www.fic.nih.gov

GLOBAL HEALTH MATTERS

MAY/JUNE 2013

FOGARTY INTERNATIONAL CENTER • NATIONAL INSTITUTES OF HEALTH • DEPARTMENT OF HEALTH AND HUMAN SERVICES

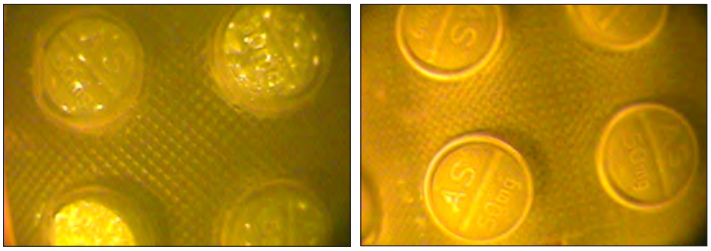
FDA acts against compromised antimalarial drugs

To counteract a global surge in counterfeit and substandard drugs, including antimalarials, the U.S. Food and Drug Administration (FDA) has announced a partnership to make a simple, hand-held device available so developing countries can more easily test if drugs are authentic or not.

In countries where malaria is endemic, falsified antimalarial medications are a growing threat. "Fake or substandard antimalarial drugs are particularly dangerous because the malaria parasite can kill a person in a matter of days and adequate, prompt treatment is necessary," said FDA Commissioner Dr. Margaret A. Hamburg. More than 660,000 people die from malaria each year, most of whom are children.

Not only do fake drugs risk patients' lives, Hamburg noted, but they cause "double damage" in allowing the malaria parasite to develop drug resistance through exposure to low doses of the active compound designed to kill it.

Photos by Nico Raniere/FDA



The FDA has launched a partnership to make available a tool that differentiates between fake malaria drugs (left) and authentic drugs on the right.

Recognizing the need for a tool to help inspectors identify diluted or falsified drugs, the FDA developed the Counterfeit Detection Device-3 (CD-3). The tool

. . . continued on p. 5

Changes needed to address AIDS as a chronic illness

Improvements to health care systems designed to handle the HIV/AIDS epidemic are priming developing countries to more effectively fight the rising threat of noncommunicable diseases, not least in the remarkable expansion underway in trained physicians, laboratory technicians and other scientists. This observation comes from Fogarty collaborator Dr. Wafaa M. El-Sadr, founder and director of the International Center for AIDS Care and Treatment Programs at Columbia University.

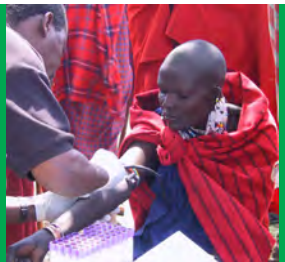
"Despite the enormous challenges, something amazing happened over the past close-to a decade," said El-Sadr, who delivered the James C. Hill Memorial Lecture, named in honor of National Institute of Allergies and Infectious Diseases former deputy director. Responding to the epidemic, health systems scaled up rapidly and by the end of 2012, about 8 million people with HIV/AIDS in developing countries had initiated antiretroviral therapy, she observed.

HIV, as a chronic lifelong disease, demanded a system that offered a continuum of care, rather than the episodic services that were previously the only option in many developing countries where HIV/AIDS was spreading rapidly, El-Sadr said. Countries needed to improve services, raise the quantity and quality of the health care workforce, establish or update information systems, develop ways to obtain medical products, finance the health system and transform leadership and governance.

"Probably at the crux of those important challenges

. . . continued on p. 4

FOCUS



FOCUS on genomics

- NIH's genome institute celebrates research milestone
- Africa's diverse DNA can reveal ways to fight disease

Read more on pages 8 - 9

Fogarty welcomes new advisory board members

Photo by Ernie Branson/NIH

Fogarty Director Dr. Roger I. Glass, left, welcomes new advisory board members (from left) Drs. William Tierney, Rebecca Richards-Kortum, King Holmes and George Hill. Not shown are Drs. Michele Barry and Michael Merson.

The Fogarty International Center recently welcomed six new advisory board members who will provide guidance on funding awards and other global health activities:

Dr. George Hill is a professor emeritus of pathology, microbiology and immunology at Vanderbilt University, and was the medical school's first associate dean for diversity. He conducted groundbreaking research to advance biomedical science worldwide, resulting in a broader understanding of the tsetse fly-transmitted "African sleeping sickness."

Dr. Rebecca Richards-Kortum is a professor of bioengineering and electrical and computer engineering at Rice University, as well as the director of the Rice 360°: Institute for Global Health Technology. Her work focuses on translating research that integrates advances in nanotechnology and molecular imaging with microfabrication technologies to develop inexpensive, portable imaging systems that provide point-of-care diagnosis.

Dr. King Holmes is the William H. Foege Chair of Global Health at the University of Washington, heads the infectious diseases section at Harborview Medical Center in Seattle, and is founder and director of the University of Washington Center for AIDS and STD. Holmes is the principal investigator for the International Training & Education Center for Health, a collaboration between UW and the University of California San Francisco, and one of the largest HIV/AIDS training programs in the world.

Dr. William Tierney is president and CEO of the Regenstrief Institute, Inc., as well as a professor at the Indiana University School of Medicine and chief of internal medicine at Wishard Memorial Hospital in Indianapolis. His research focuses on implementing electronic health record systems in hospital and outpatient venues in Indiana and in East Africa.

