Universities consider sustainable future in global health

By Ann Puderbaugh

SAN FRANCISCO – The symbiotic relationship between planetary health and human health was the overarching theme of the 7th annual Consortium of Universities for Global Health conference held in April. More than 1,800 attendees gathered in San Francisco for the three-day meeting, titled “Bridging to a Sustainable Future in Global Health.”

Envisioning a “realistic utopia” rooted in the idea of sustainable development, The Lancet’s editor Dr. Richard Horton used his impassioned keynote address to urge the group to reimagine the idea of prosperity, strive to fill knowledge gaps and collaborate to more effectively implement what is already known.

“It’s about the notion of intergenerational equity that future generations are as important as our own generation,” Horton suggested. “It’s about the oneness of all life on this planet and not only that, the symbiosis between life and our planet. It’s also about the centrality of human systems—it is down to us to shape the future.”

When global crises such as Ebola strike, those living in low-resource settings experience the greatest devastation, Horton said, noting that is when it’s more important than ever for the global community to come together. “The problem is that when we see our global systems failing, or when people think they are failing, there is a temptation, an understandable temptation, to retreat into national isolation,” Horton observed.

Horton and his colleagues on the Rockefeller Foundation-Lancet Commission on Planetary Health published a call to action in July 2015, asking the global community to adopt a more holistic approach to health.

The population explosion, escalating frequency and speed of global travel, increasing amount of livestock breeding, expanding destruction of the world’s rainforests and other human behaviors contribute to the spread of infectious diseases, said Sir Richard Feachem, of the University of California, San Francisco, during a panel discussion. “It is a new age of pandemics,” he continued, “they do keep coming and we live in apprehension of the big one.”

Weak national health systems are a key problem in pandemic surveillance and response, given that only 20 percent of WHO member countries meet the organization’s guidelines for core capacities, noted Jason Cone, director of the U.S. section of Doctors Without Borders. Many small outbreaks go unreported, he said, and there is no central validated database to track them.

... continued p. 2
Universities consider sustainable future in global health

“Our global health security architecture, while constantly improving, has some major cracks in the foundation when it comes to preparedness, surveillance, response and finally, the really broken state of affairs in the biomedical innovation system required to combat existing and emerging pathogens,” said Cone. Currently, there is a failure to connect innovation to access, so advances often don’t reach the patients in need, he added.

With deadly outbreaks of preventable diseases such as measles going unchecked, Cone suggested priorities be reexamined. “It really thrusts to the attention a real question, about how realistic is it for us to confront some of these threats when so many of the diseases we already have viable countermeasures for are not reaching the people that need them the most.”

Pandemics should be viewed as a new dimension of global security with “deep societal impact and enormous economic consequences,” said Dr. Maria Freire, president of the Foundation for the NIH and member of the Commission on a Global Health Risk Framework for the Future. The Commission, convened by the National Academy of Medicine, recently issued a report calling for a $4.5 billion investment to bolster global response capabilities. Disease outbreaks take a significant financial toll, Freire said, similar to terrorist attacks in that travel is restricted and commerce shuts down. And yet, as a society, we have chosen to prioritize our response to terrorism over pandemic preparedness, she added.

The NIH was well-represented throughout the conference, with separate satellite sessions hosted by the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases (NIAID). Representatives from the National Institute of Mental Health (NIMH) and the National Heart, Lung and Blood Institute (NHLBI) also presented information on their global health research activities and upcoming funding opportunities. NHLBI staff highlighted a new program being established to expand low-income country capacity to conduct translational research, aimed at improving the uptake of proven-effective interventions into routine clinical practice.

During the proceedings, NIAID Director Dr. Anthony S. Fauci was honored as the 2016 John Dirks Canada Gairdner Global Health Award recipient. In his remarks, he addressed the “truly breathtaking” advances in the battle against HIV/AIDS but said implementation of the findings must be improved if the U.S. epidemic is to be brought under control. “Rwanda is doing much better than we are in terms of suppressing viral load,” Fauci noted. “It’s really embarrassing, and we need to do much better.”

Globally, there are also “formidable obstacles” remaining in the battle against HIV, said Dr. Peter Piot, in a panel discussion that followed. Flat funding, sustainable drug supplies and retention of HIV-positive people in treatment are some of the challenges he detailed. Also troubling, advocates and funders have lost the sense of urgency and in some cases dropped HIV from the agenda. “The message on the end of AIDS has been quite counterproductive,” he observed. “We see lots of countries in Europe, where the perception is, it’s over.”

In another panel session, alumni of Fogarty’s Global Health Program for Fellows and Scholars presented the results of their research on topics such as the role of stigma in HIV transmission in Kenya, trauma systems development and care in Ghana, and drug use and HIV treatment in Indonesian prisons. “We feel that the greatest impact we can have on the global health community is through the training of researchers in the global health sphere, which provide tremendous returns on our investment,” said Fogarty Director Dr. Roger I. Glass.

In an effort to significantly reduce indoor air pollution and lower cardiopulmonary risk in a rural community in Peru, one program participant is studying the use of gas-powered versus traditional biomass cookstoves. Dr. Catherine Miele, of Johns Hopkins University, said her Fogarty fellowship was an “incredible experience” that enabled her to learn to set up and run a field intervention trial. “Really, none of it would have been possible without having time, an extra year to do this research, so that as I continue with my medical training I can keep my foot in the research door.” Miele and her colleagues plan to apply for additional Fogarty funding to scale up the project.

Sustainability and environmental impact are key to her initiative’s success, said Miele. “I really benefitted from the collaborations on these studies working with environmentalists, behavioralists and anthropologists, and this is really what ties it in to planetary health,” she added. “Not only am I focused on getting the cardiopulmonary disease burden down on this study but how does it impact the community around it?”

