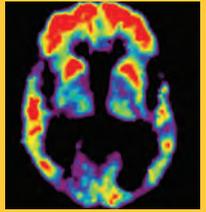


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FOGARTY INTERNATIONAL CENTER • NATIONAL INSTITUTES OF HEALTH • DEPARTMENT OF HEALTH AND HUMAN SERVICES

Brain program catalyzes research, builds capacity

A Fogarty program designed to advance research into brain disorders that affect the developing world has had “tremendous success,” according to a recently published evaluation of its first decade of activity. The initiative has resulted in “significant” scientific advances and has increased brain disorders capacity around the globe, the review stated.

A range of brain disorders emerge at various life stages, which pose particular challenges in the developing world, where expertise and treatment are lacking. In 2003, Fogarty and its NIH partners established the Brain Disorders in the Developing World: Research Across the Lifespan Program. Over the next 10 years, eight NIH Institutes and Centers joined Fogarty in providing a total of \$84 million through 156 grants that support research in the area of nervous system development, function and impairment throughout life, as well as research training to build capacity in these scientific areas.

“With broad support from across NIH, we have been able to catalyze the field of brain disorder research on topics of relevance to developing countries, where these issues

Photo by Ansem Anseri, courtesy of Photostore



A grandmother helps attend to her granddaughter's infant in Bangladesh.

pose a growing problem,” said Fogarty Director Dr. Roger I. Glass. “It is vital we build the multidisciplinary capacity required to study and treat these devastating diseases that occur across the lifespan.” . . . continued on p. 6

Lack of adherence in HIV trial has broad implications

A large, NIH-supported clinical trial in sub-Saharan Africa aiming to identify the best method to protect women from contracting HIV instead underscored that researchers cannot rely on self-reporting to gauge if study participants are following instructions.

Women assigned to receive antiretrovirals daily via a pill or vaginal gel acquired HIV at a similar rate as those on placebos. When analyzing blood samples, researchers discovered only 28 percent of women had taken the drugs, rather than the 80-90 percent compliance rate participants reported.

“It was pretty shocking,” said lead co-investigator Dr. Jeanne M. Marrazzo, of the University of Washington. “We had very little to no clue that the women were not taking the product to that extent.” A report on the study was recently published in the *New England Journal of Medicine*.

The adherence finding has implications for the design of similar randomized controlled trials. “It’s probably going to be much more impactful as a negative study than it would have been as a positive study,” Marrazzo predicted. “Other trials are now routinely monitoring adherence in real-time, or considering doing this.”

. . . continued on p. 2

FOCUS



Studying how animals spread infectious diseases

- Swine trade facilitates evolution, reach of flu
- Vaccination of pigs could eliminate cysticercosis

Read more on pages 8 – 9

HIV trial has implications

... continued from p. 1

The team investigated why women had avoided the medication and found many wanted to hide their trial participation from partners and families to avoid the stigma of being associated with HIV risk. “We heard a lot of stories where they were really anxious about having the study products at home,” Marrazzo said.

The women were also discomfited by the study’s implications that they were vulnerable to catching HIV, because they felt healthy and at low-risk. They nonetheless enrolled, and ensured they remained so, to access free medical care, sexually transmitted disease testing and contraception. They also received financial reimbursement, but it was minimal and not considered a motivator, Marrazzo said.

Although disappointing, the results were also enlightening, she observed. “We thought we were studying a biomedical intervention, but really we were studying a multi-component prevention intervention in different communities. It had everything to do with those individual women’s lives and challenges and burden of trying to remain HIV negative.”

The project involved 5,029 reproductive-age women who were HIV-negative, registered at 15 sites in South Africa, Uganda and Zimbabwe. It is part of a larger effort, the Vaginal and Oral Interventions to Control the Epidemic, or VOICE study, led by the NIH’s National Institute of Allergy and Infectious Diseases with support from the National Institute of Child Health and Human Development, the National Institute of Mental Health, CONRAD and Gilead Sciences, Inc. The VOICE study is being conducted by the Microbicide Trials Network. The project followed up

Only 28 percent of study participants actually used the daily pills or vaginal gel as instructed.



Researchers were studying methods to reduce HIV infection in women at risk.

on several smaller studies in various countries showing that prophylactic antiretroviral drugs could reduce new HIV infections by more than 50 percent in at-risk people adhering to the prescribed regimen. This trial involved different combinations of tenofovir, pills or vaginal gel, and emtricitabine pills, tested against a placebo. All participants received standard HIV risk-reduction counseling, individualized adherence counseling, condoms and hepatitis B immunization.

From the outset, the team was mindful of the need to monitor adherence, so required participants visit the clinics monthly for an interview about their compliance and to return pill bottles, all remaining pills and unused vaginal applicators. Every three months, the women also underwent a computer-assisted self-interview designed to avoid any subjective staff influence. By these measures, adherence appeared high, but 312 women tested newly positive for HIV.

The researchers found that the women most likely to take the drugs as instructed were those with the lowest HIV risk before the trial—they were older, married and had an independent income. In a number of earlier studies with higher adherence rates, participants had more motivation to take the antiretrovirals, for instance couples in which one partner was already infected or pregnant women eager to protect their babies.