Dr. Michele Barry is senior associate dean for global health and director of the Center for Innovation in Global Health at Stanford University's School of Medicine. As director of the Yale/Stanford Johnson and Johnson Global Health Scholar Award program, she has sent more than 1,000 physicians overseas to help strengthen health infrastructure in low-resource settings.

Dr. Michael Merson is the founding director of the Duke Global Health Institute, as well as a professor of medicine, global health, community and family medicine, and public policy at Duke University. Previously, he was Yale University School of Medicine's first dean of public health.

Examining manipulation in study recruitment

Researchers often find it difficult to enlist sufficient numbers of participants for their studies. They can, of course, design recruitment and consent processes in such a way to encourage enrollment through subtle manipulation. But how much manipulation is acceptable? That's the issue addressed in a paper by Fogarty bioethicist Dr. Joseph Millum and NIH Bioethics Fellow Amulya Mandava, recently published in *The Hastings Center Report.*

When designing enrollment processes, researchers should be sure not to deceive people about relevant facts or pressure them to make a decision based on immediate desires, the authors note.

RESOURCE

Paper: http://bit.ly/ZPwZP

Photo by He Yi

Varmus visits Fogarty Fellows

During a recent visit to Beijing, National Cancer Institute Director Dr. Harold Varmus (front row, center) met with several Fogarty Fellows, Scholars and mentors at the Cancer Institute and Hospital of the Chinese Academy of Medical Sciences. NCI helps to fund the Fogarty Fellows and Scholars program.

Fogarty-funded scientists help clarify dengue risk

The threat to human health from the mosquito-transmitted dengue virus is much worse than previously thought and improved surveillance is an essential part of tackling its spread and impact, according to a new study by an international team of researchers partly funded by Fogarty.

Dengue fever, a sometimes disabling or deadly disease, occurs at least three times more frequently than previously estimated, researchers said in their *Nature* paper, recently published online. They put the infection number at 390 million cases annually, versus the WHO's estimate of 50-100 million. Having a clear handle on the risk is important for policymakers and scientists tackling the disease, which the WHO describes as fast emerging and pandemic-prone.

The researchers incorporated more data than previous investigations. They analyzed dengue diagnoses records, constructed a model to map the global distribution of risk and included longitudinal information from dengue cohort studies and adjusted population census data.

Although the bulk of dengue infections go unnoticed, hosts still serve as reservoirs and can help spread the disease, so the researchers included all cases of dengue that disrupted daily routine, rather than only treatment-seeking cases.

The study yielded a global infection estimate of 96 million in 2010. Asia accounted for 70 percent—with about 34 percent of those in India—and Africa and the Americas each had about 15 percent.

"Our approach provides new evidence to help maximize the value and cost-effectiveness of surveillance efforts," the researchers wrote in their report. "Knowledge of the geographical distribution and burden of dengue is essential for understanding its contribution to global morbidity and mortality burdens, in determining how to allocate optimally the limited resources available for dengue control and in evaluating the impact of such activities internationally."

Dengue's main vector is the striped *Aedes* mosquito, particularly *Aedes aegypti.* The insects are difficult to control—feeding during the daytime, breeding in very small quantities of water and thriving with today's climate disturbance, rising urbanization and growing human populations. "We predict dengue to be ubiquitous throughout the tropics, with local spatial variations in risk influenced strongly by rainfall, temperature and the degree of urbanization," the authors noted in their report.

Along with more frequent infection comes a higher threat of serious illness—dengue hemorrhagic fever or dengue shock syndrome. This is because the virus has an unusual impact on the human immune system. Four versions exist and although humans develop lifelong immunity to the initial virus, subsequent infection by another type can disrupt the immune system reaction and make serious disease more likely. Scientists don't understand exactly why.

Currently, no therapeutics or vaccines exist and mosquito control measures have failed to rein in dengue's spread. Researchers are stepping up efforts to find interventions, including vaccines, treatments and mosquito control, and in the meantime are determining effective ways to handle any outbreaks.

The study was supported by the International Research Consortium on Dengue Risk Assessment, Management and Surveillance, the Wellcome Trust, U.S. Department of Homeland Security, Li Ka Shing Foundation and Fogarty.

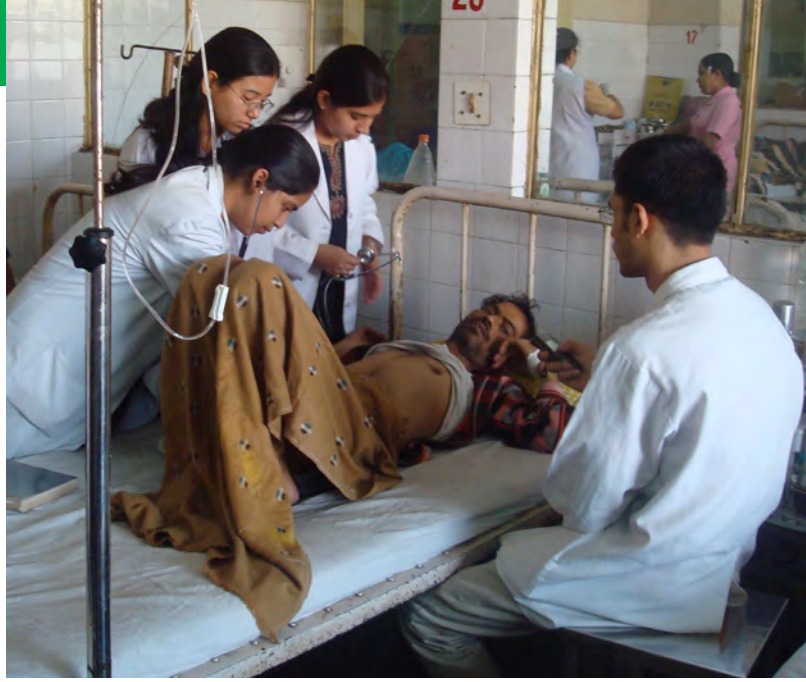


Photo by Gautam Pandey/Photoshare

Fogarty-funded researchers revealed the dengue virus is more prevalent than previously thought, with nearly half of the world's population at risk for contracting this potentially lethal infection.