RESOURCES

Academic partnerships key to success, study says

Partnerships are a key component of successful global health programs but could be strengthened by addressing inequities in relationships between high- and low-income institutions, developing additional South-South collaborations and better preparing North American students for training in low-resource settings. These and other findings were the result of a study by the Center for Strategic and International Studies (CSIS), conducted with the Consortium of Universities for Global Health (CUGH) and the Department of Global Health at the University of Washington.

The report, titled “Global Health Programs and Partnerships: Evidence of Mutual Benefit and Equity,” also presents a framework for success to guide the development of sustainable global health programs and calls for additional funding to support partnership building. The project, launched with a panel discussion at CSIS, builds on a previous analysis of the dramatic growth of interest in global health on campuses, conducted in 2009.

For the new study, researchers surveyed 101 CUGH member institutions about their partnership activities and received 82 responses. The scientists also conducted in-depth interviews with global health leaders at 15 North American academic institutions and 11 partnering international institutions. The results showed near unanimous agreement that partnerships are beneficial and that most work well. Some issues of inequities between high- and low-income partners were noted, however, in terms of decision making related to the one-sided provision of funding, lack of bi-directional student exchange and sometimes in journal article authorship.

An analysis of funding sources for global partnerships showed universities themselves are the largest supporters, with NIH ranked second. There has been a steep migration of clinical trials over the last decade, the report stated, with medical breakthroughs increasingly coming from research conducted in low-resource settings.

“The game has shifted overwhelmingly to those countries,” observed Dr. J. Stephen Morrison, co-author of the report and director of the Global Health Policy Center at CSIS. “That’s where the clinical trials are happening, it’s where programmatic implementation is happening and it’s where discovery is concentrated. So in a way, they are sitting in the driver’s seat.”

Although traditional South-North collaborations were cited as having been the most valuable to date, nearly 40 percent of respondents said expanding South-South partnerships will be their highest priority in the future.

While acknowledging North American students are a great resource, some respondents suggested they could be better prepared for assignments overseas with improved language and cultural awareness training, and more realistic expectations of the challenges and limitations of working in developing countries.

With the study findings and a review of relevant literature, the report authors developed a framework of ten key components for starting, developing and sustaining successful global health partnerships. (see chart)

It is critical that major investments are made to develop the next generation of global leaders, both in North America and internationally, said Dr. King Holmes, a co-author of the report and founding chair of UW’s global health department. “It’s amazing to see how the young people we’ve had coming in for Fogarty training, for example, are now out running their national ministries of health or universities,” he said.

The global health community should also examine partnerships and relationships to ensure they are producing the desired results, suggested Dr. Keith Martin, co-author and CUGH director. “How can we pivot so that the impacts for our colleagues in low-income countries are really much greater,” he asked, “and that in these partnerships, they are not only going to benefit us, but are also going to benefit them in the ways that they need?”

A framework for success in academic global health programs

| 1. | Gauge enthusiasm, identify champions, organize core team |
| 2. | Prepare strategic plan |
| 3. | Secure institutional support and baseline funding |
| 4. | Establish centralized presence on campus |
| 5. | Develop future leaders |
| 6. | Guide student enthusiasm and manage expectations |
| 7. | Develop existing partnerships, identify new partners |
| 8. | Establish metrics for success, monitor progress |
| 9. | Develop and maintain communication |
| 10. | Build interdisciplinary networks |

Fogarty program has catalyzed disease modeling

By Karin Zeitvogel

In just seven years, Fogarty’s Research and Policy for Infectious Disease Dynamics (RAPIDD) group catalyzed major advances in infectious disease modeling, and helped to grow the discipline from one with little impact on public health policy decisions to one that government agencies and major international groups have incorporated into their operations, veterans of the group said.

“Things have come a long way.” said Fogarty senior scientist Dr. Ellis McKenzie, who co-founded RAPIDD in 2008.

The group has punched above its weight class in the modeling world, with RAPIDD researchers publishing more than 900 peer-reviewed papers, which have been cited more than 23,500 times, and organizing 114 workshops that have drawn more than 800 scientists from 39 countries.

Supported over its 7-year existence with $17.3 million from the Department of Homeland Security, RAPIDD has achieved its main objective of improving the modeling of infectious diseases. Since it began, RAPIDD has been credited with enhancing the understanding of pathogens ranging from measles, Ebola and rabies to the less well known Nipah virus and the Leptospirosa interrogans bacterium.

RAPIDD’s work has helped to establish infectious diseases modeling as an essential weapon in the arsenals of both policymakers and scientists, said the group’s co-founder, Dr. Bryan Grenfell of Princeton University.

“Modeling is a very cost-effective way of thinking about how to control an outbreak. It helps us to summarize our biological understanding, and suggests what key data we need to collect next.” Grenfell said. “Ellis McKenzie and his colleagues are world-leading scientists in infectious disease dynamics. In RAPIDD, they were able to bring together pre- eminent researchers whose modeling work will impact policymaking long into the future.”

The 85 core faculty and junior researchers, and 13 postdoctoral fellows who were involved in RAPIDD often pivoted quickly and applied information gathered in earlier modeling exercises to new outbreaks. Modelers who worked on how dengue is transmitted, for instance, “almost instantly” produced a map showing the projected spread of Zika throughout the Americas after Brazilian officials reported a surge in infections and microcephalic births, McKenzie said. Dengue and Zika are carried by the same mosquito, the Aedes aegypti.

“RAPIDD’s small structure and lack of bureaucracy also allowed it to quickly convene workshops, often in the middle of an outbreak,” Grenfell noted. In March 2015, for example, as the WHO reported more than 10,000 Ebola deaths in Guinea, Liberia and Sierra Leone, a RAPIDD working group held a model comparison workshop, which gave rise to a months-long competition in which modelers from the U.S., U.K. and Canada tried to predict when Ebola would peak in Liberia and how it would progress between September and December 2015. Most accurately forecast the time of peak infection, and even the weakest model held useful information, showing that transmission is not exponential at the beginning of an outbreak.

