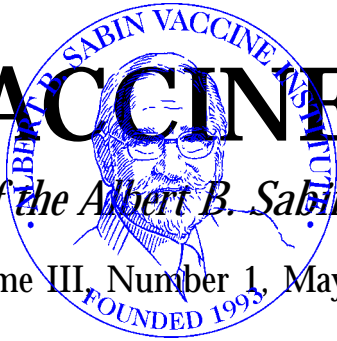


SABIN VACCINE REPORT

the newsletter of the Albert B. Sabin Vaccine Institute

Volume III, Number 1, May 2000



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Gates Foundation Awards \$18 Million to Sabin Institute Funds Awarded for Development of Hookworm Vaccine

JOHN M. CLYMER

The Albert B. Sabin Vaccine Institute has received an \$18 million grant from the Bill & Melinda Gates Foundation. The funds will be used for the development of a vaccine to prevent hookworm infection. Approximately one-quarter of the world's population is infected with hookworm.

"This grant from the Bill & Melinda Gates Foundation represents enlightened philanthropy because it will help us over the major economic barriers that have prevented development of a hookworm vaccine," said H. R. "Shep" Shepherd, chairman of the Sabin Vaccine Institute.

"This is a huge step toward democratizing health care throughout the world," said Shepherd. "Hookworms infect about one billion people, mostly in developing countries. They stunt children's growth, sap victims' energy and make them anemic. A

vaccine is the only realistic way to protect all people from this parasite."

Peter J. Hotez, called "one of the world's few hookworm experts," in a 1998 *Washington Post* article, will be the principal scientist directing the project. He is a member of the Institute's council of scientific advisors.

"Hookworm is a particularly serious problem in rural China. In some villages, more than one half of the population is infected," Hotez said. He frequently visits remote areas of China to conduct research as a visiting professor at the Chinese Academy of Preventive Medicine's Institute of Parasitic Disease and the Peking Union Medical College. The parasite is estimated to be similarly prevalent in India, and is a major health problem in certain Latin American countries, as well.

"Hookworms infect people of all ages but they are particularly devastating in children," explained Hotez. "Chronic hookworm-associated intestinal blood loss leads to iron deficiency and protein malnutrition. These conditions often retard intellectual and physical growth," according to Hotez. People who are treated for hookworm tend to become reinfected, he added.

No single sector – academia, government, industry or philanthropy – can develop a vaccine alone, Shepherd noted. The Sabin Vaccine Institute

will draw on expertise and resources from each sector to translate scientific knowledge about hookworm antigens into a real product that helps people lead healthier lives, he said.

"We are proud to support the Albert B. Sabin Vaccine Institute and its quest to find a hookworm vaccine, which will free millions of the world's most economically disadvantaged

people from this disease," said

Gordon W. Perkin, M.D., director of the Global Health Program at the Bill & Melinda Gates Foundation.

The Sabin Vaccine Institute's mission is to save lives by stimulating development of new vaccines and by increasing immunization rates. It was founded in 1993 and named for Albert B. Sabin, developer of the oral polio vaccine that has been at the heart of the nearly-complete worldwide effort to eradicate paralytic polio. This is

the Institute's first research and development program. Other Institute programs bring scientists together to share cutting-edge ideas and data to accelerate vaccine development, and advocate sound immunization strategies to combat disease.

The Bill & Melinda Gates Foundation is dedicated to improving people's lives by sharing advances in health and learning with the global community. Led by Bill Gates' father, William H. Gates, Sr., and Patty Stonesifer, the Seattle-based Foundation has an asset base of approximately \$21.8 billion. Preventing disease among poor children by expanding access to vaccines, and developing vaccines against malaria, HIV/AIDS and tuberculosis, are central priorities. Other major efforts include extending unprecedented opportunities for learning by bringing computers with Internet access to every eligible public library in the U.S. and Canada, and providing scholarships to academically talented minority students with severe financial need through the Gates Millennium Scholars Program. ❖

John Clymer is director of external affairs for the Albert B. Sabin Vaccine Institute.

For complete information and grant guidelines visit www.gatesfoundation.org.



Dr. Peter Hotez visits children at a health clinic in Beijing.

photo compliments of MHL

Doubting Vaccines Is Dangerous Business



photo by Beth Shepherd Peters

**H. R. Shepherd,
Chairman of the Sabin
Vaccine Institute**

unfounded; in fact, smallpox has now been eradicated. Yet after two centuries of success against a host of crippling and fatal diseases, vaccines are under attack from unwarranted fears once again.

Recent television, print and radio news stories in the United States, along with a growing number of Internet sites, are claiming vaccines are dangerous or even fatal. In response to rumors that vaccines are the catalysts of such wide-ranging disorders as autism, asthma and diabetes, some parents have begun questioning the wisdom of vaccinating their children. These fears are both strange and perilous. They are based not on reality or scientific evidence but on ignorance and, in many cases, the need to find a medical scapegoat when the unexplainable occurs. Those who allow themselves to be ruled by these baseless misconceptions risk undermining one of humankind's greatest medical resources. As Goethe warned, "Nothing is more dangerous than ignorance in action."

In this case, ignorance could bring irreparable harm to us all.

Before the development of a measles vaccine in the 1960s, there were some 500,000 cases each year, and thousands died

from the disease. By 1998 there were only 1,000 diagnosed cases and none of those cases were fatal. In 1968, there were more than 150,000 cases of mumps in the U.S. but by 1993, there were just over 11,500.

Vaccines have reduced infection and death from the flu by 54%. And thanks to vaccines, there has not been a single case of polio in the United States since 1975. Cholera, typhoid, German measles, whooping cough and diphtheria are only a sampling of the diseases that vaccines currently control in the U.S.

In all, vaccines have protected countless millions of lives - including yours and mine - from once-common killers. The fact is vaccines are one of the safest and most effective medical interventions of our time. Moreover, they are one of the most economical; today, every dollar spent on vaccines saves \$27 in treatment.

Unfortunately, the very success of vaccines has caused a dangerous outbreak of complacency and misunderstanding. Many of today's young parents have never encountered the diseases their children's inoculations prevent and consequently believe these horrors couldn't possibly return. Meanwhile, preventable killers such as measles, pertussis (whooping cough) and hepatitis B lurk patiently in the shadows - poised to make a widespread comeback should immunizations decline.

If we are to keep infectious diseases at bay, we must eliminate the notion that they no longer pose a serious threat. Every year in the United States, approximately 70,000 people - including 500 children - die unnecessarily from diseases that could have been prevented by existing vaccines. That's one person every eight minutes. Throughout the world, millions of people die annually from vaccine-preventable diseases.

Too often, these deaths occur because other countries' restrictive or bureaucratic policies make vaccines unavailable to their citizens. The United States works hard to help remedy this problem, but if our own citizens begin to doubt vaccines, we could initiate a dangerous chain reaction around the world. And if the number of unvaccinated children begins to grow, the worldwide benefits of immunization will rapidly erode - causing preventable illnesses to proliferate globally.

This has already happened in the past. In the 1970s, rumors associated with a pertussis vaccine lead to a drop in vaccination rates in several countries and a consequent rise in the prevalence of the disease. We must not make the same mistake again. As we enter the 21st century, vaccines are poised to play an increasingly central role in our future, saving millions of lives each year while dramatically cutting health care costs. On the near horizon, a new vaccine awaiting FDA approval promises to protect children from pneumonia and meningitis. And in the years to come, vaccines could conquer some of our century's worst scourges - malaria, dysentery, AIDS and even some cancers. However, a misinformed public outcry could delay this exciting progress and cost countless lives.

Despite early fears, vaccines never did endow people with the qualities of cows. Let us not be cowed today by the latest crop of vaccine myths. We must spread the facts - not ignorance - so that humankind will continue to enjoy the benefits of our greatest medical miracle.

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

The *Sabin Vaccine Report* is published by the Albert B. Sabin Vaccine Institute.

Subscriptions are free.

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The Albert B. Sabin Vaccine Institute is a non-profit institute dedicated to continuing the work and achieving the vision of Albert B. Sabin: to fully realize the potential of vaccination to prevent disease. Founded in 1994, the Institute strives to prevent disease by promoting the development of new vaccines and delivery systems.

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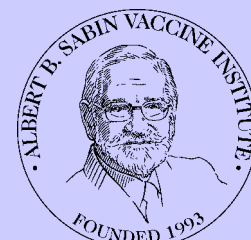
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Combination Vaccines Minimize Pain; Save Money

BY VERONICA KORN

Infant immunization schedules requiring several inoculations during each doctor's visit may become a thing of the past as more combination vaccines are developed and approved. A combined vaccine will have far-reaching affects for global immunization campaigns particularly in developing nations. The availability of a combined vaccine—a vaccine produced from cultures of a number of organisms—simplifies the actual implementation of inoculations, by enabling a single injection for application of multiple vaccines. Combination vaccines minimize pain and discomfort, cost and time; and would maximize successful immunization programs by increasing compliance.