NIAID leads hunt for safe dengue vaccine

Producing a safe vaccine for dengue is a challenge, but a leading candidate developed by NIH's National Institute for Allergies and Infectious Diseases (NIAID) was recently found to be safe and effective in early-stage trials. A single dose, costing only $1, induced an immune response in about 90 percent of participants.

NIAID called the candidate, TV003, "promising," although immune responses varied among participants, depending on their race. Phase II clinical trials to evaluate the vaccine are planned for Brazil and Thailand.

RESOURCES

Report abstract: http://bit.ly/Deng4Z
NIAID dengue website: http://bit.ly/Deng13

Reducing mother-to-child HIV transmission

Photo by WHO /Harry Anenden

An NIH/PEPFAR collaboration supports research focused on reducing mother-to-child transmission of HIV in sub-Saharan Africa.

Preventing mother-to-child transmission (PMTCT) of HIV is critical in sub-Saharan Africa, where more than 1,000 children are infected each day, primarily through mothers passing on the virus during pregnancy, childbirth or breast-feeding. Though effective preventive treatments—such as AZT, single-dose nevirapine and combinations of antiretroviral drugs—have lowered transmission rates in the U.S. to less than 1 percent, these same interventions have been less successful in many low- and middle-income countries.

In partnership with the U.S. Office of the Global AIDS Coordinator (OGAC) and the National Institute of Child Health and Human Development at NIH, Fogarty's Center for Global Health Studies recently hosted a meeting to launch a new network focused on strengthening PMTCT by promoting locally relevant, evidence-based treatment regimens and improving collaboration between HIV/AIDS researchers and program implementers. The Center will use as a platform 11 projects funded by an existing collaboration between NIH and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and, more recently, its related program dedicated an ongoing forum for grantees, policymakers and implementers on the ground.

Several of the experts attending described cultural and institutional barriers faced when scaling up PMTCT programs in sub-Saharan African countries. Dr. Amy Dubois from OGAC shared insights gained from working on PEPFAR initiatives. She explained that directives regarding how health delivery programs are evaluated, designed, budgeted and managed often come from individuals who have no knowledge of the field teams. "More coordination is needed, so we can be sure we're feeding research into our programs," she said.

The initiative—whose ultimate aim is to inform NIH and other key stakeholders on how best to design PMTCT programs to improve health outcomes—will also address obstacles and challenges identified by the implementer community. Three more network meetings are planned, with the next session to be held in sub-Saharan Africa.

"We now have some effective interventions but they're not being used widely enough in the developing world," said Fogarty Director Dr. Roger I. Glass. "This is where implementation science can make a difference."

RESOURCE

Directory of awards: http://1.usa.gov/10Eo4VG

Changes needed to address AIDS as chronic illness *. . . continued from p. 1*

was workforce shortages," she said, citing the example of Lesotho in southern Africa. When HIV prevalence reached 29 percent, the ratio of physicians to patients was 5 per 100,000. In the U.S. at the same time, the HIV prevalence was 0.6 percent and 550 physicians served 100,000 patients.

What followed was a huge investment in training in developing countries, spearheaded by the U.S. President's Emergency Program for AIDS Relief (PEPFAR) and its related program dedicated to increasing medical and scientific expertise, the Medical Education Partnership Initiative.

"It was not just didactic training but also new methods for training, including multidisciplinary teams, trying to break down walls that exist between the different disciplines, between nurses and physicians and others, and the importance of mentorship," El-Sadr said.

She discussed the spillover effects of improving health care systems for HIV/AIDS into management of other diseases. Although few studies are available to confirm the benefit, she said screening HIV/AIDS patients for co-infections has increased tuberculosis detection rates, which implies quicker treatment and less contagion. And, she said, closer scrutiny of pregnant women to prevent transmission of HIV to babies has contributed to a decline in maternal and child mortality. "Successfully responding to HIV," she said, "is essentially responding to a chronic disease."

RESOURCES

Videocast lecture: http://bit.ly/WES4554
Project website: http://icap.columbia.edu

FDA acts against compromised antimalarial drugs

. . . *continued from p. 1*

illuminates a product with a variety of light wavelengths to enable a visual comparison of an unverified product with an authentic sample. Inspectors need only minimal scientific or technical background to operate the device and can conduct testing in remote areas.

Photo courtesy of FDA

Counterfeit Detection Device-3 (CD-3)

The partnership project brings together a number of public and private entities including Fogarty. To verify the tool's use in a low-resource setting, researchers will conduct a pilot study in Ghana at sites established by U.S. Pharmacopeia, then will expand testing to other locations. The CDC and NIH will provide technical expertise and the Skoll Global Threats Fund will financially support the endeavor. Included in the partnership is the USAID-led President's Malaria Initiative. In addition, Corning Incorporated will help refine and improve the device based on data from testing sites.