RAPIDD modelers often thought creatively to find ways to produce the information that policymakers need to resolve a health problem. For example, given the reluctance of ranchers to grant scientists access to their land so that they could gather data on the movement of livestock, which would help to prepare for a potential outbreak of foot and mouth disease in the U.S., a RAPIDD postdoctoral fellow devised a way to use veterinary records and licenses that ranchers are obliged to file, and arrived at “some pretty good guesses as to what was going on,” McKenzie said.

The scientists also undertook large-scale reviews of previous modeling exercises to identify gaps in the field. One such review looked at nearly 400 models of mosquito-borne pathogen transmission, conducted between 1970 and 2010.
The analyses of previous modeling exercises, in addition to primary research done by RAPIDD, together formed a substantial body of work that McKenzie and Grenfell call “case law.” When there is a new outbreak, modelers can refer to the case law and advise decision makers that “if it is like this other pathogen, then here’s what we should do while we’re learning more,” McKenzie said.

RAPIDD helped to narrow the gap between what researchers want from modeling—information that allows them to compare strategies for tackling an outbreak and identifying knowledge gaps—and the actionable data that policymakers seek.

For instance, RAPIDD modelers estimated that around one million children in Liberia, Sierra Leone and Guinea were vulnerable to measles following the suspension of vaccination campaigns during the 2014 Ebola outbreak.

“The message was that you have to mount an aggressive vaccination campaign when Ebola subsides,” McKenzie said. That plea appears to have been heeded by public health authorities, as measles vaccination campaigns targeting several million children were launched in Sierra Leone and Guinea in October 2015 and in Liberia a few months earlier.

“RAPIDD has taught us that by modeling a wide and diverse range of diseases—not just immediate threats—we’re better prepared to react to the next threat.”

— DR. BRYAN GRENFELL, PRINCETON UNIVERSITY

Another sign of RAPIDD’s success is that most of the group’s postdoctoral fellows have gone on to tenure-track faculty positions at top U.S. universities, where they are “educating future generations of modelers to further strengthen the field,” McKenzie said. Among them, Dr. Virginia Pitzer is an assistant professor at Yale University, where her research includes an NIH-funded project to develop statistical and mathematical models that can be used to improve understanding of rotavirus immunity and transmission in developing countries. Dr. Angela Luis, who led many of the projects in RAPIDD’s small mammals working group—affectionately known as the bats and rats group—uses mathematical models in her lab at the University of Montana to predict what leads to an outbreak, when one might occur and how a disease jumps the species barrier from animal to human.

At Notre Dame University, former RAPIDD fellow, Dr. Alex Perkins, applies mathematical, computational and statistical approaches to better understand the dynamics of infectious disease transmission and control. And Dr. Juliet Pulliam, who was part of a research team that used simulations to help inform study design decisions for vaccine trials during the West African Ebola epidemic, and whose research has included work that identified what was driving Nipah virus emergence in Bangladesh, has been named director of the South African Centre for Epidemiological Modelling and Analysis (SACEMA).

Pulliam credited RAPIDD with “changing the landscape of infectious disease modeling” by pushing researchers to do comprehensive reviews of previous studies and undertake their own research.

RAPIDD’s directors hope to procure funding to allow several working groups to continue their research, covering everything from the selection of a vaccine strain for seasonal flu to drug resistance and emerging human and animal infections in small mammal reservoirs. Keeping the working groups up and running is essential to allow scientists to act quickly when “something even more unknown than Zika comes to whack us,” McKenzie said.

Grenfell agreed.

“Zika underlines to us that we never know what will emerge as the next threat,” he said. “RAPIDD has taught us that by modeling a wide and diverse range of diseases—not just immediate threats—we’re better prepared to react to the next threat.”

RESOURCE
Website: http://bit.ly/RAPIDDlinks
Japanese fellows contribute to NIH research for more than 20 years

By Karin Zeitvogel

Dr. Tomoko Yamazaki peers into a microscope and dissects a tiny mouse embryo in a National Heart, Lung and Blood Institute (NHLBI) lab. Like many Japanese researchers before her, Yamazaki traveled to NIH to learn new techniques and advance her research through a two-year fellowship sponsored by the Japan Society for the Promotion of Science (JSPS). She has stayed on to complete her research into the origins of pericytes, the mural cells that envelop the surface of vascular tubes.

The results of Yamazaki’s work could be used to treat fetal vascular malformations, leakage and hemorrhage, she says. “Furthermore, if the scenario is applied to pathological pericyte development in adults, we may be able to prevent retinopathy, a symptom of diabetes where the loss of pericytes causes leakage of blood vessels,” Yamazaki adds.

The young researcher’s work is an example of the “high-quality science” that nearly 300 Japanese fellows have undertaken at NIH since the program began in 1995, notes NIH’s Deputy Director for Intramural Research, Dr. Michael Gottesmann.

The fellowships are “very good for young researchers as they build their careers,” says JSPS executive director, Dr. Yasuhiro Iye. Many of the researchers return to Japan after their time at NIH and become leaders in their fields, says Dr. Keiko Ozato, who recently stood down after serving for nearly 20 years as chair of the review panel that helps select JSPS fellows.

At an event celebrating the 13 young scientists who began their two-year fellowships this year, Ozato urged them to “immerse yourself in asking questions that you consider important…dedicate yourselves to science.”

One of the fellows, Dr. Tetsuro Kobayashi, is part of the team in Dr. Keisuke Nagao’s National Cancer Institute (NCI) lab that found a direct interaction between an imbalance of skin microbiota and the inflammation of atopic dermatitis in mice.

Kobayashi says working at NIH has given him an opportunity he would not have had in Japan: meeting people with diverse backgrounds and life stories. He shares lab space with two Americans, one French scientist and a German.

“You don’t see that diversity in Japan,” Kobayashi says. “Japan is a very homogenous culture, which has its good points, but I think diversity is an important part of a scientist’s training. When I got to NIH, I was surprised to see that people from different backgrounds can see one phenomenon in different ways.”

