the Danish study, the fact that the risks for autism were the same between the vaccinated and unvaccinated children, regardless of the different ways that it was looked at, and that the study was very large, does not support the idea that a subgroup of vulnerable children exists. However, further studies into the causes of autism, like what we are doing here and what is being done in the U.S., will help answer some of these important questions.

**SVR** How do you explain the onset of symptoms of autism at the same time that the MMR vaccine is given?

**KM** Although most children with autism have delayed development from birth, it is often difficult to see signs of an ASD during the first year of a child’s life. The development of normal social and communication skills and normal behaviors in infants and children is a complex process and takes place over a long period of time. As the skills that parents expect their young children to have become more complex, such as beginning to say simple words around a year or so of age, then the problems that autistic children have may become more obvious to their parents. These first signs of autism are often noticed by parents around the same time that the MMR vaccine is given.

**SVR** How many children were included in your study?

**KM** About 500,000 (537,303 to be exact)

**SVR** How common is autism in Denmark?

**KM** The prevalence of autism in Denmark is around 3 /1,000 children in eight year olds. That means that when children are eight years old 3 out of 1,000 will be diagnosed with autism.

**SVR** What message do you have for parents of children of vaccine-age? For doctors, pediatricians and health care providers of children of vaccine-age?

**KM** The Danish study of about a half million children showed that MMR vaccination did not increase the risk for autism. The current scientific evidence, based on this study and others, does not support the hypothesis that measles-mumps-rubella (MMR) vaccine, or any combination of vaccines, causes the development of autism, including regressive forms of autism.

The question about a possible link between MMR vaccine and autism has been extensively reviewed by independent groups of experts in the U.S. including the National Academy of Sciences, Institute of Medicine (IOM). These reviews have concluded that the available epidemiologic evidence does not support a causal link between MMR vaccine and autism. The IOM committee also did not suggest any need to change the current U.S. vaccination schedule for MMR. However, because of some gaps in the scientific evidence, the IOM committee also recommends further research because of the seriousness of the diseases prevented by the vaccine and the seriousness of autism.

The Danish study aimed at providing some of that lacking scientific evidence.

**SVR** Who paid for your study?

**KM** We received grants from the Danish National Research Foundation, the National Vaccine Program Office and National Immunization Program in the US, and the National Alliance for Autism Research, a private organization also in the U.S.

**SVR** Thank you Dr. Madsen.
Sabin Vaccine Institute Scientist Recognized with Top Panamanian Honor

Award Presented in Appreciation for Collaboration on Tropical Medicine Center

Dr. Allan L. Goldstein of the Sabin Vaccine Institute, headquartered in New Canaan, Connecticut, received Panama’s highest national honor during a visit to that country earlier this month. The decoration as “Commander” in the Order of Vasco Nuñez de Balboa was presented to Dr. Goldstein at an awards ceremony on December 6 in Santiago, Panama.

Dr. Goldstein is a board member of the institute and also is chairman of Biochemistry and Molecular Biology at The George Washington University (GW) in Washington, D.C. The Panamanian government cited Dr. Goldstein’s valuable contributions and personal dedication in the performance of his profession dedicated to the preservation of human life throughout the world.

The medal was presented at the inaugural scientific meeting of the President Mireya Moscoso Center for Geographic Medicine and Emerging Tropical Diseases, which is a collaborative project of Panamanian and U.S. institutions. The international center is directed by Peter Hotez, MD, PhD, Sabin Scientific Advisory Council chairman and chairman of Microbiology and Tropical Medicine at GW.

“I am humbled by the great honor you have given me today,” said Dr. Goldstein. He dedicated the award to the thousands of young students and scientists from both countries whose health research efforts do not gain such attention. “These young people are my heroes and our future and I am hopeful that the scientific and medical center we are developing here in Panama will make a difference in the training and education of these young scientists and clinicians and help them to do their work.” he said.

Drs. Goldstein and Hotez are working with U.S. colleagues from GW, University of Texas Medical Branch, Texas Children’s Hospital, and Case Western Reserve University School of Medicine, along with those of Panama’s Chicho Fabria Hospital, the Central Regional University of Veraguas, the University of Panama and the Gorgas Medical Center in developing this new center for geographic medicine in Panama. The international collaboration that established the center has the strong support of Panamanian President Mireya Moscoso, who is committed to improve the health of the citizens of Panama. A goal of the partnership is to create the premier center for the study of tropical diseases.