The DTP (diphtheria pertussis polio vaccine) was among the first of such combination vaccines, being developed in 1943, and licensed for use in the US in 1948. This and others are commonly used in doctors' offices and hospitals, namely the MMR vaccine against measles, mumps and rubella (manufactured by Merck), and the DTaP vaccine against diphtheria, tetanus and pertussis (multiple manufacturers). Currently, North American Vaccines and Wyeth Vaccines and Nutrition are concentrating on further increasing the coverage in combination vaccinations to protect against up to five, rather than the standard three, childhood diseases at once.

In July 1999, SmithKline Beecham (SB) submitted a license application to the United States Food and Drug Administration (FDA) for a new combination vaccine against diphtheria, tetanus, pertussis, hepatitis B and polio. While the much used DTaP combined vaccine has existed for some time, the SmithKline product, called *InfanrixDTaP+HepB-IPV*, would now protect against five major childhood diseases and reduce the number of shots required for effective immunization from nine to three. U.S. SmithKline

spokesperson Carmel Hogan during a telephonic interview recently, said that should the FDA approve this vaccine, it would be the first pentavalent vaccine licensed in the country. The company already has had success with other combination vaccines such as *Twinrix*, for Hepatitis A and Hepatitis B, as well as *Infanrix*, the DTaP inoculation, which the FDA approved in 1997. Hogan said the success of these vaccines has largely led to a greater concentration within SB on combination vaccine development.

Valerie Manda, a medical microbiologist from the Medical University of South Africa (MEDUNSA) in Pretoria, South Africa Combination vaccines will increase compliance because they will minimize multiple shots. "Combination vaccines will increase compliance because they will minimize multiple shots. It's good for technology to go ahead...progress, but basic problems still need to be conquered." Amongst these problems, Manda cited accessibility to vaccines and vaccination clinics. In poorer countries, she noted, simple situations

such as staffing issues in clinics and basic poverty often prevent the population from receiving vaccines.

Preliminary randomized studies on over 7,000 children in the U.S. for a total of 20,000 worldwide show the combination vaccine to be as safe, efficacious and immunogenic as the monovalent vaccines. Although combination vaccines such as the SKB pentavalent require just one inoculation per visit, the pentavalent vaccine would still be repeated on the childhood immunization schedule at two, four and six months of age, said Hogan.

When asked about individual vaccines and the future of companies who manufacture them, Hogan said those vaccines will still be needed as booster, or supplemental, shots for both children and adults. SB has other combination vaccines in Phase three of development (see fig. 1). These include an MMR-Varicella, measles, mumps, rubella and chicken pox in phase IIIa and hepatitis A + *Salmonella typhi* in phase IIIb. ❖

Veronica Korn is a Research Associate at the Sabin Vaccine Institute.

OTHER COMBINATION VACCINES

<i>Twinrix</i>	Hepatitis A+B	SmithKline Beecham	Marketed
<i>Tetracel</i>	Diphtheria, Tetanus, Pertussis, Hib Disease	Wyeth-Lederle (American Home Products)	Phase II
<i>Certiva</i>	Diphtheria and Tetanus Toxoids, Acellular Pertussis Vaccine Adsorbed	North American Vaccines	Marketed
<i>Unnamed</i>	MMR+Varicella	SmithKline Beecham	Phase III

SOURCE: SmithKline Beecham PLC, American Home Products, North American Vaccines

Experts Recommend New Flu Vaccine For Next Season

BY JESSICA QUINN

The rising temperatures and blooming flowers not only signal the beginning of spring, but also the end of the flu season. Very early this season between December 25, 1999 and January 15, 2000, many people contracted the flu. This early peak in the season sent many scrambling to get flu shots for fear this was to be the worst flu season yet. Statistics compiled by the Centers for Disease Control show, however, that this year was not much different than previous years. The flu vaccine effectively preempted what would have been the worst flu season yet. "Epidemic" flu rates and hospital visits linked to the flu were fairly comparable to the last five seasons.

According to the CDC, deaths from pneumonia or those directly linked to influenza were only up 2 percent to 11.2 % during the last few seasons. The flu season lasts from October until February.

According to the Mortality Reporting System (MRS), the highest percentage of patient visits for influenza-like-illness (ILI) and patient deaths occurred in January. One

hundred and twenty-two cities contribute to the MRS data, reporting the number of deaths attributed to influenza or pneumonia. Both MRS and the State and Territorial Epidemiologists Report are part of the Centers for Disease Control's (CDC) influenza surveillance system. By this system the CDC aims to determine the strains of flu viruses circulating and monitors their effects on the United States population.

Last year's flu season was marked by people who contracted the flu although they had already been vaccinated. Health experts cannot determine whether the strain has grown less effective or whether they received more samples of this population than usual. According to the FDA, each Fall between 60 and 80 million Americans receive the influenza vaccine. Health experts choose the formula they believe will protect the most people from the most common type of the flu virus at least one month prior to the distribution of shots.

Although the flu season is behind us, health officials continue to study the virus and its effects. Work has already begun on developing next season's vaccine for our next flu season

that will counter the strains circulated this winter. The influenza viruses infecting humans and animals are isolated and studied. WHO Collaborating Centers then sequence and identify the categories of the viruses. Each February the results are discussed in Geneva and a recommendation for the composition of the next season's vaccine is made by the WHO. The composition of the vaccine for the Northern Hemisphere's flu season (November 2000- April 2001) has been determined and given to vaccine manufacturers by the World Health Organization (WHO).

In the United States a panel of experts, or Federal Health Advisors, reviewed the WHO findings and recommended a change to the formula for next season's flu vaccine. In March these experts advised the Federal Drug Administration in the United States to replace Type A strain vaccine with a new strain noted in Panama. The type A strain, common last flu season, was first identified on the South Pacific island of New Caledonia. ❖

Jessica Quinn is a Sophomore Biology major and English minor at Georgetown University.

Gary Nabel: Vaccine Research Center Head Rises to Challenge

BY PATRICIA THOMAS

On a muggy Sunday morning in Baltimore, speaking at the graduation ceremony of Morgan State University, President Clinton challenged science to develop an AIDS vaccine within 10 years. To speed this globally important effort, he announced that a



Photo compliments of the NIH.

Gary Nabel directs the nation's first AIDS Vaccine Research Center.

major new AIDS Vaccine Research Center (VRC) would be created at the National Institutes of Health. "If the 21st century is to be the century of biology, let us make an AIDS vaccine its first great triumph," the President said to great applause.

Few would have guessed that nearly two years would pass before Health and Human

Services Secretary Donna Shalala officially announced that physician-scientist Gary Nabel, known primarily as a gene therapy researcher at the University of Michigan, would come on board to lead the VRC.

The long interval between the President's May 1997 announcement and Nabel's hire in March of this year provided plenty of time for loose talk. Many vaccine researchers said that the 10-year goal was overly optimistic; others predicted that the VRC would be nothing more than a cosmetic reshuffling of current NIH researchers and resources. There was no director in sight in August 1998, when the NIH broke ground for the VRC, a five-story building expected to cost \$26-million. Top drug company executives and experienced vaccinologists were said to have turned down the job because the pay was too low, there were too many bosses and too little authority, or the whole idea was nothing more than an empty political gesture.

Gary Nabel walked into this gossipy town square with no visible signs of defensiveness or distress. Whether he's presiding over planning sessions, speaking at large scientific meetings, or meeting with AIDS advocates, he speaks his mind calmly and comes across as a solid, reasonable fellow. He's a tall lean man of 46, losing hair earlier than he would like, with expressive hands that he uses to underline his points. He listens closely to others and is quick to murmur assent when he hears something he likes.

Dark horse from Michigan

NIH Director Harold Varmus first approached Nabel about the VRC directorship in

early 1998. Although he had shepherded experimental gene therapies from the lab to the clinic, and this work was central to him, he knew that these advances could help only a limited number of people. And here was Varmus talking about the search for an AIDS vaccine, something that could potentially save millions of lives throughout the world. It was a tantalizing prospect.

But Nabel could not say yes right away. His wife, Elizabeth Nabel, is a well-known cardiologist with her own laboratory and clinical duties at the University of Michigan, where Gary Nabel himself was director of the Center for Gene Therapy. They have juggled two careers ever since they met as internal medicine residents at a Boston hospital, and it was only after Elizabeth Nabel was offered a position at NIH's National Heart, Lung, and Blood Institute that the Nabels and their children headed east. Nabel says that his favorite leisure activity is being with his family, and he wanted everyone to be happy with the move.

Although an article in *Science* described him as "a relative newcomer to AIDS vaccine work," Gary Nabel is hardly a stranger to HIV research or to the ways of the NIH. Nabel went straight from Harvard College to a joint M.D.-Ph.D. program at Harvard Medical School. "I knew that I wanted to do medicine, but I also wanted to do science," he recalled. "It was something I decided very early on." He studied immunology in graduate school, completed an internal medicine training program in Boston, and in 1985 became a postdoctoral fellow in David Baltimore's virology lab at the Whitehead Institute at the Massachusetts Institute of Technology.

This postdoc put Nabel in the vortex of AIDS research. Baltimore was not only a Nobel laureate, the founding director of the Whitehead, and an expert on HIV and other retroviruses, he was also in the innermost circle of the scientific establishment. In 1986, for example, he chaired a blue-ribbon Institute of Medicine panel that assessed the overall state of AIDS research. His lab launched the careers of many outstanding young scientists, and Nabel was among them. At the Whitehead, Nabel explored how HIV subverts the machinery of T-cells, published impressive papers, and went to seek his fortune in Ann Arbor.