JSPS fellow Dr. Shogo Takahashi is working in Dr. Frank Gonzalez’s metabolism lab at NCI, studying bile acid regulator farnesoid X receptor (FXR) to try to determine how it impacts liver health in mice. In the past two years, Takahashi has co-authored several research papers on FXR, which helps to regulate the synthesis of bile acids and their transport from the liver to the intestine. Takahashi says recent studies have shown that FXR is a novel target for drugs that treat metabolic disease, such as type 2 diabetes, fatty liver disease and obesity.

Asked what he values most about his fellowship, Takahashi responds quickly: “This is NIH. You have the chance to collaborate with smart people from around the world.”

JSPS not only brings young Japanese scientists to the United States to work at NIH, but also offers opportunities for U.S. and permanent resident scientists to work in Japan. Hundreds of U.S.-based researchers, including around 20 from NIH, travel to Japan each year on JSPS-supported invitational and postdoctoral research fellowships lasting from 14 days to two years.

JSPS collaborates with Fogarty and the NIH Office of Intramural Research to provide the fellowships.

RESOURCES


Photos by Karin Zeitvogel for Fogarty
MenAfriVac vaccine slashes meningitis cases in Africa

By Karin Zeitvogel

It’s been hailed as a public health breakthrough and one of the biggest immunization success stories in Africa: a globally developed vaccine against meningitis A that has all but eliminated the deadly disease from the continent since its rollout in 2010.

“We have achieved something truly historic with MenAfriVac—creating an affordable, effective, tailor-made vaccine for Africa,” said Steve Davis, president and CEO of the global health nonprofit PATH, which in 2001 partnered with the WHO to set up the Meningitis Vaccine Project (MVP).

With a 10-year, $70 million grant from the Bill & Melinda Gates Foundation, MVP set out to develop an affordable vaccine against meningitis A, a bacterial infection that attacks the lining of the brain and spinal cord and kills around 10 percent of those who are infected. In Africa’s “meningitis belt”—which stretches from Senegal in the west to Ethiopia in the east—tens of thousands of people died in meningitis epidemics that swept across the continent every seven to 14 years. Most of the victims of the crippling and deadly illness were children and people under the age of 30.

PATH and WHO have hailed the international effort that led to MenAfriVac being developed “in record time and at less than one-tenth the cost of a typical new vaccine.” NIH helped to transfer the conjugation technology used in the vaccine, developed by the FDA, to the Serum Institute of India at almost no cost. Serum and SyncoBioPartners of the Netherlands provided the raw materials for the conjugate vaccine, and Serum produced it for less than 50 cents per dose.

That price point is key to MenAfriVac’s success. An African health official told MVP in 2001, “Please don’t give us a vaccine that we can’t afford. That’s worse than no vaccine.”

MenAfriVac was given to 20 million people in Burkina Faso, Mali and Niger when it was rolled out in 2010. By the end of that year’s peak meningitis period—which falls during the dry season, roughly the northern hemisphere winter and spring—the three countries reported no cases of the deadly disease among those who received MenAfriVac.

Since that first round of vaccinations, 235 million people in Africa’s meningitis belt have received MenAfriVac. Cases of meningitis A have fallen from over 250,000 during an outbreak in 1996 to just 80 confirmed cases in 2015, according to scientists at the final conference of MVP, held in February 2016. Ninety percent of people who were vaccinated with MenAfriVac in 2010 had protective antibodies in their system five years later, the WHO has said.

But scientists and advocates have warned of “catastrophic resurgences in disease” if MenAfriVac vaccination campaigns do not continue.

“Our dramatic gains against meningitis A through mass vaccination campaigns will be jeopardized unless countries maintain a high level of protection by incorporating the meningitis A vaccine into their routine childhood immunization schedules,” said Dr. Jean-Marie Okwo-Bele, WHO’s director of Immunization, Vaccines and Biologicals, in November 2015. Since then, eight meningitis belt countries have applied for funding to allow them to give MenAfriVac to children and infants.

Following the success of MenAfriVac, the Serum Institute is partnering with PATH to produce another affordable vaccine, targeting meningitis A, C, W, X and Y. Clinical trials of the pentavalent vaccine are expected to begin this year.
Fogarty Scholar casts light on alcohol injuries in Ghana

By Cathy Kristiansen

Fogarty Scholar Andrew Gardner wanted to help reduce the burden of injury in Ghana, so he decided to investigate the role of alcohol. His findings came as a big surprise to Ghanaians, who generally thought dangerous alcohol use was rare in their country. But Gardner’s research showed more than a third of injured patients seeking urgent care had been drinking.

“The study helped highlight the importance of developing countermeasures and making it routine to test alcohol levels in everyone who comes into the emergency room,” said Gardner, a medical student and participant in Fogarty’s Global Health Program for Fellows and Scholars. The initiative provides a yearlong mentored clinical research experience overseas for postdoctoral fellows and pre-doctoral scholars.

Ghana is working to reduce its level of injuries, most of which occur on the roads, and by 2050 plans to halve the number of traffic fatalities from the 2010 level of nearly 2 million. But having accurate scientific data is key to identifying cost-effective interventions and Ghana has very little documentation on prevalence of alcohol-related injuries. “If you want to direct health resources, it’s important to know, ‘How common is this?’” Gardner said.

His project involved measuring alcohol concentrations in injured people admitted to the emergency room at Komfo Anokye Teaching Hospital in Kumasi to determine who was ‘acutely alcohol-positive’—meaning had been drinking—when they were hurt. He also studied whether patients were risky drinkers—for instance, tended to binge drink—even if they were sober when they entered the hospital. Alcohol levels were measured via a breathalyzer or, if the patient was unconscious, with a saliva test strip. Gardner’s team also assessed drinking habits in a face-to-face survey.