"The development of the CD-3 and the formation of this important partnership are critical steps toward the FDA's goal of improving the global product safety net in order to protect consumers in the U.S. and worldwide," Hamburg noted.

Malaria has "pandemic potential" and counterfeit drugs would seriously hamper efforts to contain it, according to Skoll's Dr. Larry Brilliant. He said CD-3's breakthrough technology offers not only a way to fight poor-quality drugs, but could also lead to new point-of-care diagnostic tools to improve early diagnosis of malaria and other diseases. "The ability to scan a medication has much in common technologically with the ability to scan the results of a blood or sputum test to diagnose or verify the type of disease that a patient has," he said.

In a pilot study in Laos last year by the CDC and Fogarty, the tool was used to screen 200 samples of artemisinin. "The FDA's device was highly accurate in detecting falsified artemisinin," said Fogarty's Dr. James Herrington. "It highlighted differences in the pills' markings, coloring and distribution of the pharmacological compounds, as well as in packaging holograms and watermarks."

The agency has successfully used CD-3 in the U.S. since 2010 to identify corrupted drugs for conditions such as cancer, depression and erectile dysfunction, as well as screen for substandard contact lenses, cosmetics, cigarettes, food and medical devices.

"The proliferation of counterfeit or substandard drugs around the world is a major public health problem and the developing world is disproportionately affected," Hamburg said. "It is imperative to come up with a way to identify these products before they are ever given to patients."

Photo by Dr. Jim Herrington/Fogarty

The FDA has developed a hand-held, battery-powered scanner that uses light wavelengths to highlight irregularities in antimalarial and other drugs.

Data use key in fighting child pneumonia, diarrhea

Developing countries need to collect and use important data as they battle childhood deaths from diarrhea and pneumonia, according to a new plan proposed by WHO and the United National Children's Fund.

The Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea (GAPPD) suggests a "cohesive approach" for tackling these two diseases, which annually kill 2 million children under five years of age.

The initiative, aimed at national governments and their partners, will help develop clear strategies and work plans, coordinate implementation of interventions, engage critical partners and take other steps to ensure maximum delivery of proven treatments to those in most need. Rather than calling for new solutions, the agencies suggest expanding the reach of steps shown to work.

RESOURCE

Report: http://bit.ly/XMYchild

PROFILE

Adapting medical practices to fit resource-poor settings

By Arthur Allen

Fogarty Fellow Dr. Mark Siedner is studying better ways to bring care to those who need it in western Uganda.

Mark Siedner, M.D., M.P.H.	
Fogarty Fellow:	2011-2012
Fellowship at:	Mbarara Regional Hospital Mbarara, Western Uganda
U.S. organization:	Harvard University
Research focus:	Determinants of care and technological interventions
Website:	http://bit.ly/Siedner

For many patients in Mbarara, Uganda, the most important medicine dispensed by Dr. Mark Siedner and his colleagues may be the text message stating that their blood test results are abnormal.

The message lets patients know that their lives may depend on a return visit to receive care from clinicians—and that's more than a simple courtesy. In resource-poor countries like Uganda, patients may live dozens of miles from the clinic and require a month of work to earn carfare. Patients who know they are ill and need to start antiviral medicines are more likely to make the decision to come back to the hospital for treatment, especially now that the drugs are widely available, Siedner says.

Transportation costs are a major obstacle to medical care across sub-Saharan Africa, contributing to the loss of up to 40 percent of patients to follow-up after a positive HIV test. Many of those who don't return will die of AIDS, often after infecting other people.

For Siedner, an infectious disease fellow at Harvard and a 2011 participant in Fogarty's Global Health Program for Fellows and Scholars, bringing care to people in marginalized populations is about finding the true determinants of health and conducting research to find better ways of getting around obstacles.

"Most paradigms for medicine have been based on what's accepted in the West and transferring it," he says. "But maybe we can leapfrog some of the dogma we use here and think about how novel technologies can serve those in resource-limited settings."

In Uganda, he and his colleagues are investigating whether there's a better way to inform patients of their CD4 counts—a key marker for progression of AIDS—than requiring a notification visit. An ongoing study, funded by his Fogarty award, has looked at the practicality and ethics of using cellphone texts to advise patients about the gravity of their HIV status. A 2012 study found that most patients at the hospital own or have access to cellphones and are enthusiastic about using them to get results.

In a follow-up study, Siedner and colleagues are testing three different messaging techniques that offer a range of privacy assurance and convenience. "It costs 2 cents to send a text message and $5 to cover their transportation. That's only one part of the equation, but we think it's an important one," says Siedner. Fewer than 20 percent of patients at the hospital return within seven days of an abnormal test result presently, and mortality rates are as high as 10-20 percent in the first year of HIV care, compared to less than 3 percent in the West.

Siedner, whose mentor at Harvard's School of Public Health is Dr. David Bangsberg, was able to hire two full-time research assistants with his Fogarty support. The students he mentored in Mbarara have submitted five academic talks or papers to journals and conferences, and he meets with five to ten local researchers and medical residents during each visit.

At a time of dwindling resources for health research in the developing world, Siedner says, Fogarty's assistance has been key. "My ability to participate in everything from research to clinical care in Mbarara, being mentored myself and mentoring others, has really set me on a trajectory to pursue my career goal of being an academic clinician focused on doing research in places like Uganda."