Marrazzo said aside from incorporating more blood sampling in trials, researchers are looking at other approaches for HIV drug delivery, such as long-term vaginal rings, implants or injections, which can lessen both the stigma and inconvenience of taking daily medication. “Taking a pill every day is hard, especially if you’re young and you feel invulnerable,” she said. Moreover, she added, some cultures regard injections as more effective therapy, so more acceptable, than pills. “There’s no one size fits all, that’s really the answer.”

RESOURCES

Journal article: www.bit.ly/NEJMHIVfail

Website: www.mtnstopshiv.org



NIH meeting advances Alzheimer's research agenda

Scientists studying dementia are making “fantastic” advances, NIH Director Dr. Francis S. Collins told attendees of the Alzheimer's Disease (AD) Research Summit held recently on the Bethesda campus. The number of people with dementia is expected to skyrocket globally over the next 35 years—especially in developing countries—but Collins expressed hope that effective interventions will be discovered soon.

Several hundred participants from academia, industry, federal agencies, foundations and advocacy groups came together for the conference, organized by NIH's National Institute on Aging (NIA), to share progress and build on previous efforts to develop an integrated, multidisciplinary research agenda. Although many challenges remain, there is cause for optimism, Collins said. “I think we've entered a new era in Alzheimer's research.”

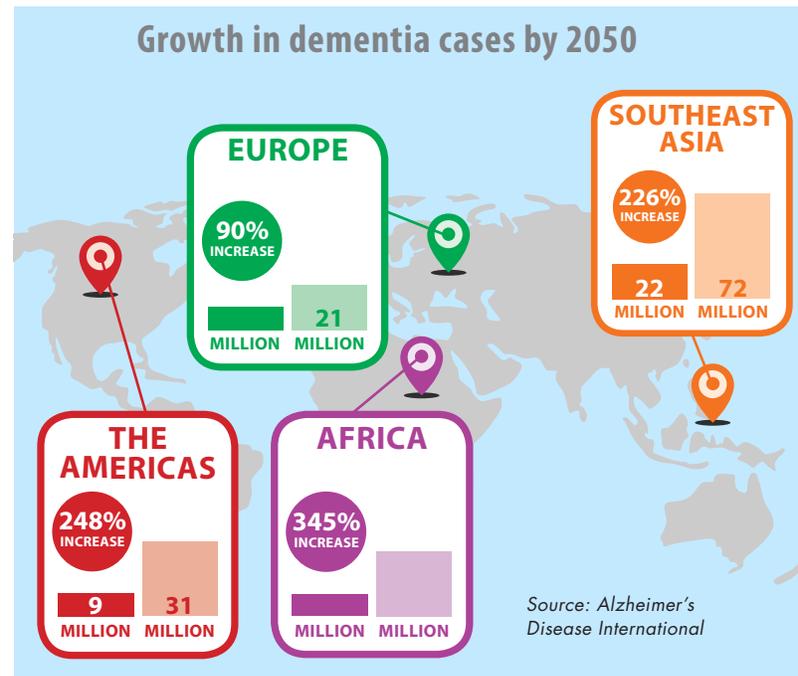
Advances in genomics, large-scale studies of individuals, and new models of collaboration and data sharing are driving progress, he said. A portal to pool complex biomedical data and analyses regarding AD has been launched by the Accelerating Medicines Partnership, an NIH-led venture designed to hasten advances.

“The enormous complexity of the human brain and the processes involved in development and progression of Alzheimer's disease have been major barriers to drug development,” said NIA Director Dr. Richard J. Hodes. “Now that we are gathering the data and developing the tools needed to tackle this complexity, it is key to make them widely accessible to the research community so we can speed up the development of critically needed therapies.”

In addition, NIA has developed a public database of research projects underway and their funding sources, known as the International Alzheimer's Disease Research Portfolio, so scientists can coordinate efforts and spot neglected areas for study. Finally, the new Precision Medicine Initiative may also aid dementia research, as it is intended to pioneer an innovative approach to disease prevention and treatment, taking into account individual differences in people's genes, environments and lifestyles.

Global burden expected to triple

For the first time in human history, the number of people older than 65 will soon be greater than those under age five, predicted Dr. Kenneth Langa of the University of Michigan. By 2050, there will be about 1.5 billion people over 65, he said. Total global dementia cases are expected to climb from 44 million now, to 135 million by 2050, according to the latest report from Alzheimer's Disease International. The annual financial burden associated with dementia is already staggering—\$200 billion in the U.S. and \$604 billion globally.



“Dementia has a large and growing health, social and economic impact around the world, with a current magnitude as great as common diseases such as heart disease and cancer,” Langa observed.

Although the current dementia incidence rates are pretty similar around the world—about 5 to 7 percent—the prevalence estimates for 2050 indicate that will change dramatically, according to Dr. Martin Prince of King's College London. The number of dementia patients is expected to double in the North, triple in Southeast Asia, and quadruple in Africa and Latin America. “It's crucial that we have a global perspective on this,” he noted.

Prevention possibilities

However, there have been some positive developments, Langa reported. Age-specific risk of dementia has dropped in high-income countries over last 25 years. There is some evidence that the expansion of educational opportunities is driving that decline, he said.