In addition to revealing the large proportion of patients who had been drinking when they were hurt, the study held other surprises. The first was that drinking was prevalent in all subcategories, including sex, age, religious affiliation and educational status. Second, more than 40 percent of pedestrians who were hit by a vehicle had been drinking.

“That was very interesting, because many people in the emergency department had tended to blame the driver when a pedestrian got hit,” Gardner said. “But now we realized it may not have always been the driver’s fault.”

During his fellowship, Gardner also helped triage newly arrived patients and saw vividly how much injury road accidents can cause in developing countries like Ghana. “The pre-hospital and ambulance care of patients is still being developed, so when there were traffic accidents, the police would show up in a pick-up truck with the victims,” Gardner recalled. “This made it palpable how serious injury is in low-resource settings and how it can affect families on a daily basis, forever changing them.”

When he arrived in Ghana, Gardner had already nurtured an interest in improving health in disadvantaged populations as a Peace Corps volunteer in Madagascar and clinic volunteer in Malawi. Then at the University of Michigan, he helped establish a student-run free clinic for a disadvantaged rural population and began to wonder how their backgrounds related to their health risks. “I started to realize how important it is to generate new information to provide the most value for the community and the patient,” he said. “It took me a while to realize, that’s called research!”

Gardner says he learned many skills during his fellowship, such as project design, different research methodologies, data organization and analysis, and manuscript writing. He also learned how to build and manage a team of people from different backgrounds, using their individual strengths. “The Fogarty year really helped me sharpen my focus career-wise and reaffirm the importance of research,” he said. “It has also helped reaffirm my passion for global health equity.”
**What is the GACD’s unique role?**

I remember the discussions at the very first board meetings were a bit like, “We’re trying to boil the oceans here. This is a huge undertaking—how can we make a difference?” We identified a number of priority areas and implementation science research was at the top of the list. The second was research conducted in partnership with research users, if possible policymakers. This is something we will have to push further as we consider bringing some of our results to scale and working even more closely at the national level with some of the research users. Another goal was ensuring the creation of implementation science networks—sharing good practices. That’s where a consortium like the GACD plays a critical role. Rather than having different countries do superb things in isolation, it’s almost a GACD club within the networks of the funded researchers—networks on implementation science in hypertension, diabetes and soon chronic pulmonary diseases. And they collaborate with each other, given their similar approaches and issues in implementing the interventions. What is really striking is that putting these bright minds together in an international setting is enabling far more powerful sharing of good practices than occurs with countries working in isolation. And also, in due time, this will give us the capacity to work with other organizations—I’m thinking the WHO, which is already an observer at the GACD and is taking a keen interest in the research we are developing, but also the World Bank, the Gates Foundation and others. This is ensuring an international level of scientific excellence in what we are funding.

**What has GACD learned so far?**

We’ve learned that these networks take on a life of their own—and to me that’s the most exciting thing. They have elected leaders and have started meeting regularly, standardizing their approaches for gathering data, and are actually writing together. They’ve put out papers on implementation science, developed the methodologies they share and are now discussing developing repositories for the data they produce. So, there’s been huge progress and it evolved because we did something right in the first place by bringing the teams together to form international networks.

The other thing that we’ve realized is that, in some countries, we were not explicit enough about involving decision makers and research users that would be integral to formulating the research objectives, defining research protocols, and fully integrating them into the projects to ensure an uptake and dissemination of the results in due time.

**What’s the next phase?**

With each call for applications, we’ve actually increased the pressure and the need to have integrated knowledge translation rather than token involvement of knowledge users. As we move forward, we have to go even further. We need to discuss at a national level the possibility of true partnerships within countries to scale up some of the successful interventions. For instance, hypertension 2.0 should not be a mere renewal of prior grants with the same group and they go on forever. It has to be something more. We have to progress, be innovative, be creative. And we have to use the tremendous lobbying power that comes from so many countries represented and working together around the same table and investing jointly. The GACD is a fairly young organization and we’ve invested more than $100 million already and that’s going to go on increasing. We have to use our impact to ensure sustainability and scale-up of successful interventions.

**Does GACD plan to target mental health research?**

It will come in due time. One issue is the huge difficulty on the diagnostic side. In hypertension, the diagnosis is pretty straightforward, but in mental health, it’s a little more complex. There’s huge stigma issues everywhere, more pronounced in some countries than others. The GACD is focused on implementation science, intervention research, and working with decision makers and policy-makers to better understand interventions, why programs are effective or not, how we can make effective programs sustainable and cost-efficient, and how we can increase access to these programs. We’re moving toward better describing the research questions around mental health and I feel confident that we’ll be able to tackle this issue.
Advancing research on alcohol abuse and dependence

Alcoholic beverages are consumed in a variety of forms with wide-ranging cultural and local traditions for its use. However, alcohol abuse is a global problem that kills 3.3 million people a year, according to the WHO. To advance understanding of alcohol’s effects and to develop new prevention and treatment strategies, NIH’s National Institute on Alcohol Abuse and Alcoholism (NIAAA) funds research and fosters collaborations among U.S. and international investigators.

Dependence and misuse have health, social and economic consequences for drinkers, their families, and society at large. A psychoactive substance, alcohol impacts every organ in the body and is linked to cancer, tuberculosis, injuries and 200 other conditions. Violence, crime, unemployment and absenteeism are other outcomes of excessive consumption. Globally, harmful use of alcohol is the top risk factor for death and disability among people aged 15-49.

“As the world’s leading research institute on the causes, consequences, treatment and prevention of both alcohol use disorders and the wide-ranging health effects of alcohol abuse, NIAAA partners with scientists in both the developing and the developed world to advance our understanding of how alcohol acts on the brain and body to create pathophysiology,” says NIAAA Director Dr. George F. Koob. “By joining forces we are able to move the science forward that will lead to important improvements in global public health.”