Q&A

AMBASSADOR LESLIE V. ROWE, M.A., M.ED.

Ambassador Leslie V. Rowe joined the new U.S. Office of Global Health Diplomacy in January 2013 to manage its day-to-day operations. Together with Ambassador Eric Goosby, she is supporting U.S. efforts to advance global health and move developing countries toward fully managing their health care needs. Rowe is an experienced diplomat, having served as ambassador to Mozambique (2010-2012) as well as Papua New Guinea, Solomon Islands and Vanuatu (2006-2009). Her previous postings include stints in Kenya, Thailand, Portugal, Chile, Brazil and Costa Rica. She spoke recently at the Center for Strategic and International Studies:

What are your goals for the new Office?

Our Office will support U.S. ambassadors and their teams, the deputy chiefs of mission, health teams and others to make global health a priority and part of the daily diplomatic dialogue that ambassadors engage in.

As Ambassadors, we have access to many different people at all levels of government and in communities, and have multiple opportunities to discuss global health. And so, for instance, if I was going to have a meeting with the president, the prime minster or the ministry of finance or health, I would always ask our country team: "I'm going to talk about 'X' but is there something we need to get more high-level attention on and can I raise that issue?" While such questions are already standard for many ambassadors, we want to make it even easier for them to do this by creating some tools that they can easily pull out of their toolbox, such as talking points and useful information. They will be promoting country ownership of health systems, health systems strengthening and also sharing responsibility with our partners and seeking donors or expanding their support.

How can all parties work more efficiently?

We are all concerned about the fiscal difficulties in this country and among our partners. We have to be sensitive to everyone's concerns, and we have to look for even better coordination among our partners to make sure the countries in which we are working are aware of all the resources available. In the U.S., we want to make sure that every dollar spent on our global health and assistance programs is being managed effectively. We take those responsibilities seriously and will be paying a lot of attention to this as we move more and more into country ownership, as countries take over all their own planning and implementation, all their monitoring and evaluating, and eventually manage all their expenditures in global health.

What's the importance of country ownership?

It's one of our major goals. We don't define it simply as ownership by the government. Country ownership runs throughout civil society, community groups, women's groups and local and nongovernmental organizations. We've relied on the national government for decades working with NGOs to implement our very effective health programs. Now it's definitely a thrust of embassies abroad to go out into the communities, because we feel it's at the local level, the community level, that people really take ownership and become advocates for their own global health. That will necessitate their putting pressure on their local officials and eventually national officials to provide the kind of health care that they really want.

How do collaborations advance global health?

Let me give you an example: While I was in Mozambique, we signed a trilateral agreement to work together with Mozambique, Brazil and the United States on health issues and also on food security, presenting a good example of participation of an emerging economy. I served in Brazil when it was a recipient more than a donor-partner and it's really gratifying to see this evolution, the way Brazil has taken responsibility for its global health and now is in the position to reach out to the Lusophone communities in Africa.

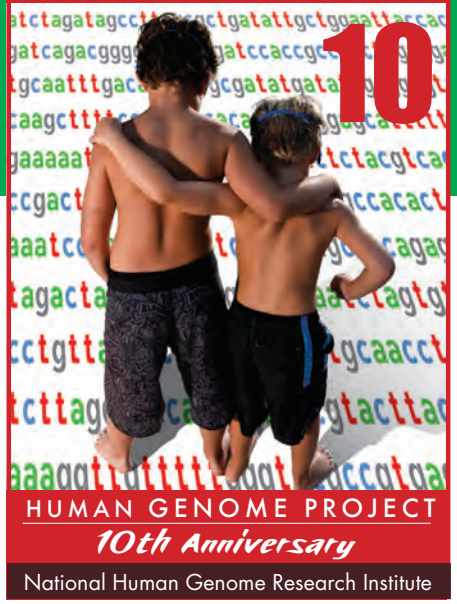
In addition to expanding partnerships with emerging economies, I also feel that we need to work more closely with the private sector. While we've had fantastic support from governments around the world, I think we can do more with private enterprise. There's tremendous interest among American companies to get engaged in Africa, and great opportunities there.

What backing does the new Office have?

We have very strong support, starting with Secretary John Kerry, who cares deeply about global health, and has a long track record of accomplishment on this issue in the Senate. In his first public speech as Secretary, he talked about working toward an AIDS-free generation, eradicating polio, reducing maternal mortality and supporting efforts to avoid malaria, TB and other diseases. It's a great start for our Office to have that kind of support from the top.

RESOURCES

Website: www.state.gov/s/ghd
CSIS webcast: http://bit.ly/RoweDip



Genomics breakthroughs mount to fight disease

Scientists have produced a remarkable volume of human DNA data, but now they need to decipher it faster and produce interventions against disease, according to speakers at the 10th anniversary of the Human Genome Project. The conference was hosted by NIH's National Human Genomics Research Institute (NHGRI).

One of the intended outcomes of the project was that scientists would use the explosion of genomic information about disease pathogenesis and pathways to try to identify new possibilities for intervening in common diseases, said NIH Director and former NHGRI Director, Dr. Francis S. Collins. "We really haven't taken advantage of that as we might have—and it's time."