Gaining something in translation

At Michigan, Nabel began to inject foreign genetic material directly into human tumors, in hopes of inducing the patient's immune system to attack the cancer. When preclinical studies showed promise, he arranged for Vical, a San Diego-based biotech company, to package the genetic material in tiny lipid beads called liposomes. (In the world of HIV vaccines, Vical is better known for the DNA vaccine technology it licensed to Merck.)

Nabel soon discovered that moving a radical

new therapy into humans is no easy task. "I wrote the clinical protocol, I wrote the IRB (request to experiment on humans) and the FDA application, we developed the production process, I went down for the IND (Investigational New Drug) meetings with the FDA, I treated the first patient, I even wrote the informed consent," Nabel recalls, sounding glad to have done this but relieved that it's over. "I saw every aspect of what's needed to bring something forward into a clinical study, and I learned from that." This product is now being tested in a Phase III study enrolling patients with advanced melanoma, and in a Phase I trial with head and neck cancer patients.

Bridging the gaps

Although Nabel has never designed an HIV vaccine, his lab is working on a vaccine for Ebola virus. More relevant to the VRC's mission is his "translational" experience with gene therapy. Nabel hopes that the VRC will remove stumbling blocks from the path of vaccine developers. Some vaccine efforts, for example, are stymied when their academic inventors don't have the resources to make test batches. Other ideas languish in the labs of corporate scientists, who must put all their energy into the company's lead technology instead of exploring new approaches.

The VRC will enable vaccine scientists "to see it through," an opportunity that he hopes will lure new talent to the enterprise. Instead of reorganizing long-time NIH personnel, Nabel has the go-ahead to recruit about 100 full time employees, including researchers and support staff. Completion of the Dale and Betty Bumpers Vaccine Research Center, honoring the former Senator from Arkansas and his wife is expected in August 2000, and the facility will provide containment facilities for handling dangerous organisms, a small GLP manufacturing facility for making test batches, and a research group focused on developing assays for clinical trials. These resources can be used to help researchers elsewhere at NIH, in academia, or in corporate settings. The point is to keep promising ideas from withering on the vine.

Research agenda evolving

Nabel and his new scientific team will be closely watched as they set their scientific priorities. Nabel reports to an executive committee of top NIH administrators, including not only NIH director Varmus but also Tony Fauci of the National Institute for Allergy and Infectious Disease and Richard Klausner of the National Cancer Institute. The VRC also answers to an intramural scientific board and to an external advisory committee that will probably be an offshoot of the AIDS Vaccine Research Committee. David Baltimore, Nabel's former mentor, chairs the AVRC.

Fortunately, Nabel is no stranger to the world of NIH committees. He was a member of the NIAID's AIDS Research Advisory Committee from 1993 to 1997, and chaired the group during his final year of service. In 1994, Nabel was among the majority of ARAC members who voted not to expand clinical testing of the recombinant gp120 vaccines owned by Chiron and Genentech (now VaxGen). Over the years he's kept track of candidate vaccines for HIV, and expects the VRC to throw its early support behind combination strategies that appear to elicit both antibodies and CTL-activity. In the long run, Nabel expects good results from DNA vaccines or live vectors.

AIDS VACCINE RESEARCH ENTITIES OF THE NATIONAL INSTITUTES OF HEALTH

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FOR RESEARCH
RESOURCES
DIVISION OF AIDS

OFFICE OF
AIDS
RESEARCH

NATIONAL INSTITUTE OF
ALLERGY AND INFECTIOUS
DISEASES (NIAID)
DIVISION OF AIDS

China Holds First International HIV Vaccine Workshop

BY MYRNA E. WATANABE, PHD

Nabel wants the VRC to play an active role in developing vaccines for the world, not just the United States. Although there are clear genetic differences among HIV subtypes from different parts of the globe, "it's still an open question what these differences mean in terms of immune responses," Nabel said, vowing that the VRC will help back international clinical trials. Africa and other parts of the developing world are suffering mightily from the AIDS pandemic, and the U.S. should support international trials mainly because "it's just the right thing to do."

While the pursuit of a vaccine that can protect millions against AIDS is the central mission of the VRC right now, "I hope that we're going to be developing, as much as possible, a set of rules or lessons that we can apply to other vaccines," Nabel said. There's every reason to expect that new epidemics are waiting in the wings, and Nabel hopes to be better prepared when they step onstage. ❖

Patricia Thomas was editor of the Harvard Health Letter from 1991 to early 1997. Since then, she has been at work on a book about the search for an AIDS vaccine, which will be published in 2001 by Public Affairs. Thomas was among the earliest healthy volunteers to be injected with an experimental DNA vaccine for AIDS, in a National Institutes of Health trial conducted during 1997 and 1998.

On November 18-23, 1999, the National Center for AIDS Prevention and Control (NCAIDS), Chinese Academy of Preventive Medicine, Ministry of Health, and Ministry of Science and Technology of the People's Republic of China hosted their first International AIDS Vaccine Workshop. Nearly 40 foreign scientists and about 70 Chinese researchers, clinicians, government officials, graduate students, and post-doctoral students attended the workshop. The goals of the meeting were to introduce foreign HIV research to Chinese scientists, especially those unable to travel extensively, and to introduce the data China already has compiled on its growing HIV problem to the international scientific community.

The meeting began in Beijing and ended with a trip to Yunnan Province to visit a vaccine manufacturing facility and a primate facility and to meet Chinese HIV patients. The dogged work of Yiming Shao, deputy director of NCAIDS, and his colleagues yielded significant international support. The foreign sponsors included the Joint United Nations Programme on HIV/AIDS, the US National Institutes of Health (NIH), the European Union, the International AIDS Vaccine Initiative, the Henry M. Jackson Foundation, and NIH funds via Harvard University and the University of North Carolina-Chapel Hill.

Chinese epidemiologists estimate that there are 400,000 people infected with HIV in the country. By the end of September 1999, 15,088 cases of HIV infection were identified. As of that date, a total of 240 deaths in China were attributable to AIDS.

HIV was first identified in China in the mid-1980s in hemophilia patients who received contaminated factor VIII (a blood-clotting factor that is given to hemophiliacs), in several foreigners, and in a few (people of Chinese ancestry who live abroad, according to a paper

given by Shao at the meeting. The next group in which HIV was identified was intravenous (IV) drug users in Yunnan Province who injected pure heroin. Cases also were identified along China's coast and in its large cities.

Yunnan, in southwestern China, adjacent to the Golden Triangle region of Myanmar (formerly Burma), currently has the highest HIV infection rate in the country. According to Hehe Cheng of the Yunnan Center for AIDS Prevention, Care and Research in Kunming, 89.3% of the people from Yunnan infected with HIV are IV drug users.

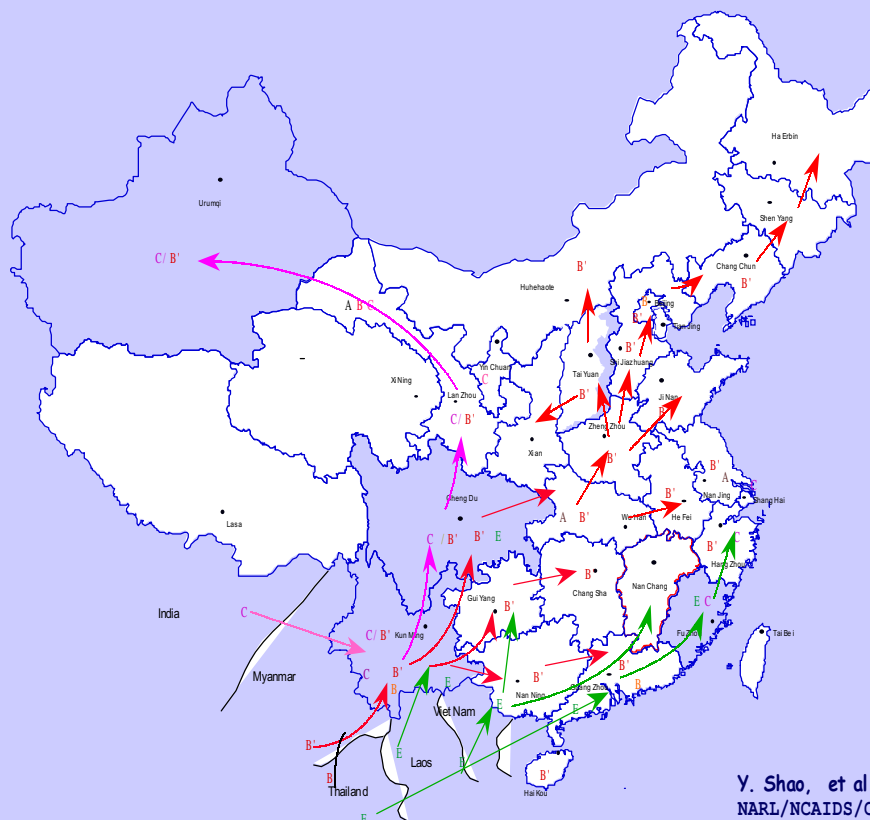
Molecular epidemiological evidence indicates that the infection spread in a northeasterly direction into Sichuan Province, then eastward into Hebei and Henan. It also spread northwest from Sichuan, into Gansu and Xinjiang. Xinjiang, in the far northwest of China, is estimated to have between 15,000 and 25,000 people infected with HIV, according to Yuanzhi Zhang, director of the Center for AIDS Detection and Supervision, Station of Hygiene and Epidemic Prevention of Xinjiang Uygur Autonomous Region. Ninety-seven percent of Xinjiang's 2,341 diagnosed cases of HIV infection are IV drug users.