NIAAA, which was established in 1970, uses its nearly $470 million annual budget to examine alcohol’s effects across the lifespan and develop and test effective approaches to the prevention and treatment of these health effects. Neurobiology, genetics, pharmacology, epidemiology and other disciplines are applied to a range of issues—treatment of alcohol use disorders, alcohol-related liver disease, Fetal Alcohol Spectrum Disorders (FASD), and alcohol’s complex relationship with HIV/AIDS.

The Institute’s Global Alcohol Research Program encourages international scientific exchange. To combat FASD, NIAAA supports research collaborations in several countries, including a wine-producing region in South Africa that has an unusually high prevalence of the condition.

The Institute also supports research that examines the relationship between alcohol and HIV/AIDS. Science has shown that alcohol use and abuse can contribute to the spread of the disease and affect treatment for infected patients. Studies to better understand the alcohol-HIV relationship are underway in sub-Saharan Africa, where HIV prevalence is high, and in Russia, where heavy drinking also occurs.

NIAAA works with scientists and health experts in other high-income countries. For example, a strong collaborative relationship has been developed with NIH’s French counterpart, INSERM. The research partnerships between U.S. and French investigators span several areas of NIAAA’s portfolio and French scientists contribute to some of their most productive consortia, such as the Integrative Neuroscience Initiative on Alcoholism. Additionally, NIAAA supports a “brain bank” at the University of Sydney, Australia that collects and distributes autopsied human tissue to facilitate neurological studies conducted throughout the world. This resource takes advantage of a unique population of people who abuse alcohol but no other substances.

In low- and middle-income countries (LMICs), NIAAA works with local experts to identify some of the specific problems poorer individuals experience as a result of alcohol abuse and addiction. Lack of adequate health care, treatment programs, support networks, and safe roads and vehicles all increase the risk of illness and deaths related to unsafe levels of consumption. Individuals in LMICs also drink more home brew that can be inexpensive, associated with heavy drinking and contain unsafe and even lethal ingredients.

NIAAA helps build capacity in LMICs as a longtime partner on Fogarty training projects, and by sharing information and building collaborative partnerships through support of scientists’ travel to conferences and meetings, and dissemination of research via its peer-reviewed journal, Alcohol Research: Current Reviews.

Because alcohol consumption generally increases with wealth, the health and social burden in developing economies is expected to grow, as noted in the WHO’s most recent status report on alcohol and health, increasing the need for collaborative research on this global health challenge.

FOCUS ON THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

Studying alcohol and HIV: a dangerous combination

There is no safe level of alcohol consumption for people being treated for HIV, scientists say, yet it commonly occurs among those living in low-income settings, compromising drug therapy and encouraging the spread of disease through risky behavior. More than two-thirds of the global population living with HIV is located in sub-Saharan African. More than half are women and 1.4 million new cases are diagnosed annually, according to UNAIDS. One strategy to combat the epidemic is to address the alcohol use and abuse that help fuel it.

“Alcohol is a driver of the epidemic both from a prevention and treatment point of view,” says Dr. Kendall J. Bryant, director of HIV/AIDS research at NIH’s National Institute on Alcohol Abuse and Alcoholism (NIAAA). Drinking impairs judgment and cognition, which can lead to unprotected sex, multiple partners, and failure to follow the antiretroviral therapy (ART) regimen that keeps the virus in check. Alcohol causes biological problems, too. By damaging the liver, alcohol can interfere with the body’s ability to process antiretroviral medications, for example.

NIAAA grantees are working with collaborators in sub-Saharan Africa to better understand alcohol's role in HIV, and identify interventions that decrease consumption, reduce the spread of disease and improve adherence to ART. Researchers look at what people drink and where they gather to do it. Traditional homemade brew is believed to make up the highest proportion of alcohol use in the region. It’s unregulated, untaxed so cheaper, and often stronger and more toxic than commercially produced beverages. The Kenyan brew chang’aa, for example, is the equivalent of two standard U.S. drinks, according to an NIAAA study.

“Another issue in low- and middle-income countries is that there are a lot of migrant worker populations—primarily men who will be drinking heavily and often engaging in higher risk sexual behavior that forms kind of a framework for transmission,” Bryant observed.

NIAAA grantees are conducting a number of studies to identify interventions aimed at patrons of drinking venues, where people often meet new sex partners. One study in Cape Town, South Africa found that alcohol was commonly used as a currency for sex and contributed to the risk of HIV because it often led to unprotected intercourse with multiple partners. Through observations of heavy drinking in the bars and in-depth interviews with regular patrons, field workers noted it was accepted practice for men to buy alcohol for women, in exchange for sex, with women having little ability to negotiate for safe terms. Women reported going to the venues and drinking out of boredom and to escape poverty, unemployment and other pressures at home. The findings, researchers note, suggest the need for interventions that address alcohol abuse and dependence, as well as ways to help women find jobs and healthier entertainment options.

Cognitive behavioral therapy (CBT), which teaches people coping skills, is being investigated as a way to reduce alcohol use. A pilot study in Kenya found that 69 percent of people who received CBT abstained from drinking for 90 days, compared to 38 percent who got the usual care. A larger trial is now underway.

Researchers in Uganda are investigating how heavy alcohol use affects the progression of HIV. One study of patients in an HIV clinic found that people reduced their drinking when starting HIV care, but couldn’t sustain it while on ART. Scientists say they believe this was the first study to use a blood test that looks for biomarkers of alcohol in addition to the patient’s self-reporting of alcohol use. Investigators say augmentation increases the accuracy.

“When I first came to NIH, alcohol was not an issue in HIV, no one paid any attention to it,” Bryant says of the evolution that’s taken place over the past 20 years. Now there’s so much interest, a conference to explore new tools for addressing alcohol and HIV in LMICs is being planned to coincide with this summer’s International AIDS Conference in Durban, South Africa.
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NIAAA advances fetal alcohol exposure research

Fifty years ago, alcohol wasn’t widely considered a danger to the developing fetus—some doctors even infused pregnant women with high doses of it to prevent premature labor. But, by the 1970s scientists began to recognize the connection between alcohol consumption by mothers and birth defects and developmental problems in their children. Today the consequences are well documented, yet millions of babies born worldwide continue to be affected by the conditions known as fetal alcohol spectrum disorders (FASD).