Researchers are on the right path, he said, citing cancer as an example. Under the umbrella of the Cancer Genome Atlas, scientists are sequencing and analyzing more than 11,000 cancer tumor genomes, which they hope will point to new diagnostic biomarkers and therapies. "We have great hopes this will lead us not only to better ideas about how to identify subsets of cancers, but also to target therapies more effectively," Collins said. The atlas is a collaboration between NHGRI and the National Cancer Institute, supported by public and private institutions.

New technology to sequence genomes at very high volume and speed has exponentially increased the supply of genomic data, noted NHGRI Director Dr. Eric D. Green. In 1990, DNA sequencing took six to eight years and cost $1 billion, but today takes two to three days and costs between $4,000 and $6,000. In 1990, scientists had identified the molecular basis of 61 diseases and this number has surged to 4,847.

The Human Genome Project has also accelerated discovery of DNA influences on individuals' responses to pharmaceuticals. U.S. regulators now require genomic information on the labels of more than 100 products, up from four in 1990. "In short," Green noted, "this additional label information now notifies physicians to consider the patient's genomic makeup when prescribing."

Physicians have begun to do this, for instance in identifying whether their breast cancer patients should take the drug Herceptin, which works only on tumors with a specific genomic profile. The same goes for lung cancer drugs Iressa and Tarceva.

The Human Genome project opened the door to making sense of the so-called "junk DNA." Although mapping the genome identified about 20,000 protein-coding genes, these comprise only about 1.5% of total DNA, with the rest of unknown function at the time, but now recognized as key to many genomic functions.

Collins said massive undertaking though it was, the Human Genome Project succeeded because it was "so compelling, so game-changing, so interdisciplinary. It had such opportunities for creativity from multiple perspectives that it attracted some of the best and brightest scientists of our generation."

About NHGRI

The National Human Genome Research Institute was established in 1990 to carry out NIH's role in the International Human Genome Project. With an annual budget of around $500 million, the Institute supports the development of resources and technology that will accelerate genome research and its application to human health. It studies the ethical, legal and social implications of genome research, supports the training of investigators and disseminates genome information.
Website: www.genome.gov

Articles in this section are by Cathy Kristiansen

Africa's genetic diversity holds promise

A richness of genomic information remains hidden in Africa, origin of anatomically modern humans 200,000 years ago, and research findings there will reveal much about diseases everywhere, according to Dr. Sarah A. Tishkoff, an expert in human evolutionary genomics. She spoke at a recent conference held by NIH's National Human Genome Research Institute to celebrate completion of the human genome mapping 10 years ago.

"Despite the importance of studying African genomic variation, there has been relatively little work done in the region," noted Tishkoff, of the University of Pennsylvania, whose Africa work is supported in part by NIH funding, including a prestigious Pioneer Award. "There's an urgent need to include ethnically diverse Africans in genomic studies, to identify unique, rare and common variants which may be of functional significance, including those associated with disease risk."

Africa's extensive genetic diversity is evident in Tishkoff's research. In one project, her team analyzed the genomes of just 15 individuals in three different populations and identified 13 million variants, including 3 million not previously found anywhere—expanding all known human genetic variation by 8 percent.

African populations suffer from an array of infectious diseases, such as malaria, tuberculosis and HIV/AIDS, but their disease burden is shifting toward many of the chronic diseases more common in developed countries, including hypertension, diabetes and cardiovascular disease. Tishkoff emphasized, "If we want to understand risk factors for these diseases, we need to be looking at Africa."

Efforts to expand African genomics capacity are on the rise, not only from independent research collaborations, but also from partnerships. The Human Heredity and Health in Africa Initiative (H3Africa), supported by NIH and the Wellcome Trust, aims to develop African genomics expertise, establish a continent-wide bioinformatics network and create biorepositories for use in scientific investigations. Tishkoff noted, "The H3Africa project hopefully is going to have a major impact on training and capacity building to do genomics research in Africa."

In more than a decade of genomics research in Africa, Tishkoff and her collaborators have produced findings about many different African populations, especially little-studied minorities. At least 2,000 ethnic groups exist on the continent and their genes have adapted to a broad range of environments. She noted, "It's thought that mutations associated with common diseases in modern

Photo by Dr. Sarah Tishkoff/University of Pennsylvania

Research collaborations and partnerships will help build genomics capacity in Africa, home to the world's broadest range of genetic diversity.

populations may have been selectively advantageous in the past."

Her team has collected more than 10,000 blood samples, conducted detailed ethnographic surveys about diet, nutrition and other environmental influences and measured phenotypic variation ranging from height to blood types to metabolic function.

One study focused on the short-statured Pygmy people of western Africa, whose average height of 60 inches compares with an average 80 inches in neighboring Bantu populations. Pygmies dwell in tropical forests where shortness may be advantageous, Tishkoff suggested. The researchers found numerous genomic differences that influenced not only height, but also neuroendocrine signaling, reproduction, metabolism and immune function.

In another study, Tishkoff and her collaborators investigated why some African populations digest lactose with ease in adulthood. They found three relevant genomic variations, none of which matches the mutation that brings lactose tolerance in many people from Northern Europe. Tishkoff estimated the African adaptations evolved 3,000 to 7,000 years ago, along with cattle domestication.

One area of research that needs urgent attention is pharmacogenomics. Tishkoff noted, "There can be differences in how people respond to drugs and . . . we need to have better characterization of variation."

"If we want to learn more about the African diaspora and African-American ancestry, we need to be looking at Africa," she concluded. "We are just at the beginning of characterizing that extent of variation, particularly across diverse populations."