Shao explained that almost all known subtypes of the HIV-1 virus have been found in China, although the majority of cases are B' and C. A unique C/B' recombinant strain has been traced through its transmission via the drug trafficking routes from southern China north to Xinjiang, where it is the only strain of HIV found. HIV has been identified in samples from all of China's provinces and autonomous regions. Recently, several cases of HIV-2 were identified in Shanghai, Shao noted.

The question the Chinese now confront—and which they posed to the meeting attendees—is how China can best interface and cooperate with researchers worldwide to stop the spread of HIV before the country faces an

Continued on page 5

Molecular Epidemiology of HIV-1 Infection in China



Y. Shao, et al
NARL/NCAIDS/CHINA
Unpublished data

Testimonials Bring Deeper Meaning To the Burden of Hookworm

The Albert B. Sabin Vaccine Institute and the Medical Helminthology Laboratory at Yale University under Dr. Peter Hotez have worked and collaborated extensively with China since 1994, and more recently with India. Reprinted below are two examples of how urgent the hookworm problem is and how desperate medical personnel from these countries feel in regards to the disease. The following letters were instrumental in securing funding to make a vaccine against hookworm possible.

A Letter From India:

Hookworm Weakens an Already Impoverished Nation

The problem of hookworm disease in Third World countries has been the subject of investigation for several decades. It perhaps outranks all other worm infections of human misery, debility and morbidity. In India more than 130 million people are infected with hookworms due to either *Ancylostoma*

duodenale or *Necator americanus* or both. The former parasite, a more virulent pathogen, is distributed exclusively in the north while the latter is prevalent in the rest of the country. Both parasites are voracious blood suckers as

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duodenale or *Necator americanus* or both. The former parasite, a more virulent pathogen, is distributed exclusively in the north while the latter is prevalent in the rest of the country.

Both parasites are voracious blood suckers as

each one sucks 0.1 to 0.2 ml of blood per day. The vast majority are the same individuals who suffer from malnutrition, lethargy and poverty. The highest incidence of infection is in wet areas and in coalmines. The epidemiological study in India reveals that the 15 to 20 year age group is commonly infected and a larger segment of this population have enough worms to cause clinical symptoms of anemia, loss of vitality and chronic illness.

Though the disease is never spectacular like some other diseases but is essentially insidious year after year, generation after generation and undermines the health and efficiency of whole communities. Since there are hardly any sanitary indoor toilets in homes, people have the habit of releasing themselves in open fields where hookworm eggs are discharged with faeces.

In course of time they pick up infection and reinfection from their own contaminated environment which is a

major public health problem. Drugs are available but are cost prohibitive. The people who are infected are extremely poor and cannot afford the cost of medicines in view of repeated reinfections in endemic areas. So there is a pressing need for vaccines that can prevent hookworms from penetrating and establishing in the gut, a normal site for the parasite.

It is unfortunate that the problem of hookworm infection has been ignored by public health officials in this country as the disease does not cause instant death. [Nevertheless,] the hookworm disease undoubtedly is one of the major impediments in the socio-economic progress in India and warrants immediate attention for containment of the parasite.

With warmest regards,

DR. H.G. SEN
Senior Scientist
Hindusthan CIBA-GEIGY

A Letter From China:

Experts Hope For a Vaccine To Combat Emerging Drug Resistance

Hookworm infection is a major public health problem in the rural areas of our country. Based on a nationwide survey between 1988 and

A successful vaccine could prevent the problem of rapid reinfection which occurs almost immediately several months after anthelmintic chemotherapy.

1992 organized by our Ministry of Health, we had determined that the overall prevalence of hookworm is 17%. This number is based on 1,477,742 fecal examinations. Therefore we calculated that there are an estimated 194 million cases of hookworm. Over the last decade, the prevalence of hookworm has decreased in some areas where aggressive economic reforms have occurred. The best example of this is in suburban areas of Jiangsu Province which are close to the large cities, including Shanghai and Wuxi. This study was published together with Peter Hotez in the *Southeast Asian Journal of Tropical Public Health* (September 1998).

However, in the highly rural areas of Hainan, Sichuan and even Anhui Provinces hookworm continues to be a

major health threat. Working with Peter's group we published papers this year in *Acta Tropica* (in press, 1999) which show that the prevalence and intensity of hookworm is the same or even higher than it was 10 years ago! There are several reasons for this, including the continued use of human feces as fertilizer and inadequate sanitation. This is essentially the situation in this part of China for hundreds of years. In the absence of aggressive economic reforms in these rural areas, it is not reasonable to expect this situation to change anytime soon. Therefore we anticipate that hookworm rates will decline only in suburban areas close to major cities.

Unfortunately, albendazole and other anthelmintic drugs are not adequate for controlling hookworm in these rural areas. Unless we administer the drugs several times a year, the people remain infected with not only hookworm, but also ascariasis as well. However, it is usually not possible to administer the drugs to large populations on this frequent basis. Therefore the people remain infected. Now we are also worried about anthelmintic drug resistance, especially to albendazole.

In many ways the problem of hookworm is similar to the problems of many helminth infections in China, including schistosomiasis. For that reason,

we are working with Dr. Hotez's group to develop an alternative strategy through anti-hookworm vaccination. This is a new idea, but one which we are excited about. A successful vaccine could prevent the problem of rapid reinfection which occurs almost immediately several months after anthelmintic chemotherapy, and would help us lessen use of anthelmintic drugs. Therefore use of an anti-hookworm vaccine might also help us prevent emerging drug resistance. We could anticipate using a vaccine as part of an overall anti-helminth control strategy.

Therefore we at the Institute of Parasitic Diseases, which is the major parasitic disease component of the Chinese Academy of Preventive Medicine, hope that you will seriously consider the Hookworm Vaccine Initiative proposal submitted by Dr. Hotez. We anticipate that our Institute will continue to collaborate closely with Peter on this project. As you may know, there are not many U.S. scientists like Dr. Hotez who have the commitment to work with institutes such as ours to solve problems in developing regions of Asia. We greatly enjoy working with Peter.

Sincerely,
Feng Zheng, Professor
Institute of Parasitic Diseases
Chinese Academy
of Preventive Medicine

Few Lured To Study Hookworm Despite Its Global Prevalence

BY CHARLENE A. FLASH

"As it was when I first saw it, so it is now, one of the most evil of infections. Not with dramatic pathology as are filariasis, or schistosomiasis, but with damage silent and insidious. Now that malaria is being pushed back (sic) hookworm remains the great infection of mankind. In my view it outranks all other worm infections of man combined... in its production, frequently unrealized, of human misery, debility, and inefficiency in the tropics."

In the 1960's Professor Norman Stoll of the Rockefeller Institute eloquently described the disease burden caused by hookworm in an address to the New York Society of Tropical Medicine. Four decades later hookworms infect more than 1.3

billion people in Asia, Africa and South America, haunting the world's poorest children and consigning them to lives marred by stunted mental

and physical development. Hookworm bears the dubious distinction of being the second most prevalent infection of humans; nevertheless, only two laboratories in the entire world are exploring solutions one being the Medical Helminthology Laboratory directed by Dr. Peter Hotez, chair of the Scientific Advisory Board of the Albert B. Sabin Vaccine Institute. His lab is on the front lines of battle as the search for an anti-hookworm vaccine draws ever closer to success.

Labeled the "germ of laziness," hookworm is indescribably debilitating even though it does not yield the dramatic clinical manifestation of Ebola virus or HIV.

It takes a unique individual to spearhead these types of efforts, and one is found in Dr. Peter Hotez. As Dr. Peter Hotez graciously accepted the 1999 Henry Baldwin

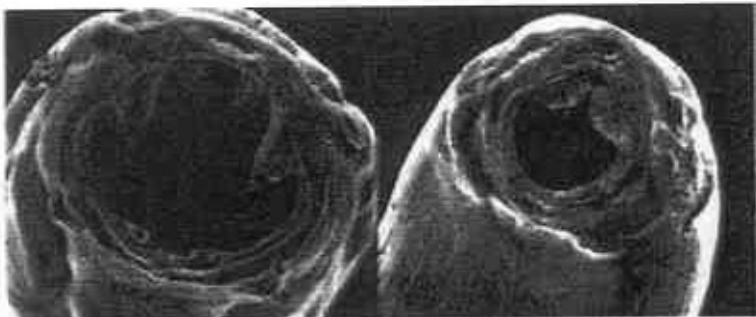
Ward Medal from the American Society of Parasitologists, he shared his earliest scientific pursuits when as a child he would look at the murky waters of a nearby pond under his microscope and marvel at the wonders he saw. In that watery microscopic world he encountered *daphnia* and learned of their symbiotic

relationship with ducks and geese.