In low-resource settings, a complex combination of biological, social and economic factors may contribute to prenatal alcohol exposure. Pregnant women may lack information about risky drinking, have limited access to health care resources and suffer from poor nutrition. In some communities, where alcohol abuse is part of the culture, women may face social pressure to drink and struggle to stop because of dependency and the need for social interaction. Another issue is that many women don’t change their drinking habits until they realize they are pregnant, often in the second trimester, when damage to the fetus may already have occurred.

Researchers funded by NIH’s National Institute on Alcohol Abuse and Alcoholism (NIAAA) have been studying concentrations of risky-drinking populations in countries including South Africa, Ukraine and Russia to increase awareness of the issue, prevent or limit the impact of alcohol exposure, and help improve the lives of children who suffer permanent damage from it.

Preventing fetal alcohol spectrum disorders

A significant advance came in the 1990s with the discovery of a large number of alcohol-exposed children in a wine-producing region of South Africa. Two decades of NIAAA-supported studies document the area as having the highest prevalence of FASD in the world, with as many as 26 percent of children in some communities affected.

“"It was pretty amazing. We had never seen rates that high in a general population," says NIAAA grantee Dr. Philip May of the University of North Carolina. He and his team have been conducting in-school studies in communities throughout the Western Cape Province since 1997 to determine the prevalence of FASD and identify the characteristics associated with disorders across the spectrum.

He and other researchers attribute the high rates of FASD to the practice of giving farm workers alcohol as part of their payment. Now outlawed, it left behind an established pattern of weekend imbibing—including among women, who report consuming as many as 16 alcoholic beverages.

“"In the communities in which we work, drinking is the major form of socialization and recreation," says May. "There’s so much social pressure to be with the group and continue to drink. Trying to quit pulls them out of their normal social network, so it’s very hard.”

May’s research has shown that women at high risk of having a child with FASD can be helped to stop drinking or drink less while pregnant through motivational interviewing, a type of counseling that encourages positive behavior changes. His team has been studying the use of trained social workers and nurses as case managers who help women set goals to abstain from or reduce drinking during pregnancy: understand the growth and development of the child they are carrying; and identify friends, family and organizations they can turn to for emotional support.

The studies found drinking decreased six months into the program, but increased at 12 and 18 months after the baby was born. May says clinics in the area don’t have the funding to regularly provide this type of counseling, but the educational pamphlets and videos used in case management are now the standard of care.

May’s team also provides liquid nutritional supplement drinks with protein, an array of major vitamins and other nutrients to pregnant women who have low body mass index (BMI), because his prior research has shown a link between low BMI, a number of nutritional deficiencies, and the severity of FASD in children.

Understanding alcohol’s impact on the brain

Neuroimaging is providing important clues on how alcohol consumed during pregnancy affects children’s brains. Drs. Sandra and Joseph Jacobson, husband and wife researchers from Wayne State University in Detroit, have also been working with collaborators in South Africa since...
FOCUS ON THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

the 1990s and conducted the first prospective, longitudinal study of fetal alcohol syndrome. They interviewed the mothers about their drinking habits throughout their pregnancies and continue to follow the children, some of whom are now 15 years old.

To advance understanding of the cognitive effects on children, the Jacobsons use a number of neuroimaging techniques including MRI, which measures the brain’s structure, functional MRI (fMRI), which documents brain activity while completing a task, and diffusion tensor imaging, which assesses white matter integrity.

Some of their earliest Cape Town fMRI studies looked at number processing, a known problem in FASD. Alcohol-affected children and controls were each given a math problem to solve while in the scanner. Both groups could perform the task but there was a telling difference—children with FASD had to use more extensive brain regions to do so.

“The interpretation is they had to use a lot more neural resources to do what is a very simple and automatic processing problem for normal children,” explains Dr. Joseph Jacobson.

When the Jacobsons began their work in South Africa, there was no capacity to conduct fMRI, but Dr. Ernesta Meintjes, at the University of Cape Town, wanted to learn the technology. With a Fogarty grant, Meintjes traveled to Vanderbilt University to learn how to implement an fMRI study and analyze the data. The collaborators went on to produce 19 papers from that initial Fogarty grant.

Diagnosing FASD can be difficult because not all alcohol-exposed children have the facial abnormalities and other physical traits associated with the condition and the neurobehavioral deficits are often similar to those seen in other conditions, such as attention deficit hyperactivity disorder. Using a method known as eyelink conditioning—in which people learn to blink in anticipation of an event—the Jacobsons found that none of the children with the most severe form of FASD met the criterion for this type of learning compared to 75% of the controls. “This is dramatic and possibly is a good behavioral biomarker for alcohol effects,” notes Dr. Sandra Jacobson. Data from neuroimaging studies conducted by Jacobson and colleagues suggest this deficit may be attributable, in part, to slower processing of information due to deficits in the brain’s white matter, which transmits signals across brain regions during a task.

Improving outcomes of children with FASD

Children with FASD can improve their academic performance with specialized coaching, research has shown. For instance, May’s team has demonstrated the students can improve language and literacy skills by learning to identify first and last sounds of words, becoming aware of and producing rhymes, and using word picture cards to build sentences. Other researchers have had success using visual imagery to teach math concepts.

The researchers are also investigating additional approaches. One avenue is nutrition—May and other scientists are studying whether regular consumption of calorically rich multivitamin drinks can improve the children’s cognitive function. Another track is engaging and training parents to coach their children at home.

“With special attention to stimulate them, their brains can repair to some degree,” says May. “Usually some problems with impulsivity and working memory persist, but overall their performance and behavior can be improved significantly.”