Prevention is beginning to rise on the research agenda, Prince said. A review he conducted of existing studies found robust evidence for four associations—education in early life, hypertension in midlife, and diabetes and smoking across the lifespan.

Although the disease burden is growing rapidly, research funding is also rising, up 42 percent since 2011, Collins observed. “Scientific opportunities have never been better and the public health need so compelling.”

RESOURCE

www.bit.ly/ADresources

PROFILE

Fogarty Fellow studies trauma, injury in Ghana

By Cathy Kristiansen

Research wasn't part of his original career plan, but Dr. Rockefeller Oteng found he was lacking the skills to adequately measure the outcomes of his work. Part of a team in Ghana to train physicians and establish the country's first emergency medicine department, he discovered it was difficult to determine if they had actually improved patient outcomes over the first two years of the program.

Oteng was on assignment from the University of Michigan to Komfo Anokye Teaching Hospital (KATH), where the paper medical record system was incomplete and patients received multiple identification numbers as they moved through the different hospital departments. Part of capacity building is being able to document there's a problem and that the solution you are proposing will help, he said. "As I grew as a clinician and as a global health worker, I realized I needed more of an understanding of clinical research and its effect and possible uses in my work."

After some thought, Oteng applied to Fogarty's Global Health Program for Fellows and Scholars to venture into this new field. "For me, the Fogarty fellowship was that next step of learning how to do research, how to describe my thinking and how my discoveries could be translated to others."

Oteng said without the fellowship, it would have been difficult to carve out time from his clinical and teaching work. But he flourished under the direction of two experienced mentors, Dr. Cheryl Moyer from his home institution and Dr. Charlie Mock from the University of Washington. His learning was well-structured, he recalled. For instance, Moyer assigned chapters from a research methods book and followed up with regular calls. "I would explain my interpretation and we would talk about how to apply those concepts to what I was doing," he said. "It was 'read and apply,' which for me is a super effective way to learn new material and absorb it and make it a part of my daily activities."

For his fellowship research project, Oteng tackled his question of how patient outcomes had changed because



Rockefeller A. Oteng, M.D.

Fogarty Fellow:	2013 - 2014
Fellowship at:	Komfo Anokye Teaching Hospital, Ghana
U.S. organization:	University of Michigan
Research Project:	Road traffic injuries and trauma outcomes

of the new emergency care department. He managed to locate and analyze records on 50 trauma patients and produced two recommendations: include more sepsis training in the curriculum, because it was a common diagnosis, and give patients only one identification number for all departments, so they are more easily tracked.

Frustrated by the paucity of data at the hospital, he obtained a supplemental grant to establish an emergency medicine research office in Ghana. That enabled him to create an electronic data base, which now provides a searchable collection of patient information to better document treatment outcomes, spot trends and identify teaching topic priorities. Oteng recently submitted an NIH grant application to expand research training in the country. "The fellowship has paid multiple dividends," he observed.

Preventable deaths from injury, trauma or treatable infections are a heavy health burden throughout sub-Saharan Africa. It is Oteng's hope that the expertise developed in Ghana will be shared throughout the region. Some of the support comes from the Medical Education Partnership Initiative (MEPI), which is co-administered by Fogarty. A dozen African countries make up the MEPI network, which is designed to share expertise. "We're trying to build something that is respectful and sustainable," Oteng said. "It's difficult but it will create leaders who can go on to do incredible things, not only in their country, but for their neighbors."

Oteng was born in Ghana, but moved to the Washington, D.C. area when he was nine years old. Although he initially leaned toward journalism, he decided he could make more of a difference in people's lives as a doctor. "Emergency medicine became my definition of what a doctor is," he said. "You're trained to be ready for anything, so that anytime, anyplace you can have a positive effect on what is happening."

RAJIV SHAH, M.D., M.B.A

Dr. Rajiv Shah stepped down as USAID Administrator in February 2015, having led for five years nearly 10,000 staff in more than 70 countries to advance USAID's mission of ending extreme poverty and promoting democratic societies. Previously, he served as Undersecretary and Chief Scientist in the U.S. Department of Agriculture. Prior to that, he spent eight years at the Bill & Melinda Gates Foundation, where he managed efforts in global health, agriculture and financial services. He is a graduate of the University of Michigan, the University of Pennsylvania School of Medicine and the Wharton School of Business.



What are your thoughts as you leave USAID?

I am really proud to have had the opportunity to reflect, and represent, the best of what America is about—enterprises that started in the fight against the earthquake and the recovery of Haiti, to the more immediate effort to stop Ebola in its tracks in West Africa. I am deeply proud of efforts that so many of you have partnered with myself and our teams on in the past years to build bold new public-private partnerships to end hunger, to eliminate preventable child death, to deliver electricity to hundreds of millions of people who still live in the dark, and to create an opportunity for justice and basic human aspirations.

There are so many people around the world that still, incredibly, live and subsist in conditions that—despite our thoughtfulness—we can hardly empathize with, and hardly experience ourselves. Taken together, my experience over these past years has really taught me that when we pursue this mission with humility, respect, and a focus on partnership with results, we can build the kind of political support that is required for America to really lead the charge to end extreme poverty in the coming decade-and-a-half.

How have you changed how the agency operates?