RESOURCES

Tishkoff lab website: http://bit.ly/TishLab
H3Africa website: http://h3africa.org

OPINION

By Dr. Roger I. Glass, Director, Fogarty International Center

New rotavirus vaccine provides hope

Science advances certainly require good ideas, hard work and perseverance. But I've found serendipity, personal relationships and good partnerships can also play a significant role.

In 1985, I traveled to Calcutta for a WHO meeting on diarrheal diseases, where I met a young Indian pediatrics professor, Dr. Maharaj "Raj" K. Bhan.

Since we were housed at a convent with strict rules forbidding alcohol, we decided to leave the premises together for a drink. Our casual conversation that night spawned nearly three decades of fruitful collaboration. This May, it's my pleasure to join Raj and our now many other partners in New Delhi to review the results of a clinical trial of an affordable and effective rotavirus vaccine that is the result of this unplanned meeting 28 years ago.

During that long-ago happy hour, Raj mentioned he was following a rotavirus outbreak in the newborn unit at the All India Institute of Medical Sciences (AIIMS). He noted it was surprising the infected neonates didn't develop diarrhea. At the time, I was working on an NIH effort studying an unusual group of rotaviruses collected from newborns on four continents that also did not cause the disease. And so began our joint efforts to see if these infections could protect children against subsequent severe rotavirus disease.

After three years of informal collaboration, the Indo-U.S. Vaccine Action Program (VAP) was launched by the Indian Department of Biotechnology and NIH's National Institute of Allergy and Infectious Diseases (NIAID) and our project was approved for funding. Further study of the AIIMS strain of rotavirus indicated it was safe in adults and that it might be a good candidate for a vaccine for children. In 1998, a meeting organized by VAP brought investigators together with a group of Indian vaccine manufactures, including Dr. Krishna Ella, CEO of Bharat Biotech. His enthusiasm was infectious and we began the vaccine development process.

There have been bumps along the road and many wonderful partners joined the project—most importantly the Gates Foundation and program at PATH. By 2011 we were finally ready to launch a trial with 6,800 infants at three sites in India conducted by an NGO, the Society for Applied Studies, that grew out of the need for larger field trials. Thankfully, the results have been positive. We hope the vaccine will be licensed so that it can be introduced in several sites in India. We're confident this will make a huge impact and go a long way to preventing the 100,000 rotavirus deaths that currently occur in that country every year.

> It's significant that this new vaccine was derived from an Indian strain, identified by an Indian scientist, developed by an Indian company, studied in Indian populations, with support from the Indian government.

We've accrued other benefits during this long and winding journey. As we studied the epidemiology of rotavirus in India, we discovered vast differences in the epidemiology of disease between low- and high-income settings. We learned there are more diverse rotavirus strains circulating in India at any time than anywhere else in the world and that Indian children are more likely to be infected with several strains rather than a single strain. While rotavirus infections are highly seasonal in the U.S. and Europe, they occur year-round in India. Eighty percent of Indian children are infected in the first year of life with fatalities occurring for about 1 in 200.

Through our many years of partnership, we also provided more than a dozen investigators and young scientists with significant research training, which has prepared them to tackle other remaining health challenges.

Finally, it's significant that this new vaccine was derived from an Indian strain, identified by an Indian scientist, developed by an Indian company, studied in Indian populations, with support from the Indian government. It's likely the first entirely new vaccine developed in India in over 100 years! There is still much to be done to take this vaccine to India's children—but I am encouraged this will have an immediate and considerable impact on reducing the global burden of rotavirus.

RESOURCES

Papers: http://bit.ly/Rota25
http://bit.ly/11TRzqz

PEOPLE

Hideyo Noguchi Africa prizes awarded

The Japanese government has awarded Fogarty Fellow mentor Dr. Alex Coutinho, of Makerere University in Uganda, its Hideyo Noguchi Africa Prize for Medical Services. The award recognizes Coutinho's efforts to combat infectious diseases in Africa and his contributions to medical research.

The Noguchi Africa Prize for Medical Research will go to Dr. Peter Piot for his pivotal research on diseases endemic to much of the African continent, including HIV, Ebola, chlamydia, tuberculosis and gonorrhea. Piot is Director of the London School of Hygiene and Tropical Medicine. The awards will be presented on June 1, 2013 in Yokohama.

Gairdner honors for researchers Holmes, Alter

Fogarty Board member Dr. King K. Holmes was honored with the 2013 Canada Gairdner Global Health Award for his work in sexually transmitted diseases. Holmes heads the University of Washington's department of global health.

Dr. Harvey J. Alter and two colleagues jointly received the 2013 Canada Gairdner International Award for critical contributions to the discovery and isolation of the hepatitis C virus. Alter is an infectious diseases researcher and clinician at NIH's Clinical Center.

Former Fogarty director Keusch receives award

Dr. Gerald T. Keusch, Fogarty director from 1998-2003, has received the 2013 Distinguished Leadership Award from the Consortium of Universities for Global Health. Keusch, now at Boston University School of Public Health, was recognized for his exceptional contributions to global health.

Lorsch is chosen as NIGMS director

NIH has selected Dr. Jon R. Lorsch to direct its National Institute of General Medical Sciences. Lorsch, a professor in Johns Hopkins University's department of biophysics and biophysical chemistry, earned his doctoral degree from Harvard University and was a postdoctoral fellow at Stanford University.