The complexities of symbiosis would continue to intrigue Dr. Hotez, as his scientific pursuits for the next three decades focused on worms and parasites. At age fourteen, Dr. Hotez volunteered at the Connecticut State Department of Health compiling records of parasite incidence in fecal samples. In high school he studied earthworms. In college he analyzed the proteins of a parasitic worm specific to the African continent. Dr. Hotez received both his medical degree and his PhD from R Rockefeller University, and it is there that he began studying hookworms in particular.

Labeled the "germ of laziness," hookworm is indescribably debilitating even though it does

not yield the dramatic clinical manifestation of Ebola virus or HIV. When these worms attach their teeth-like appendages to the walls of their



Ancylostoma Duodenale (l) and *Necator Americanus* (r) are the most prevalent species of hookworm found on the continents of South America, Africa, and Asia. *Necator Americanus* is also found in Australia.

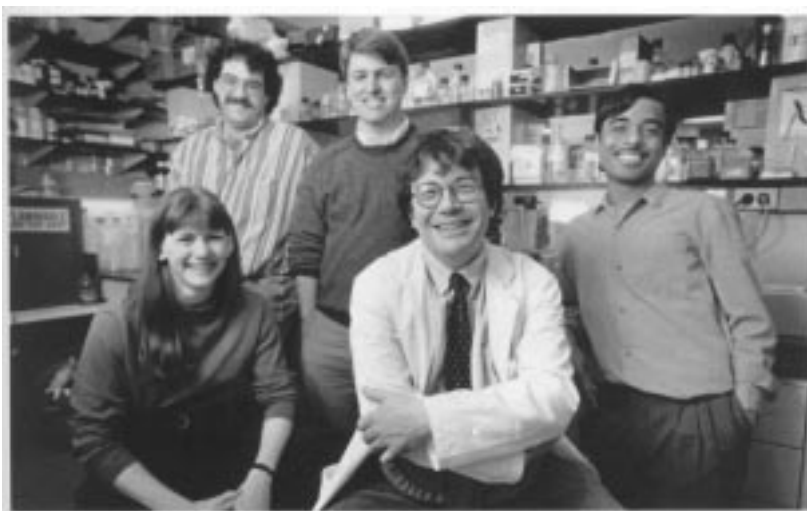
intestinal homes in a human host, hemorrhaging results. Hookworms cause chronic blood loss and thus anemia and protein deficiency; they inhibit physical development in children and retard intellectual development. The large-scale social affects hookworm infections have on education and economic progress explain hookworm's ability to quietly cause the deterioration of entire communities.

Charles Wardell Stiles, one of the early champions in the battle against hookworm played a key role in eradicating hookworm from the Southern United States. In the international arena, the solutions Stiles discovered and helped implement will not work because they require changes in agricultural, religious and social

practices in China, India, and sub-Saharan Africa that have been ingrained for decades. Hookworm's affects can be best nullified by implementation of an anti-hookworm vaccine in

tandem with improved sanitation, use of antihelminthic drugs, and new fertilization techniques.

Charlene Flash is a research fellow at the Albert B. Sabin Vaccine Institute and Editor-in-Chief of the Sabin Vaccine Report.



Dr. Peter Hotez's Medical Helminthology Laboratory has committed themselves to developing an antihookworm vaccine.

Hookworm Glossary

Helminthology: the study of parasitic worms.

Nematodes: a zoological phylum of worms. These include parasitic and free-living species. Therefore it is frequently qualified to talk about "parasitic nematodes" or "intestinal nematodes."

Ancylostoma: one of two genera of human hookworms. The other is *Necator*.

Necator: one of two genera of human hookworms. The other is *Ancylostoma*.

Albendazole: a major benzimidazole drug used for treating hookworms.

The other is mebendazole.

Eukaryotes: organisms with a

Hookworm Glossary

China Aids Conference (cont' from page 5)

extremely serious problem. Vice Minister of Health Da-kui Yin invited foreign assistance: "I welcome everyone to enhance our communication and collaboration in this field." He asked, "Why don't we cooperate together and contribute to this important work?" The important work includes development of vaccines against HIV.

China already has several ongoing projects to develop HIV vaccines. Shao noted that among these are: 1) construction of virus-like particles from HIV-1 subtypes B', C, C/B', and E that have been placed in a baculovirus system and were expressed in insect cells (in cooperation with University of Regensburg, Germany); 2) using yeast systems to express HIV proteins; 3) development of a DNA vaccine (*gp120* and *gag p55* clones in a DNA vector) (also in cooperation with University of Regensburg); 4) development of a vaccinia virus vector (Tiantan strain); 5) development of a fowl pox vaccine expressing subtype B', C, C/B', and E; and 6) development of an adenovirus expressing B', C, C/B', and E.

China also has facilities for testing vaccines in primates and for vaccine production. The country's main problems are financial resources. The Chinese researchers and administrators hope that with this meeting, foreign researchers will see the opportunities for joint research, clinical trials, and epidemiological monitoring in a country that has good science and technology, a good public health and epidemiology infrastructure, large populations for clinical trials, and a commitment to HIV vaccine development.

WHO, UNICEF, CDC, Rotary Intensify Polio Eradication Efforts

BY NISHIENA GHANDI

Global polio eradication as defined by World Health Organization (WHO) involves the complete interruption of wild polio transmission. Efforts to achieve eradication by the year 2000 have been underway since the late 1980s. In fact, the Polio Eradication Initiative was launched in May 1988 at the World Health Assembly's annual meeting in Geneva. At that time this governing body of WHO resolved to eradicate polio from the world by the year 2000. The success of this initiative, however, depends on collaboration of many public and private partners, including the United Nation's Children's Fund (UNICEF), which provides the oral polio vaccine; the U.S. Centers

for Disease Control and Prevention, which offers technical expertise; and the service organization Rotary International, whose 1.2 million members in 159 countries have made polio eradication the main focus of their fund-raising and volunteering.

The polio eradication initiative is currently in its final and most crucial phase. Although some observers have suggested that the campaign may take until 2003 to eliminate paralytic polio, the World Health Assembly delegates and two independent expert advisory groups to WHO, The Global Technical Consultative Group for Polio Eradication and the Scientific Advisory Group of Experts at their 52nd annual meeting in May 1999 in Geneva, Switzerland, asserted that "established eradication strategies, when fully implemented, will achieve eradication by the target date." Accelerating efforts in reservoirs such as Angola and Bangladesh make eradication by the end of the year 2000 is still a reasonable goal.

The strategy developed by WHO and its partners to eradicate polio is four-pronged:

- a strong routine immunization program via the effective and inexpensive oral polio vaccine,
- supplementary additional doses of OPV

during National Immunization Days (NIDs),

c) acute flaccid paralysis surveillance whereby every single case of child paralysis must be investigated, and

d) "Mopping up" immunization activities which are in place to re-immunize children in high-risk areas.

The last case of polio in the Western hemisphere occurred in Peru in 1991 and in the Western Pacific region in Cambodia in 1997.

There were only 6000 cases of polio reported world-wide in 1998 which represents a decrease of 85 percent of cases as compared to the 350,000 cases reported in 1988. Although significant progress has been made to date, there are still three major reservoirs where polio transmission occurs: South Asia, West Africa, and Central Africa. Forty-eight countries are presently known or suspected to be endemic, and recent polio outbreaks such as those in Angola and Eastern Europe call for an intensification of eradication activities. The Polio Eradication Initiative has in particular identified India, Bangladesh, Pakistan,

Sudan, Somalia, Democratic Republic of Congo (DRC), Ethiopia, Angola, Afghanistan and Nigeria as priority countries.

In its final and most crucial phase, the major challenges in the initiative have been identified as stopping polio transmission in endemic countries especially those in conflict, and strengthening surveillance and laboratory networks. To achieve the termination of transmission, WHO urges its member nations to improve vaccine coverage beyond the already impressive rate of nearly 90 percent. They are advocating, "Immunizing every child because every child counts."

Rotary International, a nonprofit organization which has played a leading role in polio control, addressed Gro Harlem Brundtland, the WHO's Director-General, to offer its 1.4 million volunteers as "foot soldiers" in the eradication effort. Dr. Brundtland warned, "One of the paradoxes of an eradication initiative is that control efforts must be intensified as the disease disappears. We need to accelerate house-to-house delivery of the vaccine ... and continue negotiations with

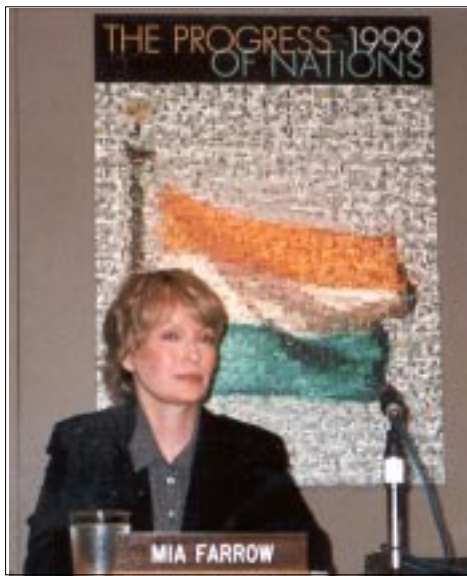
warring parties, and we need to improve surveillance systems so that every paralyzed child is investigated for polio and we can confidently say that countries, regions, and eventually the entire world are polio-free."