We've embraced transparency, demanded new standards of rigor and efficiency, and made tough trade-offs in our projects and our programs—including shutting down 38 percent of our total program activities. That includes shutting down 30 global health programs in countries around the world, and about that many agriculture programs as well. Those were tough cuts to make—because I know that, even in their least effective form, those are good projects and programs that make a difference in the lives of the poor. But we made those trade-offs so we could invest in where we thought we could get the greatest value for our investment, we could operate at scale, and we could really transform the face of global hunger, of child death, of access to water, of access to education.

We made those tough calls in order to convince Congress to help us recapture our budget authority (which they supported), rebuild our staff (which we have accomplished),

and diversify our community of partners so we are working with more local organizations and private sector partners in particular. Taken together, these efforts have formed the foundation of a new model of development that tries to harness the power of business, investment, and innovation to end extreme poverty. Instead of just hiring a contractor to build a road or write a check to deliver health services, we built the U.S. Global Development Lab, to have an entity that would connect us to the brightest minds and best new technologies that can achieve our objectives faster, cheaper and more efficiently. With partners like Cargill and Coca-Cola, Texas A&M and Duke, the Lab's investing in high-impact innovations—from a low-cost infant resuscitation device, to new protective suits for health care workers.

What lessons have you learned?

First, I believe we must celebrate the people who do this work as national heroes. They do not often wear uniforms or win medals, but they do risk their lives in service of our country and our mission of helping those in need. Second, we know that achieving this mission requires not only celebrating exceptional people with great hearts and strong minds, but also a strong, empowered and accountable development agency. Third, as part of that commitment, we do have to enshrine some of these recent successes into law through legislation. Fourth, we will always have to balance competing legislative and Administration priorities. But our commitment to the values that underlie America's success and American assistance can never waver. And that's why—across all of our work and all of our programs—we should have strong and capable democracy, rights and governance programming. Fifth, while it's understandable that American global leadership is not going to touch or transform every part of the world, there is at least one area where we fall far short of our capabilities. In infrastructure, there is a more than \$1 trillion deficit annually in just Africa alone, and it remains the single greatest barrier to creating true, broad-based growth.

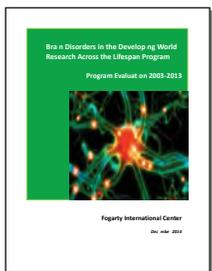
This is a condensed version of Dr. Shah's final speech as USAID Administrator. Complete text is at www.bit.ly/ShahExit

Brain program catalyzes research

. . . continued from p. 1

The brain initiative, managed by Fogarty's Dr. Kathy Michels, is structured to support exploratory or developmental research grants (R21s), full research project awards (R01s), as well as an annual network meeting. During the R21 award period, applicants have two years to initiate preliminary studies and training, and to prepare information to apply for a more comprehensive R01 award that incorporates both research and, importantly, capacity building. The program model allows investigators in the U.S. and other high-income countries to gain experience working in low- and middle-income country (LMIC) settings while strengthening the research base of the U.S. and foreign institutions in LMICs through research collaborations.

The program evaluation was conducted with information from a survey, NIH databases and interviews with NIH staff, grantee investigators and foreign collaborators. Portions of the data collection and analysis were conducted by the Science and Technology Policy Institute, a federally funded research and development center chartered by Congress to advise U.S. government agencies. Data collection and analysis was designed and overseen by Fogarty's science policy division. Representatives from NIH partners with equities in the brain program reviewed and approved the report.



Evaluation details program's achievements

One metric of the program's success is the number of publications produced, which enable grantees to share relevant and important research evidence with the brain disorders community. Investigators have generated discoveries in topics across the spectrum, from

mental health and substance abuse, to peripheral nervous system trauma, to gene-environment interactions. During the first 10 years of the program, participants published 435 peer-reviewed articles in 249 unique journals, in addition to 14 books or book chapters, the evaluation stated. In addition, grantees also produced tools for clinical assessment in the LMIC context, developed and evaluated new interventions, and identified novel lab tools or methods.

Nearly all program participants reported their projects included training or mentoring at the LMIC site, in skills, methods or procedures essential to the research project, the survey found. About 70 percent also held training in a high-income country, as well as hosted a variety of workshops on specific brain disorders topics or clinical or research skills. The majority reported training in research

Photo by Curt Camermark/World Bank



ethics as a component. Almost half supported training for developing country personnel at an LMIC site that was not a primary collaborator on the project. The program supported in-depth instruction for at least 138 scientists, for an average of 23 months.

In the survey, a number of grantees reported the program had a significant impact on advancing their careers and creating a research path. One noted the initiative helped upgrade his university's ranking due to the increased research capacity. Participants also commended Fogarty for hosting annual network meetings, maintaining an active Listserv and facilitating communication through social media.

Discoveries inform policy

In addition to contributing to a growing scientific field and building research capacity in developing countries, there are several examples where data generated by program participants have provided critical evidence used to inform international and national practice and policy. While the evaluation acknowledges it is difficult to determine the direct influence of projects on policy decisions, grantees reported a number of compelling anecdotes that are presented as case studies in the evaluation's appendix. These include identifying and helping remove a global barrier to availability of an anti-epileptic drug in Africa, increasing awareness of fetal alcohol syndrome on a national level in Russia, and convincing the Peruvian government to institute acyclovir treatment for Herpes Simplex Virus encephalitis.