Fogarty collaborator El-Sadr is honored

Fogarty collaborator Dr. Wafaa M. El-Sadr has been named one of "50 Women Who Shaped America's Health" by the publication, *Huffington Post*. A professor at Columbia University, El-Sadr was recognized for developing family-centered care in HIV/AIDS.

Global HEALTH Briefs

Preparing for rise in NCDs

With noncommunicable diseases set to rise around the globe, scientist should study the related research questions, according to a series of policy briefs, "Addressing the Gaps in Policy and Research for Noncommunicable Diseases," published by Johns Hopkins University.
Full report: http://bit.ly/YVWW9U

World Bank offers policy tool

The World Bank has released an online policy resources toolkit that can facilitate private sector contributions to important developing country health goals.
Website: http://bit.ly/PvtTool

WHO kit improves vital statistics data

The WHO is offering materials to help countries produce reliable statistics. Titled "Strengthening registration and vital statistics for births, deaths and causes of death," the kit was developed by numerous technical partners and institutions.
Website: http://bit.ly/33kyyxm

WHO briefs on inequities

The WHO has compiled expert policy briefs on how to further health equity around the world. "Closing the Health Equity Gap" covers such topics as working toward universal health coverage, ways to measure inequities and cross-government actions helpful in urban settings.
Report: http://bit.ly/75EETyJ

UN report notes South's rise

Prospects of people in the South have improved at an unprecedented pace, according to the UN's "2013 Human Development Report." The report notes inequality in health and education declined, even as income inequalities rose. Mothers' education was found to raise child survival more than household income levels.
Full report: http://bit.ly/HDrpt33

Countries in flux need to measure health

Health impact assessments are important tools for maximizing health promotion, but many countries do not conduct them systematically while under the pressure of population growth, urbanization, natural resource pressure and global climate change, the WHO reports in an article "Untapped potential of health impact assessment."
Article: http://bit.ly/55ZmkWd

Funding Opportunities

Funding Opportunity Announcement	Details	Deadline
Fogarty HIV Research Training for Low- and Middle-Income Country Institutions (D43)	http://bit.ly/HIV43D	July 24, 2013
Critical HIV Research Infrastructure for Low- and Middle-Income Country Institutions (G11)	http://bit.ly/ZnZn88	July 24, 2013
Planning Grant for Research Training for Low- and Middle-Income Country Institutions (D71)	http://bit.ly/LTD724	July 24, 2013
International Research Scientist Development Award (K01)	http://bit.ly/V9wRRF	March 4, 2014

For more information, visit **www.fic.nih.gov/funding**

Global Health Matters

May/June 2013

Volume 12, No. 3 ISSN: 1938-5935

Fogarty International Center
National Institutes of Health
Department of Health Human Services
Publication No. 07-5369

Managing editor: Ann Puderbaugh
Ann.Puderbaugh@nih.gov

Editor/writer: Cathy Kristiansen
Catherine.Kristiansen@nih.gov

Photo editor/writer: Jeff Gray
Jeffrey.Gray@nih.gov

Writer: Arthur Allen

Web manager: Anna Pruett Ellis
Anna.Ellis@nih.gov

Designer: Carla Conway

READ
DOWNLOAD
SUBSCRIBE

SUBSCRIBE:
www.fic.nih.gov/subscribe

Obama plan aims to unlock secrets of the brain

Much of the human brain is mysterious, clouding scientists' understanding of devastating diseases such as Alzheimer's and Parkinson's. To accelerate the development of innovative technologies that can help reveal the secrets of this complex organ, President Obama recently launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative.

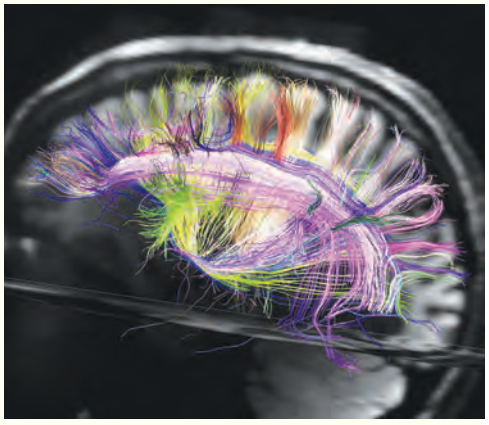


Photo by Dr. Van Wedeen, MHG/Harvard

President Obama recently proposed an initiative to encourage researchers to unlock the mysteries of the human brain.

"We can identify galaxies light years away, we can study particles smaller than an atom," Obama said. "But we still haven't unlocked the mystery of the three pounds of matter that sits between our ears."

The project aims to illuminate how the human brain develops, thrives and succumbs to disease. Improved understanding could bring new treatments and prevention strategies for conditions such as Alzheimer's disease, autism and epilepsy. WHO estimates that one in four people globally are affected by mental or neurological disorders at some point in their lives.

Obama said expanded brain research would also generate economic activity. "Ideas are what power our economy, it's what sets us apart," he said. "We do innovation better than anybody else—and that makes our economy stronger." He cited another major initiative supported by the U.S., the Human Genome Project, which greatly enhanced scientific understanding and generated significant returns for the U.S. economy—$140 for every $1 invested.

Obama proposed BRAIN receive $100 million for first-year funding to support research by NIH, the Defense Advances Research Projects Agency and the National Science Foundation. He intends the initiative to attract matching private sector investments.

RESOURCE NIH website: www.nih.gov/science/brain/index.htm