Dr. Jose Miguel Alemán, Panama’s Minister of Foreign Affairs, presented the award. Dignitaries at the ceremony included Dr. Fernando Gracias, Panama’s Minister of Health, and Panama Special Ambassador Dr. Adán Rios. The honor given Dr. Goldstein carries the title Knight-Commander, is named for the Spanish explorer who trekked through the jungles of what is now Panama in 1513 to become the first European to see the eastern shore of the Pacific Ocean. The award has been given since 1941 to citizens and friends of Panama who have made significant scientific or artistic contributions to the country.

In Santiago, Panama, at the presentation ceremony are, from left, Dr. Fernando Gracia, Panama’s Minister of Health, Dr. Allan L. Goldstein, recipient of the Order of Vasco Nuñez de Balboa, and Dr. Jose Miguel Alemán, Panama’s Minister of Foreign Affairs.
Dakar, Senegal, was the venue for the Second Partners’ Meeting of the Global Alliance for Vaccines and Immunization (GAVI) on November 20-22. Representatives from international organizations, developing country governments, industry, research institutions, and philanthropy gathered to review strategies and lay plans for their shared assault on global diseases.

GAVI was formed two years ago as a public-private partnership to address worldwide concerns in disease control. GAVI and its financial arm, the Vaccine Fund, invited the world’s 75 poorest countries to submit proposals for immunization financing.

Of these, 55 countries have already received vaccines or cash support with a total value of $130 million, while others have proposals pending. GAVI’s award commitments total $900 million to date. The Vaccine Fund was established with $750 million from the Bill & Melinda Gates Foundation, supplemented by grants from the governments of the United States, the Netherlands, Norway, the United Kingdom, Canada, Denmark, and Sweden, as well as private donors.

The first priority identified by GAVI is for every country to boost immunization rates of the “basic six” vaccines: diphtheria, tetanus, pertussis, polio, measles, and BCG. Once a country has achieved 50% coverage rates with these vaccines, it is eligible to apply for assistance with other vaccines such as yellow fever, hepatitis B, and Hib.

During the Dakar meeting, UNICEF executive director and GAVI chair Carol Bellamy argued that expanding immunization coverage is the best investment the world can make. “Vaccines are among the most cost-effective public health interventions. Today, no child should die from a vaccine-preventable disease. We need to invest more—and more rationally—in vaccine coverage and research, and ensure access in all corners of the globe.”

Representatives of participating Ministries of Health and Ministries of Finance signed the Dakar Declaration, a statement committing their countries to the implementation of Financial Sustainability Plans for immunization, and calling upon all governments to recognize that “immunization and the sustainability of immunization is a national priority, a global concern and a shared responsibility.”

Advocacy was stressed as a key component of a minister’s job. Ministers of Health shared tips with each other on how to lobby for immunization financing within their governments, and Ministers of Finance responded with their perspectives on what kind of “sales job” it takes to loosen government purse-strings.

Social mobilization is equally important. An unusual example was seen in the efforts of Bhutan’s Minister of Health, Dr. Lyonpo Sangay Ngedup. Participants watched a film documenting his 15-day, 560-kilometer trek across this small Himalayan kingdom to raise awareness of immunization and public health and to promote the Bhutan Health Trust Fund. He collected two million dollars in donations, mainly from domestic sources in this cash-strapped country. Dr. Ngedup emphasized that even aside from the money raised, his walk impacted thousands of people’s lives with messages as simple as the value of hand-washing. He believes that even a country with a small gross national product can achieve a large “gross national happiness.”

But every country faces unique challenges. Afghanistan provides a case in point. Dr. Suhaila Siddiq, the new Health Minister of Afghanistan, brought two urgent requests to the GAVI leadership:

First, she explained that her country, while already approved for assistance in the “basic six” vaccines and approaching the 50% immunization benchmark, is suffering an epidemic of hepatitis B. She therefore asked for accelerated approval for hep B vaccination support.