Projects generate spin-offs

In the survey, many grantees described how they successfully extended the reach of their brain program-funded activities through additional funding. Specifically, 65 percent of awardees report having submitted applications to other funders for spin-offs, or new research projects that were catalyzed or otherwise enabled by the brain program. Nearly half of these have been funded—a dozen by NIH, three by Canada, 15 by LMIC countries and 19 by foundations and other organizations.

Review identifies areas for improvement

Despite the program's successes, there are areas for

improvement, the evaluation concluded. Participants expressed concern that review panels are not always well informed about the program's intentions in terms of capacity building versus research, nor did they always possess a good understanding of some of the mitigating factors involved in international research. In addition, the process of transferring funds tends to be a slow and time-consuming procedure, some reported.

“With broad support from across NIH, we have been able to catalyze the field of brain disorder research on topics of relevance to developing countries, where these issues pose a growing problem.”

– FOGARTY DIRECTOR DR. ROGER I. GLASS

Several grantees suggested the program promote further engagement in LMIC cultures or governments. One survey respondent stated that there should be a greater emphasis on the cultural or international variations in health factors. Another discussed the need for better dialogue between the NIH and governments; with approvals for protocol and funds substantially different in LMICs, improved communication could be valuable in avoiding delays in funding. Other awardees reported the lack of sufficient skills among LMIC partners posed a barrier to collaboration and suggested training be provided for research methodology and advanced statistical analysis. Finally, it was recommended that the program should facilitate a multi-country approach.

Specific instances would be encouraging multi-site projects in different LMICs or allowing lead investigators and funds to move among institutions more easily so they can set up additional research centers and sites in various countries. The evaluation recommended future iterations of the program should enhance collaboration and networking to more firmly establish a community of practice, strengthen the focus on implementation science and develop a systematic approach to measuring capacity building. In addition, efforts should be made to develop funding partnerships beyond NIH and encourage grantees to dovetail research efforts with other international, large-scale, longitudinal or cohort neuroscience studies. However, the report suggested the program should maintain its existing flexibility in how capacity building is defined

Number of Awards by I/C (FY2003-FY2013)		
	R01	R21
NIAAA	1	2
NIA	5	8
NIDA	2	8
NIMH	7	20
NIEHS	2	12
NINDS	10	18
NICHD	8	8
FIC	2	43
TOTAL	37	119

and continue to support research on a range of disorders occurring at different points in the lifespan.

Program enjoys broad support

NIH partners listed on program solicitations over time have included the National Eye Institute, National Institute on Aging, National Institute on Alcohol Abuse and Alcoholism, National Institute of Child Health and Human Development, National Institute on Drug Abuse, National Institute of Environmental Health Sciences, National Institute of Mental Health, National Institute of Neurological Disorders and Stroke, and the Office of Dietary Supplements. Other partners that have provided funding are the Institute of Neuroscience, Mental Health and Addiction at the Canadian Institutes of Health Research, the National Council of Science and Technology in Mexico, Autism Speaks and the National Alliance for Autism Research.

The evaluation is part of a larger brain disorders-related initiative spearheaded by Fogarty's Center for Global

Health Studies, which will result in a journal supplement outlining gaps, opportunities, and emerging priorities in brain disorders-related research and training as they relate to LMICs.

“With mental, neurological and substance use disorders forecast to climb in the next decades, it is critical we continue to support this valuable program,” Glass noted.

“Because the rise will be steeper in developing countries—due to the continuing and long-lasting effects of early life trauma, infectious diseases and malnutrition—we must strengthen our efforts to reduce this terrible burden.”



RESOURCE

Evaluation report: <http://bit.ly/BrainEval>

Global swine trade facilitates evolution, spread of flu

Live pigs are transported between many parts of the world, spreading the influenza viruses they carry, and allowing them to mix and evolve in ways that could produce another influenza pandemic. To prepare against future outbreaks in humans, countries must step up swine surveillance and encourage vaccination of swine workers, according to recent studies.

In research published in *Nature Communications*, Fogarty scientists Drs. Martha Nelson and Cecile Viboud and their international collaborators investigated how swine trade can spur the evolution of influenza, including in the 2009 H1N1 pandemic.

“The central question is how a flu virus jumps from animals to humans, and we understand so little,” Nelson said. “We must gain more understanding of viral evolution in animal hosts or we’re going to be just as flat-footed when the next pandemic occurs.” In the 2009 pandemic, the influenza virus transmitted from swine to people, with the first human outbreak in Mexico. “But we have no idea where that virus evolved undetected in pigs for many years or how it got to Mexico.”

In their study, the largest of its kind to date, the team analyzed live pig trade data from 146 countries and whole-genome swine influenza sequences from 10 countries. Viral movements correlated strongly with trade patterns. Europe and North America—major swine exporters—were the main sources of viruses found in Asian countries, but a surprising discovery was that China had very little influence on its neighbors, largely because it keeps most of its farm-raised pigs for the large domestic market. Surveillance data were very limited in many places that import pigs from different continents and are likely to be mixing grounds for viral evolution, including Russia and Southeast Asia.