To address the changing needs of the initiative in the last and final phase of eradication, a new set of priorities were identified during the 1999 meeting of the Social Mobilization Advisory Group for Polio eradication which included UNICEF, WHO, Rotary International, Basics, Change, Voice of America, CDC, USAID, World Bank, ARCH (Harvard University) and PCS (Johns Hopkins University).

The need to improve the quality of National Immunization Days was discussed and it was determined that in order to obtain a better understanding of the immunization status of a region and deliver vaccines comprehensively, disaggregated data on coverage needed to be generated so that populations with inadequate coverage can be identified. This would improve the accuracy of the target population and enable immunization efforts to be more focused. Additional efforts focus on giving children in regions of conflict access to immunization, increasing support for the ten priority countries, and improving surveillance methods.

The number of worldwide cases of polio has dropped by almost 90% since the campaign began 10 years ago. The great majority of countries are already polio-free, and the 6,415 confirmed cases in 1999 came mostly from the Indian subcontinent and sub-Saharan Africa. From now on, WHO hopes to investigate each singular case to better understand the specifics around the infection. Specific populations have been targeted and surveillance efforts have increased. With continuing effort on the part of WHO and other health and volunteer agencies, a polio free world seems possible within the next three years if not the next 11 months. ❖

Nishiena Ghandi is a Master's Candidate at the Yale University School of Public Health.



Mia Farrow, actress and mother of a son with polio, speaks at the Progress of Nations at the UN in 1999.

Photo by Charlene Flash

Remembering Polio: Karen Veronica Recalls the Polio Scourge

BY CHARLENE FLASH

In these first months of the new year, those of us trying to clean up and clean out encounter memorabilia of days long gone. Karen Veronica, Executive Director and Founder of an HIV/AIDS hospice in Connecticut called Bread & Roses, chanced upon a single wrinkled sheet documenting the day she received her polio vaccination. Ms. Veronica remembers the seemingly never-ending line outside the newly constructed Junior High School in her home town of Berea, Ohio population 20,000, where her siblings, parents, and neighbors patiently awaited their turn to take the contents of a little white cup holding the precious white

cube containing the Sabin oral polio vaccine dose. After the days when the townspeople lined up for their sugar cubes, she recalls they breathed a "collective sigh of relief."

During that post-World War II era, a general sense of fear cloaked adults and children alike with the beginnings of the Cold War and the shroud of infectious diseases like influenza and polio.

Foremost however was the fear of Polio. In those days, "People were always thinking about it," according to Ms. Veronica. During the hot summers parents, rich and poor alike, restrained their children from swimming for fear they might contract this dreaded viral illness by ingesting



The iron lung was used in the first half of the century to enable paralyzed polio victims to breathe.

Photo by Charlene Flash

International Leaders Seek Solutions to Developing World Challenges Cold Spring Harbor Colloquium Tackles the Issue of Affordable Vaccines

BY PETER HOTEZ

While most of us think of December 7 as a day that will “live in infamy” because of its association with the bombing of Pearl Harbor, in 1999 that date also witnessed a remarkable day of human compassion. Between December 5 and 7 last year, the Sabin Vaccine Institute held a colloquium at Cold Spring Harbor Laboratory, which brought together leading economists, international health policy experts, philanthropists, vaccine manufacturers, and physician-scientists in order to tackle one of our greatest social challenges - namely how will we afford the next generation of vaccines for developing countries. Over these two days an extraordinary team of experts selected from such diverse organizations as the White House Office of Science and Technology, the U.S. Treasury Department, the National Security Council, World Bank, UNICEF, Global Alliance for Vaccines and Immunization (GAVI), WHO,

Our technical abilities to employ modern biotechnology for the manufacture of these desperately needed vaccines have outpaced our vision.

Merck, Wyeth, SmithKline Beecham, and Glaxo Wellcome debated and explored innovative solutions for a pressing issue that will affect hundreds of millions of children in less developed countries.

The problem we focused on was how we can encourage the development of desperately needed vaccines for which the markets either do not exist or are grossly inadequate. For instance, falciparum malaria kills an estimated 1-2 million children under the age of 5 every year. This disease is arguably the single leading killer of young children in the world. The biotechnology is now available to begin making a serious attempt to develop a safe and effective malaria vaccine. Yet,

this disease predominantly afflicts not only the poorest countries in places regions as sub-Saharan Africa, but in particular the poorest of the poor in these developing nations. What then is the incentive for major vaccine producers to invest the hundreds of millions of dollars in R&D, manufacture and post-license marketing that would be required to produce an anti-malaria vaccine? Case studies presented for not only



Dr. Peter Hotez (left) of Yale University and Dr. Jeff Sachs (right), Director of the Center for International Development at Harvard University, co-chaired the colloquium at Cold Spring Harbor.

malaria, but also HIV, dengue fever and hookworm infection illustrated over and over again that “business as usual” would never result in the successful development of vaccine to fight these devastating illnesses.

The colloquium reaffirmed that combating infectious diseases must be accorded a central role in international strategies for improved public health, poverty reduction, and economic development ...

Thus, although it is now possible to apply modern techniques developed by academia and the biotechnology industry to make vaccines for these ancient and emerging scourges, we now find ourselves in an unusual and distressing situation. Our technical abilities to employ modern biotechnology for the manufacture of these desperately needed vaccines have outpaced our vision. Our technology is exceeding our wisdom. This is occurring at several different levels, regarding the

issues of R&D, payment structure and macroeconomics. Yet for the most part, our political and spiritual leaders, our legal and medical scholars, our ethicists and artists, have remained silent about our ability to combat the great plagues of AIDS, TB, malaria, dengue, hookworm. In this sense there is a conspiracy of silence. Our colloquium attempted to break the conspiracy of silence about development of vaccines for the great neglected diseases of humankind, such as AIDS, TB, malaria, dengue, hookworm. This meeting broke the silence.

The colloquium reaffirmed that combating infectious diseases must be accorded a central role in international strategies for improved public health, poverty reduction, and economic development in the heavily indebted poorest countries (HIPCs). A number of novel push and pull funding strategies were outlined to provide mechanisms by which to solve these issues. These were put forward with some urgency because of a series of key actions anticipated in the YR 2000. These include finalization and submission to Congress of the FY 2001

Administration budget; parliamentary budget cycles in Europe, Japan, and Canada; a White House meeting early next year, following up on President Clinton’s U.N. address this Fall; ongoing preparation for the G-7 Summit in Japan in June 2000; a planned Summit of African Leaders on Malaria next Spring to be hosted by Nigeria and supported by the WHO; the launch of the enhanced HIPC initiative on debt relief; decisions by the Executive Board of the World Bank.

The Colloquium has launched a concerted effort by the pharmaceutical industry, GAVI, and other participants to work intensively over the next year. Extraordinary interdisciplinary leadership of vision and wisdom is needed to seize this unique opportunity and find solutions. Our goals will be to ensure that an expanded global vaccine effort is brought to fruition. ❖

Peter J. Hotez is the director of the Medical Helminthology Laboratory at Yale University and is also an Associate Professor at the School of Public Health and Epidemiology.

water contaminated by infected feces.

Ms. Veronica chuckles as she remembers preparing for her family vacation to northern Michigan by picking out an extra bathing suit—an extravagance at other times—but a necessity because she was not allowed to even sit by the crystal clear lake in a wet bathing suit. Though she could not understand how the crystal clear waters of the lake could hold anything infectious or bad, she was excited at the prospect of a new bathing suit.

In about the fifth grade one of Ms. Veronica’s classmates contracted polio. News spread through her community as pity

for his parents and siblings filled each house. Although he left school, the constant hum of conversation about his ailment made his presence felt. “That’s all we talked about. We all sent cards.” Paralysis of individual muscles is one of the symptoms of polio, and a few years later he returned to school with a “bad limp.” Many of her friends did not know how to approach the topic of his limp, the calling card of his bout with polio. It was a tragic curiosity. He and his family later moved away from Berea.

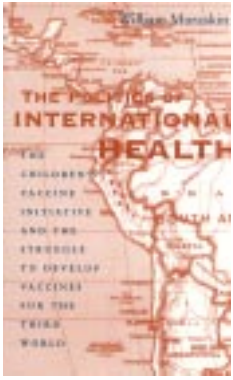
The actual vaccination process stands out in Ms. Veronica’s memory as one of her best public health experiences. She recalls her polio vaccination as a positive experience among a host

of negative health encounters such as being treated as a second-class citizen when going in for STD testing. This experience was proactive, clean, upbeat, all-inclusive and it made sense. Most importantly it erased the fear.