A second problem is the administration of GAVI funds in a war-torn country like hers. Currently, GAVI investment in Afghanistan is channeled through UN...
agencies. Dr. Siddiqi felt that vaccines could be delivered with lower administrative costs if the assistance were channeled directly to the Health Ministry. In reply, GAVI executive secretary Dr. Tore Godal said that GAVI would consider her request, but a non-governmental organization such as UNICEF would still be needed to reach populations living in rebel-held zones outside the government’s control.

The worldwide polio eradication campaign has been central to GAVI efforts and received close scrutiny at the meeting. Delegates debated whether it would ever be feasible to stop polio immunization, and how the campaign infrastructure could be applied to a stepped-up measles control initiative. Some delegates argued that the emphasis on polio eradication had come at the expense of more pressing disease problems in their countries and argued for more flexible approaches.

There were impassioned pleas for more research toward malaria and AIDS vaccines. The prospects for future vaccines were discussed in a breakout session, while other sessions examined issues such as the regulatory process for new vaccines and logistical problems in vaccine delivery.

Also released at the meeting was the report *State of the World’s Vaccines and Immunization*, a joint publication of the World Health Organization, UNICEF and the World Bank. This is a long-awaited update of the first edition published in 1996. The report examines the progress made in the field of immunization and presents the remaining challenges of the access gaps and emerging and neglected diseases. It also outlines the vaccines research agenda for the 21st century, including the expanding role of alliances between the public and private sectors. It is available free of charge from UNICEF in English, French, or Spanish; ISBN: 92 4 154578 X. Email requests to pubdoc@unicef.org. It also can be downloaded from www.unicef.org.

—by David Bedell

David Bedell, Sabin Vaccine Institute, left, with Dr. Yankuba Kassama, Gambian Minister of Health.
An age in when the media uncovers more about politicians and government officials than we may necessarily want or need to know, when little goes unrecorded, unreported or unanalyzed, it’s hard to imagine that the death of Franklin D. Roosevelt was a shock to a nation during one of the most pivotal moments in U.S. history. Despite his iconic status, President Roosevelt, at 62 years old, was deathly ill – a fact that was carefully shielded from the American public during the election of 1944.

In *The Hidden Campaign*, a study 10 years in the making, Dr. Hugh Evans explores the efforts to conceal the truth about Roosevelt’s declining health from the American public, the world—even from some of his own staff. Dr. Evans takes a medical ethics perspective of FDR’s 12 years in office, with a focus on the wartime pressures and politics that pushed him into a fourth campaign, compromised his health, and ultimately led to his death.

“There was ignorance, denial, a deliberate campaign of misinformation, and a level of medical treatment below what would have been provided another citizen,” Evans explains. “The medical history of Roosevelt offers paradoxes, enigmas, and conflicts which parallel, and are interwoven, with the larger tapestry of his presidential career.”

In this comprehensive study of one of the most loved and iconoclastic leaders of the 20th century, Evans points out the extent to which modern medicine fails in the context of extraordinary celebrity and national need. Drawing on the medical notes of the physician treating Roosevelt at the time, and in-depth interviews with FDR’s cardiologist as well as other key figures and confidants of the World War II era, *The Hidden Campaign* reveals fascinating new insights into one of the most successful cover-ups in U.S. history.

Evans goes on to explain the impact and relevance of FDR’s administration today, calling into question the role of the White House physician, with an emphasis on how full, timely disclosure by neutral, nongovernmental physicians is nothing short of imperative in the nuclear era, particularly in light of recent events.

“The scenario that played out across the nation and the world sends a clear warning for the future,” says Evans. “The public’s right to know the facts of high-risk illness in a chief executive should be paramount, transcending the ‘privacy rights’ of the president or presidential candidate. While events evolved favorably in 1944-45, the potential consequences of future cover-ups are likely to be more devastating.”

The Presidency is a “killing job” for its occupant. On average, presidents die much earlier than their counterparts in the general population. Critics have always charged that in 1944 the Democrats ran a dead man whose health undermined negotiations with the Soviets on the postwar world order at Yalta in early 1945, the year of the President’s death. This volume makes it clear that FDR boasted excellent health at least during his first two terms and that he generally enjoyed himself until the end, despite suffering from serious hypertension. Evans points out that both the presidential and vice-presidential candidates on the 1940 Republican ticket, seemingly in robust health, died in 1944.