Despite trade’s role in fueling the risk of pandemics, Nelson acknowledged that limiting such live pig

movements—except perhaps quarantining noticeably sick pigs—would be impractical and not necessarily

prevent outbreaks because of the ease with which humans can infect pigs. Human-to-pig transmission of influenza is the topic of another paper by Nelson, co-authored by Dr. Amy Vincent of the U.S. Department of Agriculture, and recently published in *Trends in Microbiology*. Their review highlighted the surprising frequency with which humans infect swine with influenza viruses, far more than the other way around.

The circulation of human influenza viruses in pigs is likely to contribute to the next pandemic. Genetic research is revealing the extent to which influenza viruses can reassort in pigs by exchanging RNA. The H1N1 pandemic virus was a reassortant, with gene segments from North America and Eurasia. “Reassortment allows the virus to evolve rapidly and unexpectedly, and to overcome evolutionary hurdles that might be impossible through simple mutation,” Nelson said. “It can make big leaps in mutational space.”

Nelson and Vincent urged more attention be paid to the human-pig pathway, for instance by enhancing vaccine strategies in swine workers, learning more about the mechanisms enabling the virus to move between the two species, and further expanding global surveillance of the influenza virus in pigs.

Although pig surveillance has picked up around the world since the 2009 pandemic, the animals receive much less attention than birds, another particularly accommodating host for influenza genetic diversity and reassortment. Bird deaths spark media headlines, intense surveillance and prophylactic killings, but while sick pigs may lose weight, they typically stay alive. “You can have viruses lurking in pigs that might be more dangerous to humans, but we’re not detecting them, they’re not in the news,” Nelson said. “In some ways, the pig viruses may be even more dangerous because they’d be silent threats.”



Photo courtesy of USDA/ARS

Global trade of live pigs increases the risk of an influenza pandemic, research shows.

RESOURCE

www.bit.ly/swinefluresources



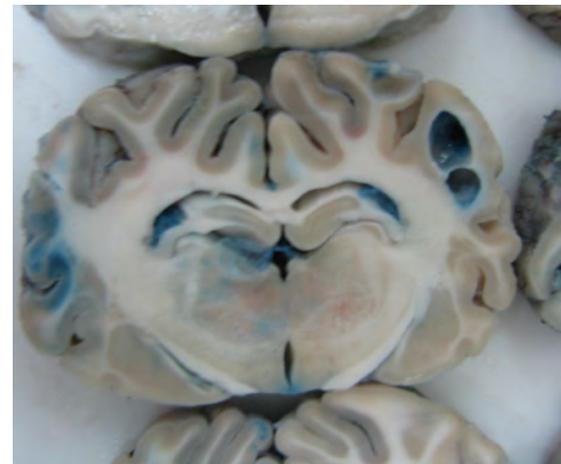
Photos by Miguel Marzal/Universidad Cayetano Heredia

form the basis for the established standard of care for neurocysticercosis. Their complex, multidisciplinary studies require an understanding of epidemiology, genomics, imaging, data analysis, animal models, bioethics and clinical trials. Since 2006, Fogarty has provided support to train more than 90 Peruvian scientists to participate in this critical work, including 25 who earned master's degrees and five who received their Ph.D.s. Garcia says that has created a solid research structure attracting funders, such as the NIH's National Institute of Allergy and Infectious Diseases (NIAID), the Wellcome Trust and the Bill & Melinda Gates Foundation, which is supporting the Tumbes eradication program.

Garcia's team has studied several elimination strategies, including an effective vaccine for pigs that was developed in Australia. "We have had major successes," noted Garcia. "Demonstrating that we can wipe out the disease with focused efforts in targeted villages provides a major advance in the control and possible elimination—and perhaps eventual eradication—of this terrible disease." But barriers remain before the intervention can be scaled up and adapted for other locations, he acknowledged. Especially challenging is the fact that the vaccine must be administered in two doses, requiring staff to catch each pig twice. "It's logistically complicated, we need to find a vaccine that works in a single dose," he said.

Garcia recently visited NIH to present his work, in a lecture sponsored by NIAID. He said although the disease was identified in the 1800s, only recently have sophisticated imaging tools allowed scientists to better understand the disease. After exposure in humans, it takes about three months for brain cysts to grow. Three to five years later, they begin to die and calcify, which is when seizures and other issues frequently develop.

Simple blood tests can determine the presence of the disease, Garcia noted, but CTs or MRIs are required to see if the parasites are alive or dead. Even then, scientists are split on the best treatment. Some recommend sufficient doses of drugs to kill the parasites but others caution that can lead to harmful brain inflammation. "You have to use common sense," Garcia suggested. "In general, we think killing the parasites is beneficial."



Peruvian scientists have tested antiparasitic drugs in pigs. The blue dye indicates disruptions in the blood-brain barrier.

A vaccine has proven very effective at eliminating cysticercosis in Peruvian pigs but requires two doses.

Scientists work to eliminate disease carried by pigs

Pigs are an important source of nutrition in many parts of the developing world but can spread a neurological disease that poses serious human health hazards. Cysticercosis is a preventable parasitic infection of the central nervous system caused by the pork tapeworm, *Taenia solium*. A person can get the disease through unhygienic practices, by consuming eggs that have been excreted by someone with an intestinal tapeworm. The larval cysts can infect brain, muscle or other tissue and are a major cause of adult-onset of seizures in low-income countries. People with the disease may also experience chronic headaches, depression, strokes and other problems.