Now as executive director and founder of Bread & Roses, Karen Veronica strives to create positive health experiences for people suffering with HIV or AIDS. She and her staff “walk alongside people with AIDS, through direct care, education, outreach and advocacy.” ❖

Lessons learned; opportunities missed

The Politics of International Health:



Children's Vaccine Initiative and the Struggle to Develop Vaccines for the Third World William Muraskin, State University of New York Press, 1998

BY VERONICA KORN

Published shortly before the controversial dissolution of the Children's Vaccine Initiative (CVI) in March 1999, William Muraskin's *The Politics of International Health: The Children's Vaccine Initiative and the Struggle to Develop Vaccines for the Third World* is an in-depth exploration of that organization's vision and effort to bring together the private and public sectors to target vaccine development for the nations of the Third World. Muraskin's predictions that the future of the CVI seemed precarious were accurate, as it turns out. Through many short and lively interviews and quotes, the author highlights the difficulties in this process and the differences in the organizational cultures of the key players.

Created at the World Summit for Children in 1990, the CVI was born out of inspiration and humanitarian vision on the cusp of a revolution in biotechnology that would make vaccine production more affordable and carve out a place for vaccines as a profit-making entity. Co-sponsored by the United Nations Children's Fund (UNICEF), the UN Development Programme (UNDP), the World Health Organization (WHO), the World Bank, and the Rockefeller Foundation, the CVI was a unique global coalition of public, non-governmental, and private organizations. Its original goal was to develop a single oral vaccine that could be given to newborns shortly after birth to prevent more than twelve deadly diseases. Vaccines are the least expensive and most effective means of disease prevention against many infectious diseases that still

ravage children of the Third World.

When formed in 1990, the CVI was intended to act as a facilitator in the product development aspect of vaccine research, especially on the international level. Immunization efforts in the Third World were severely hampered by a communication gap between the public and private sectors, and the founders of the organization that would evolve as the CVI hoped to bring together researchers, developers, and health networks. Muraskin described the process of vaccine development as "a disarticulation." As he clearly explains in writing to both the scientific and the lay community:

...shelves of research facilities were filled with vaccines...not picked up as a usable commodity. [Health agencies] delivering vaccines...had little interaction with scientists or commercial interests. They are forced to work with whatever vaccines the other two groups [researchers and private sector developers] have decided to work on."

Although the coordination of a three-fold system that would involve researchers, developers, and those ultimately responsible for delivering vaccines in the field was one of the CVI's initial undertakings, the real impetus lay in involving the public sector more in vaccine product development.

Muraskin takes the reader on a journey through the private sector, beginning with the attitude of complacency towards vaccines, despite their potential to change the face of the Third World, and then describing the dawning realization that new biotechnology would make vaccines very profitable. All the while, the author intertwines the role of the public sector in this process as it endeavored to put aside its suspicion of the private sector's commercial interests and the subsequent formation of the CVI for a fascinating historical account.

Despite the unfortunate timing of the CVI's origins from an economic standpoint, as the world economy entered a recession in 1990, Muraskin points out that its failures and frustrations were really more the result of decision-making and in-fighting among the players in such health network giants as the WHO and UNICEF. He describes the dissimilar corporate cultures, personality clashes, and cultural differences that oftentimes fueled a heated competition between the two agencies. Most vividly, he describes the absorption of the CVI into WHO, the ensuing struggle between the agencies, and WHO's inability to reach the important private sector

once CVI was officially based inside WHO. In addition, Muraskin predicts what can best be described as the slow death of the CVI once it was subordinated by WHO. He writes:

"...CVI leaders believed WHO was incapable of doing what the CVI did: [being] flexible...seizing opportunities, attractive to outside agencies, working comfortably with the private sector, seeking out the best people. The tendency of WHO to subordinate expertise to equal representation of nations and regions...differentiated it from the CVI. The WHO's corporate culture was simply the wrong place for the CVI. In addition, groups [like] UNICEF would not financially support programs implemented by WHO."

Indeed CVI Coordinator Roy Widdus wrote in the final issue of the *CVI Forum*, the organization's newsletter (no.18, July 1999), that because WHO was a public-sector agency, it could not "formally integrate" private partners into a true coalition, as had been the initial vision of the CVI.

It seems almost inevitable that the CVI itself would eventually become something of the past. Muraskin's work describes a relatively simple solution to some international health problems: a diverse coalition cooperating to find and deliver vaccines to the Third World, where immunization rates are extremely low and disease rates are enormous. Yet, each chapter is filled with power struggles and competition among key international players with good intentions but without the ability to play together as a team. Muraskin concludes his book by focusing on the far-reaching successes of the CVI: its legacy of stirring interest in vaccine development and production across the international health scene; the renewed interest of organizations like WHO in taking on effective roles in health; the establishment of the International Vaccine Institute in Seoul, Korea, which is wholly dedicated to vaccine research and development; and a revolutionary plan to coordinate the work of private and public sectors involved in vaccine production from beginning (development) to end (delivery). The lessons learned from the endeavors of the CVI are thought provoking, especially when one considers the challenges of immunizing almost 4 million children who, without vaccines, will die annually from vaccine-preventable diseases.

Find out more about the Children's Vaccine Initiative at <http://www.vaccines.ch>.

Merck CEO and Honduran First Lady to Receive Sabin Awards

Celebrating Health in the Americas

BY JOHN M. CLYMER

The Albert B. Sabin Vaccine Institute has selected Raymond V. Gilmartin to receive the 2000 Sabin Lifetime Achievement Award and Mary Flake de Flores to receive the Albert Sabin Humanitarian Award. The awards will be presented at a black tie dinner on Wednesday, May 31 at The Pierre Hotel in New York City.

Mr. Gilmartin is chairman, president and chief executive officer of Merck & Co., one of the principal vaccine research and development companies in the world. Mr. Gilmartin has invested heavily in vaccine research. During his tenure, Merck has introduced the only vaccine that prevents chickenpox, as well as vaccines against hepatitis A and *Haemophilus influenzae* type B (meningitis). The company's pipeline features vaccines to prevent HIV/AIDS, human papillomavirus/cervical cancer,

and rotavirus, a major cause of acute diarrhea and dehydration in infants.



Ray Gilmartin, Chairman, President and CEO of Merck & Company

Compliments of Merck & Co.

Mr. Gilmartin's emphasis on recruiting and retaining a talented workforce has helped Merck be named the best pharmaceutical firms to work for in the U.S. by Fortune magazine.

The theme for the dinner is "Celebrating Health in the Americas." It will focus attention on the eradi-

cation of polio throughout the Americas, and the ongoing campaign to eradicate measles from the Western Hemisphere.

Merck is an established leader in solving health problems in developing countries. After Merck discovered that one annual dose of its Mectizan® (ivermectin) drug prevents river blindness, it decided in 1987 to donate Mectizan® free of charge to all people affected by river blindness. It formed a partnership of industry, nongovernment development organizations, and nongovernment organizations to help it distribute the drug in African and Latin American countries where river blindness is prevalent. The company donates approximately six million doses of Mectizan® annually. And, it has created a donation and distribution model that can be used to address other disease threats.

The first lady of Honduras, Mrs. Flores,

Cancer efforts at Critical Stage Show Promise

Report from Walker's Cay Cancer Vaccine Colloquium

BY ALLAN GOLDSTEIN

Thirty of the leading U.S. cancer researchers presented work at the 2nd Annual Walker's Cay Colloquium on Cancer Vaccines that indicates we are on the verge of a major victory in the "war on cancer." "We are seeing meaningful results in the development of weapons to treat and prevent various types of cancer," said Allan Goldstein, Chairman of Biochemistry and Molecular Biology at George Washington University School of Medicine and a participant in the meeting. "Recent advances in immunology are now being applied to develop novel vaccines for cancers and the results are encouraging," he said.

The goal of the meeting convened by the Albert B. Sabin Vaccine Institute was to shorten the time needed to translate scientific discoveries to meaningful treatments for cancer. The work presented there "indicates that we are at the stage of fine tuning therapeutic and prophylactic cancer vaccines," Goldstein observed.

A number of novel cancer vaccines using combinations of the patient's own cancer and dendritic cells plus cytokines have now entered human trials, have shown remarkable regression of advanced tumors and restoration of anti-tumor immunity. These results provide proof of principle for a vaccine approach to cancer treatment.

"Scientists in multiple disciplines have made extraordinary advances in molecular biology and genetics over the past few years," Goldstein observed. "These advances have vastly increased our understanding of the role of cellular components of the immune system and the soluble growth factors and cytokines produced by T-cells, NK cells, macrophages and dendritic cells responsible for antitumor activity. This knowledge has resulted in the development of novel cancer vaccines which are now being tested in humans," he added.

That approach to treating cancer and the colloquium's impact on scientific progress were

underscored by Dr. Carl June, Director of translational research programs at the Leonard and Madlyn Abramson Family Cancer Research Institute at the University of Pennsylvania Cancer Center. June, a participant in the 1999 and 2000 meetings, reviewed a case in which he developed a new biochemotherapy for a patient with a recurrence of ovarian cancer in April 1999. He incorporated experimental material developed and disclosed by other



Participants enjoy the surroundings at the Walker's Cay

participants in the 1999 meeting. June's therapy appears successful at this juncture; the cancer is in remission and the patient is physically active. "Without this sharing of

unpublished data and information at last year's meeting, I would not have known about these brand new therapies, so I could not have incorporated them into this cocktail. I contacted these investigators and they were extremely helpful in sharing additional data and providing material to me," June said. His clinical protocol therapy has just been approved for a Phase I trial in patients with advanced ovarian cancer.