—review by Veronica Korn

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About The Author

Hugh Evans, M.D., author of *The Hidden Campaign*, is a well-known clinician, educator, researcher and administrator whose career spans four decades. He has published over 140 peer-reviewed articles, a medical textbook, and numerous abstracts. As a grand rounds speaker, he has been an associate director, director and chairman of academic departments. Dr. Evans has served on numerous regional and national committees, and has chaired a committee of The American Academy of Pediatrics. His research on the medical history of FDR, which represents a decade of focused study, has been presented to numerous professional and community groups and noted on television.
The Vaccine Education Center at the Children’s Hospital of Philadelphia (CHOP) has introduced a new parent education resource entitled Vaccines and Your Baby, a 28-minute video designed to answer frequently asked questions about immunization. The video covers common questions including how vaccines are made, how they protect against disease and how they are regulated and tested for safety. A parent handbook accompanies the video and outlines major childhood illnesses, which are now preventable through the miracle of vaccines.

Paul A. Offit, MD, chief of Infectious Diseases and director of the Vaccine Education Center at The Children’s Hospital of Philadelphia, says “Well-documented scientific evidence overwhelmingly supports the protective qualities of vaccines, yet some parents resist immunization for their children. For parents to make the best decisions about their children’s health, it is essential they understand the nature of vaccines and how they work, the diseases they prevent and why it is so important to immunize against diseases. Parents will be reassured when they learn of the rigorous testing and evaluation involved in the development of the vaccines to make them safe.”

According to Dr. Offit, a decision not to have a child vaccinated presents much greater risks and therefore, Vaccines and Your Baby includes vignettes about the adverse outcomes for families who did not have their kids immunized based on misperceptions about vaccine safety.

With many once-common childhood disease now virtually eliminated and widely unseen, substantial numbers of parents today question whether particular vaccines are still necessary. Many times these doubts are fueled by inaccurate or scientifically questionable information.

The Children’s Hospital of Philadelphia founded the Vaccine Education Center in 2000 to educate healthcare professionals and the public by providing complete, up-to-date, science-based information about vaccines and the diseases they prevent.

Pediatricians may obtain their first two copies at no charge and subsequent copies for $5 each; others may purchase the video for $5 by emailing vaccines@email.chop.edu or calling CHOP at 215-590-9990.

### Institute Volunteer Appreciation

Volunteers provide welcome assistance at the Vaccine Institute headquarters. Recent volunteers include:

- Brett Wasserman, Port Chester, New York, who solved a number of computer problems and wired computer networks.
- George Holland, Danbury, Connecticut who lent a hand to update the Library Files Database.

Thank you Brett and George! Anyone interested in volunteering in the New Canaan office can contact Vanessa Santiago at 203-972-7907 or vanessa.santiago@sabin.org.

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Save the Date

**Wednesday, May 14, 2003**

**Sabin Vaccine Institute Annual Awards Dinner**

**The Pierre Hotel**

**New York City**
money for both producing vaccines and discovering new and improved vaccines.

“Vaccines are difficult,” Reilly said. “Vaccines have more production problems than any other category in any pharmaceutical or medical area. You are working with biological processes, not with chemical processes, and it is just a tougher activity to manage.”

Mr. Reilly placed security of vaccine supply and price in the context of the past 30 years. Business decisions in the industry have during that time been governed according to three thresholds: an operating level, a capital level, and a discovery level.

To illustrate this point, he suggested that the threshold for operating a vaccine manufacturing operation at a given capacity of production might not be exceeded under circumstances as normal production and perhaps with tiered pricing. However, if called upon to invest in new facilities or to make expensive innovations, the threshold could be exceeded. Far more market return would be warranted if capital investment would be required to increase capacity or for mandated regulatory requirements. Such thresholds govern the vaccine manufacturing business and guide business decisions.

With a measure of reassurance, Reilly explained that every company confronting a decision whether or not to discontinue a product, be it a pharmaceutical or a vaccine, will assess if there is a medical need that will be left unmet. “If you have a marketplace for vaccines that is not huge, I am not sure you can expect to see three or four suppliers in there, all fighting for a share of that,” Reilly said. “So, in a way, with old product it is not very surprising to see a reducing number of suppliers.”

Reilly suggests that despite consolidations among the vaccine manufacturers supplying the global market, a core of companies that are committed to vaccines have kept most production facilities operational. These companies, however, are dealing with economics and dynamics of manufacturing vaccines that have changed.