Cysticercosis mainly affects rural farming communities, where poor families allow pigs to roam free to search for food that includes feces. "That's the reality in many little towns around the world," according to Dr. Hector "Hugo" Garcia, a Fogarty grantee who has spent his career studying cysticercosis. Garcia, a microbiology professor at both the Universidad Cayetano Heredia in Lima, Peru and Johns Hopkins University in Baltimore, has been leading a decade-long effort to eradicate the disease in Peru's northern coastal region of Tumbes. He is also a researcher at the National Institute of Neurology in Lima.

The research discoveries he and his team have made

OPINION

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

Brain disorders research: a decade of progress



The breadth and complexity of brain disorders make them some of the most difficult conditions to diagnose and treat, especially in the developing world, where there may only be one psychiatrist or neurologist in an entire country. These disorders occur throughout the lifespan—from infants starved of oxygen during difficult births, to children whose development is stunted due to malnutrition or

exposure to infections or toxins, to adults who develop depression or dementia. Such mental and behavioral issues cause the world's largest burden of disability, according to the Institute of Health Metrics and Evaluation.

That's why Fogarty has been working with its NIH partners for more than a decade, to catalyze this field of research and develop badly needed expertise in low- and middle-income countries (LMICs). As we celebrate this milestone, it's important that we stop to review our progress and consider how best to move forward. I'm pleased to report we recently completed an evaluation of the program, which highlighted some important accomplishments and provided useful guidance for its next iteration.

With a total investment of about \$84 million awarded through more than 150 grants, investigators have generated discoveries detailed in 435 peer-reviewed articles and 14 books or book chapters. Scientists developed clinical assessment tools designed for low-resource settings, produced and tested novel interventions, and identified new approaches that show promise. To help sustain this significant momentum, the funding enabled long-term training of at least 138 scientists.

As we and our partners consider the program's next phase, the evaluation suggests we enhance collaboration and networking to more firmly establish a community of practice, strengthen our focus on implementation science and develop a systematic approach to measuring capacity building. For more details of the evaluation, please see the story on pages 6-7 in this issue.

One of the most heartbreaking and costly brain disorders is Alzheimer's Disease. By 2050, the number of people living with dementia around the world is expected to triple, reaching 135 million. Nearly three-quarters of them will reside in developing countries, which are least well-equipped to bear this burden.

Despite these distressing predictions, I was encouraged by some favorable news presented at the recent NIH Alzheimer's Disease Summit. Age-specific risk is declining in high-income countries, likely due to rising levels of educational attainment. This is a welcome development since literacy levels are climbing in LMICs—even among women and girls. With the increasingly wired world and growing libraries of free online learning tools, this trend should continue. Researchers believe other modifiable risk factors are also likely to curb dementia, especially diabetes, smoking, depression and physical activity. To learn more about this important meeting, please see page 3.

It is vital that countries monitor the dementia epidemic closely so scientists can study changes in prevalence and relate those to differences in exposure to risk factors. By pooling this type of data and working together as a global community, we might someday be able to prevent and treat this dreadful disease.

Finally, in March, I had the great pleasure to travel to a scientific meeting hosted by our grantees at the Center for Cysticercosis Elimination in Tumbes, Peru. The Center's dedicated team—including a significant number of scientists trained with Fogarty support—has made great strides in studying how to diagnose and treat cysticercosis, a parasitic infection that often infects the brain and is a major cause of adult onset seizures. They have also made significant progress toward their long-term goal of eliminating the disease altogether by vaccinating pigs, which spread the disease. You can read more about this incredible success story on page 9.

By continuing to build the human scientific capacity that is so badly needed in low-resource settings, we can begin to make real progress against the full scope of brain disorders, which are the cause of so much global suffering.



Goosby is appointed as UN Special Envoy on TB

Ambassador Eric Goosby has been selected as the UN Secretary-General's Special Envoy on Tuberculosis. Goosby—a professor at the University of California, San Francisco's medical school—previously served as the U.S. Global AIDS Coordinator, overseeing implementation of the President's Emergency Plan for AIDS Relief (PEPFAR).



NIH Foundation awards Lurie Prize to brain expert

The Foundation for the National Institutes of Health has awarded Dr. Karl Deisseroth its 2015 Lurie Prize in Biomedical Sciences, for the development of scientific approaches for studying cell function, especially neurons. Deisseroth is a professor at Stanford University and is a Howard Hughes Medical Institute Investigator.



Fogarty bioethics trainee promoted in Egypt

Dr. Azza Saleh, a former trainee in the Fogarty-funded bioethics program at the University of Maryland, Baltimore, has been chosen to head the central administration for development and research at Egypt's Ministry of Health. Saleh also is co-coordinator of the Egyptian Network of Research Ethics Committees.

Bioethics commission studies Ebola

The U.S. Presidential Commission for the Study of Bioethical Issues met recently to consider the Ebola epidemic and has issued recommendations regarding the ethical dimensions of restrictive public health measures, the use of placebos for treatment and vaccine trials, and collecting and sharing bio-specimens for future research.