Formation of a vaccine biomedical consortium, which the Sabin Vaccine Institute has advocated for several years, was discussed at the 1999 colloquium. This year, Dennis Panicali, chief executive officer of Therion Biologics, reported on an industry-government-academia consortium formed by his company. Therion, a closely-held biotechnology company,

A number of novel cancer vaccines using combinations of the patient's own cancer and dendritic cells plus cytokines have now entered human trials...these results provide proof of principle for a vaccine approach to cancer treatment.

will be recognized for leading both public and private efforts to prevent disease and improve healthcare in Honduras. Her involvement in this arena began in the 1970s, long before her husband's January 1998 election as president. She is an outspoken advocate for immunization. Her leadership helped the XIX Vaccination Crusade in May 1999 reach 95% coverage nationwide. She obtained a donation from Merck of one-third million doses of measles, mumps and rubella vaccine, which were used in the crusade.

Mrs. Flores formed Fundación María, a nonprofit organization dedicated to ameliorating poverty, and improving health conditions, education, recreation and sustainable development for Hondurans. In the aftermath of Hurricane Mitch in October 1998, the foundation distributed humanitarian aid to people left homeless by the storm,

an effort led by Mrs. Flores. Currently, Mrs. Flores is raising private funds to build a children's hospital in the country's capital, Tegucigalpa. She is founder



Mary Flores de Flores, First Lady of Honduras

and honorary president of the Honduran Foundation for Children with Cancer. She donates the prof-

has several cancer vaccines in its R&D pipeline, most of which have produced encouraging results in clinical testing. "No one can do it alone," Panicali said. "Every one of the promising products in our pipeline is the result of this consortium that allows the NIH, academic research centers and our company to stick to our strengths and combine our best efforts to develop effective cancer immunotherapies."

The Walker's Cay Colloquium is a think tank-style meeting. Ralph A. Reisfeld, professor of immunology at the Scripps Research Institute and co-chair of the colloquium, said the meeting is "distinctive for its small size and its emphasis on lively, open discussion." The colloquium atmosphere encourages free exchange of data and information about the latest advances being made in cancer vaccine design and immunotherapy. Participants share unpublished data and conclusions in discussions that spark new ideas and experiments.

The site of the meeting, Walker's Cay, is a small island in the northern Bahamas owned by Robert Abplanalp, chairman and chief executive officer of Precision Valve Corporation. Richard Nixon was a frequent visitor to Walker's Cay during his presidency. The secluded tropical island provided solitude as he pondered major decisions. He was at Walker's Cay when he decided to commit the United States to a "war on cancer."

The "war" began with enactment of the Cancer Control Act of 1971 which greatly increased National Institutes of Health funding for cancer research. Elliot Richardson, secretary of Health, Education and Welfare at the time, "directed [funds] into areas of basic research that offered significant promise of shedding light on the fundamental causes of cancer" such in molecular biology, he wrote in a 1999 letter to Sabin Institute chairman H. R. Shepherd. Twenty-nine years later, that research is paying off with experimental vaccines to prevent and treat a variety of cancers.

Allan Goldstein is a Professor and Chairman of the Department of Biochemistry and Molecular Biology at the George Washington University in Washington, D.C.

its of her book, *Virgencita de Suyapa*, to the foundation.

"Mary Flores de Flores is a tireless advocate for better healthcare for Hondurans and all peoples of Central America," said Sabin Vaccine Institute chairman H. R. "Shep" Shepherd. "Like Albert Sabin, she is dedicated to preventing disease. She rolls up her sleeves and does the heavy lifting that is required to truly make a difference."

Mr. Shepherd praised Mr. Gilmartin as "an extraordinary corporate leader who is focused on more than meeting Wall Street's expectations for the next quarter. He has strengthened Merck's commitment to preventive health care, investing in research, bringing innovative vaccines to market, and creatively applying Merck's resources to prevent disease in all corners of the world, rich and poor alike. Although Ray is young, he already has established a legacy as an astute executive and a global citizen," Shepherd said.

Victor J. Menezes, chairman and chief

NEWS FROM THE INSTITUTE

CYRO DE QUADROS RECEIVES SABIN GOLD MEDAL



Ciro de Quadros,
Director of the Pan

Compliments of PAHO

Dr. Ciro de Quadros, director of the Pan American Health Organization's Division of Vaccines and Immunization, will receive the Albert Sabin Gold Medal for his roles in the eradication of polio and

measles from the Western Hemisphere.

"Ciro de Quadros is an extraordinarily apt choice for the Sabin Gold Medal because he upholds Albert Sabin's ideals and quest to conquer disease with vaccines," says H.R. Shepherd, chairman of the Sabin Vaccine Institute. "Dr. Sabin showed us that, just as viruses know no borders, vaccine research

and immunization can transcend political boundaries and tensions. Dr. de Quadros continues to blaze trails in vaccine diplomacy, working to make all peoples healthier and to break down barriers to peace."

Dr. de Quadros earned his medical degree in 1966, and a master's in public health in 1968. He joined PAHO in 1977 after working on smallpox eradication in Ethiopia. He led polio eradication efforts in the Americas, from 1985 to 1991 when Peru reported the last case of polio. Efforts continue to globally eradicate polio by 2003. PAHO, which also serves as the Regional Office for the Americas of the World Health Organization, works to improve health and living standards in the Americas.

Dr. D.A. Henderson, a 1999 Sabin Gold Medal recipient who led the successful global smallpox eradication program, will present the award to Dr. de Quadros at the 3rd Annual Conference on Vaccine Research in Washington, D.C. on April 30. ❖

Sabin Institute Establishes Satellite Office in Research Corridor

"A consistent mission pursued through dynamic programs," is chairman H. R. Shepherd's assessment of the Albert Sabin Vaccine Institute. The Institute was founded in 1993 to carry on Albert Sabin's commitment to disease prevention through immunization. That is our guiding principal even as the Institute evolves," he explained.

Based in New Canaan, Connecticut since its founding, the Institute recently moved its Washington satellite office from the Georgetown University campus to Rockville, Maryland. The New Canaan executive office coordinates all research advancement, educational, and advocacy programs, and communications including the *Sabin Vaccine Report* and the Institute's World Wide Web presence. The satellite office headed by Dr. Philip K. Russell, the Institute's founding president, supports the Institute's research advancement initiatives. The satellite office is located closer to the National Institutes of Health and the Food and Drug Administration in Maryland's biotechnology corridor.

Fran G. Sonkin recently joined the Sabin Institute at its New Canaan headquarters as Executive Vice-President. Reporting directly to the Chairman H.R. Shepherd, Sonkin will direct all major operations of the Institute. She received her Masters in International Relations at Columbia University.

You may contact the Sabin Vaccine Institute at the following locations and numbers:

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Fax 301-231
www..sabin.org

sabin calendar

The Institute is not responsible for non-Institute events listed below.

April 30, 2000

*Albert B. Sabin Gold Medal Awards
Renaissance Hotel, Washington, DC*

DR. CIRO DE QUADROS, DIRECTOR OF THE PAN AMERICAN HEALTH ORGANIZATION'S DIVISION OF VACCINES AND IMMUNIZATION, WILL RECEIVE THE ALBERT SABIN GOLD MEDAL FOR HIS ROLES IN THE ERADICATION OF POLIO AND MEASLES FROM THE WESTERN HEMISPHERE.

October 5-7, 2000

*Cold Spring Harbor, NY
INTELLECTUAL PROPERTY IN A
PHILANTHROPIC WORLD
Sponsored by the Sabin Vaccine
Institute and organized by Jeffrey
Sachs, M.D. Ph.D. and Peter
Hotez, M.D. Ph.D.*

May 31, 2000

*Dinner to Honor Ray Gilmartin
Pierre Hotel, NY, NY*

RAY GILMARTIN, CEO OF MERCK PHARMACEUTICALS WILL RECEIVE THE LIFETIME ACHIEVEMENT AWARD FOR HIS OUTSTANDING CONTRIBUTIONS TO VACCINE DEVELOPMENT.

July 5-8, 2000

*Washington, DC
Marriot Wardman Park Hotel
34TH NATIONAL IMMUNIZATION
CONFERENCE*

September 7-10, 2000

*New Orleans, LA
38TH ANNUAL MEETING OF THE
INFECTIOUS DISEASE SOCIETY OF
AMERICA*

Gilmartin, Flores (cont' from page 10)

5th Annual Vaccine Colloquium

*Vaccines for Developing Economies,
Who will pay?*

précis

5 December – 7 December 1999
Cold Spring Harbor Laboratories
Cold Spring Harbor, NY 11724-2213

Compiled by
Charlene A. Flash
Research Fellow

**Sponsored by
The Sabin Vaccine Institute**

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