Full report: www.bit.ly/BioEbola

US malaria initiative unveils strategy

The U.S. President's Malaria Initiative (PMI) has launched its next six-year strategy to further reduce malaria deaths and substantially decrease malaria illness, toward the eventual goal of elimination. The plan pledges support for long-term partnerships with scientific institutions and operational research to overcome bottlenecks and test new tools.

Full plan: www.bit.ly/PMIstrat

Book examines health rights in Africa

A newly published resource explores approaches to strengthen sexual and reproductive health rights in the African region. The free, downloadable book—produced by the Pretoria University Law Press—addresses emergency obstetric care, HIV/AIDS, adolescent sexual health and rights, early marriage and gender-based sexual violence.

Free book: www.bit.ly/AfrBook

Epigenomic data catalog is available

NIH-supported researchers have mapped the epigenomes of more than 100 types of cells and tissues, providing new insight into which parts of the genome are used to make a particular type of cell.

News release: www.bit.ly/epiGenome

WHO releases health literacy toolkit

The WHO has produced a health literacy toolkit for low- and middle-income countries, consisting of fact sheets to empower communities and strengthen health systems.

Toolkit: www.bit.ly/HealthToolkit

Scientists approve of public engagement

Most American scientists support active engagement in public policy debates, according to a recent Pew Research Center report. Although scientists believe they face a challenging environment, about 87 percent say it's necessary to participate in discussions with citizens and journalists to further their work and careers.

Full report: www.bit.ly/PewSci

HHS expands public access to research

An estimated 110,000 peer-reviewed scholarly articles will be made available each year under the new U.S. Department of Health and Human Services (HHS) public access plan, announced recently. Other HHS operating divisions—including CDC and FDA—will follow the practice developed by NIH a decade ago to make federally funded research results public. More than 3 million papers are currently available through the NIH's National Library of Medicine's PubMed Central, a free archive of biomedical and life sciences journal literature. New areas to be included are public health, comparative effectiveness and emergency preparedness research. Another component of the plan aims to capture and make public research data, building on the existing collection at www.healthdata.gov.

"Together we can accelerate the movement of science and research into the hands of as many as possible," said HHS Secretary Sylvia M. Burwell in a letter accompanying the policy notice.

As part of the effort, NIH will be issuing for public comment a policy proposal to require all NIH-funded investigators generating digital scientific data to submit a plan addressing how, when, and where their data will be managed and shared. The policy will apply to research funded through grants, contracts, and the intramural program, and will replace the current policy, which applies only to extramural awards that request \$500,000 or more in any given year. The plan was developed in response to a White House directive that federal research agencies increase access to peer-reviewed scientific publications and digital data developed by researchers.

HHS blog: www.bit.ly/HHSAccess

Funding Opportunity Announcement	Details	Deadline
International Research Ethics Education and Curriculum Development Award (Bioethics) (R25)	http://bit.ly/Fogbio	May 22, 2015
NIAID Global Infectious Disease Research Administration Development Award for LMIC Institutions (GID) (G11)	http://bit.ly/GIDJly15	July 15, 2015
Global Infectious Disease (GID) Research Training Program (D43) (D71)	http://bit.ly/GIDJlyD43 http://bit.ly/GIDJlyD71	July 29, 2015 July 29, 2015
Fogarty HIV Research Training Program for LMICs (D43) (D71) (G11)	http://bit.ly/FogHIVD43 http://bit.ly/FogHIVD71 http://bit.ly/FogHIVG11	July 30, 2015 July 30, 2015 July 30, 2015
Fullbright-Fogarty Postdoctoral Awards	http://bit.ly/FogFul2015	Aug 3, 2015

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

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NIH examines lead's impact on dementia, bone density

Lead is toxic to the human brain and its use as an additive in gasoline has largely been stamped out, greatly reducing new human exposure. But some scientists wonder whether lingering traces of the metal stored in the body might reenter circulation later in life, fueling dementia and reducing bone function.

The NIH is seeking information on various aspects of these topics, as well as unique opportunities to conduct studies in related areas. Fogarty—in partnership with the National Institute on Aging, National Institute of Child Health and Human Development, and National Institute of Environmental Health Sciences—has issued a Request for Information, with responses to be submitted by June 30, 2015.

Lead was added to gasoline globally to stop vehicle engine knocking and thus became airborne in exhaust. Populations in the U.S. were exposed from the 1920s until 1980, while residents in many other countries also breathed it in for decades. Leaded gasoline continued to be sold in some places until just two years ago, according to the UN's Environmental Program.

Research has shown that lead impairs cognitive function in the developing brain, but much less studied is the metal's impact in the adult and especially the aging brain. Animal and human studies have identified that lead can remain in the body for many years, primarily in bone. Scientists want to know whether this interferes with bone function later in life thus raising the risk of fracture and, if osteoporosis develops, whether this releases lead more generally into the body again, where it could compromise brain health.

RESOURCE

NIH Request for Information: <http://bit.ly/RFI4lead>

Photo by Elson T. Elizaga, courtesy of Photoshore



An elderly woman sits by a door in Cagayan de Oro, Philippines.