Some progress on policy, but issues remain

In the years after pockets of high prevalence were established by May and his NIAAA-funded team of scientists, the South African government convened global experts and established some policy guidelines for prevention and management of FASD. They also enacted legislation restricting the sale of alcohol, governing its advertising and mandating labels include health messages, such as warnings that drinking during pregnancy can harm unborn babies.

“When you go to the antenatal clinics, there are posters all over: ‘If you drink, your baby drinks.’ There’s a major effort to cut down or stop drinking,” says Dr. Sandra Jacobson. “But, when you are dealing with alcoholism and poverty, it’s challenging and there aren’t enough services to provide support for the women.”

FETAL ALCOHOL SYNDROME

Low Nasal Bridge

Epicanthal Folds

Short Palpebral Fissures

Flat Midface and Short Nose

Indistinct Philtrum

Micrognathia

Thin Upper Lip

Minor Ear Abnormalities

Courtesy of NIAAA

13
We spend much of our time at the NIH pondering how to improve human health, but give much less consideration to the issue of planetary health. At the recent Consortium of Universities for Global Health annual meeting, the bravura keynote address framed the situation in stark terms. In a provocative manifesto delivered by The Lancet’s Dr. Richard Horton, we were encouraged to view the two concerns in a holistic manner. For if the planetary systems continue to be compromised at the current rate, no vaccines we produce will preserve our health.

That spurred me to ponder how we prioritize the issues we face and how we determine the difference between “important” and “urgent” global health problems. I view “urgent” problems as those that present suddenly and are responded to in crisis mode. We saw that with Ebola, when numerous organizations and governments sent floods of health care workers, epidemiologists, portable labs, treatment centers and other resources to West Africa.

Much of the assistance, unfortunately, came after the virus had already spread through cities and villages, taking an enormous death toll and making it more complex to trace the contacts of those infected, which was necessary to contain the outbreak. We’re seeing it now with the Zika virus, which has been around for a while but suddenly started causing heartbreaking cases of microcephaly in infants and Guillain-Barré syndrome, which can be very serious and even fatal in adults.

“Important” global health problems seem to me to be those big issues—HIV, malaria, TB, polio—that we’ve been working on for a long time, require sustained effort and commitment, and can produce fatigue on behalf of the donors, as well as implementers. The burden of disease they cause is huge—for TB alone it amounts to 4,000 deaths per day. This mortality dwarfs that for most of the diseases that are considered “urgent.” We have grown more complacent in thinking that these major killers here defined as “important” are not also “urgent.”

Since we don’t have the resources currently available to fix all the global health problems, we must prioritize. Politicians and health officials responded unreservedly to the public’s fear of Ebola, particularly when Americans became infected, which is understandable. At the same time, it’s important to note that globally, more people died from HIV in three days than from Ebola during the entire outbreak. And it’s imperative that we all work together as quickly as possible to learn what we can about the Zika virus, figure out how to control the mosquito population and develop a vaccine. But we also must keep our eye on the long-term need to strengthen research capacity and health systems in low-resource countries. In terms of infectious diseases, we have seen that we are all only as safe as the weakest link. And we know that preparedness is less expensive to support than emergency response.

We need to prepare for future outbreaks, of whatever agent arises. At Fogarty, our core mission is to build research capacity in low- and middle-income countries—and I believe that’s a long-term investment that pays huge dividends. If we look at the case of the Ebola outbreak, the countries with little or no infrastructure suffered the most, and the cost of unpreparedness soared above $1 billion. The amount needed to sufficiently strengthen local institutions, train health leaders and link them to the global network of experts would take just a fraction of this. We know people with Ebola traveled across borders into some of the countries surrounding Guinea, Liberia and Sierra Leone. Why didn’t outbreaks occur there? Because well-trained epidemiologists, lab technicians and others were on hand, prepared to identify and treat those who were infected, and ensure the disease did not spread. They were linked to global resources, and had access to technical advice and support.

This expertise is essential for responding to pandemics. That’s why Fogarty issued a call for applications to spur partnerships that will create sustainable research capacity in the Ebola-affected countries. Only by addressing the “important” issue of global capacity development, can we hope to be prepared for the next “urgent” pandemic that is sure to come.

This column first appeared in the Global Health Now news bulletin. To subscribe, visit http://bit.ly/GHNsub
Fauci recognized for HIV work in developing world
For his pioneering contributions to the understanding of HIV/AIDS and his leadership bringing successful treatment to the developing world, Dr. Anthony S. Fauci, director of the NIH’s National Institute of Allergy and Infectious Diseases, is receiving the 2016 John Dirks Canada Gairdner Global Health Award. The awards are Canada’s most prestigious medical honor.

Leading HIV prevention researcher Cates dies
Dr. Willard (Ward) Cates, a leader in the field of HIV prevention and women’s reproductive health, died in March. He chaired the executive committee of NIH’s HIV Prevention Trials Network for more than a decade and was a scientific advisor for the Office of Global AIDS Coordination and UNAIDS. Cates spent two decades at the CDC before joining the nonprofit, FHI 360.

Fogarty grantee wins international excellence award
The Endocrine Society has honored Fogarty grantee Dr. Ghada El-Hajj Fuleihan with its International Excellence in Endocrinology Award for making contributions to the field in a region with limited resources. El-Hajj Fuleihan, a professor of medicine at the American University of Beirut, directs the Scholars in Health Research Program (SHARP), a Fogarty-supported capacity building project.

Former Fogarty fellow takes up new position in SA
Dr. Juliet Pulliam, a former postdoctoral fellow in Fogarty’s Research and Policy for Infectious Disease Dynamics (RAPIDD) program, will become director of the South African Centre for Epidemiological Modelling and Analysis (SACEMA), effective July 1. SACEMA, a government-supported Centre of Excellence, builds capacity in infectious disease modeling and other quantitative aspects of health research in sub-Saharan Africa.

Fogarty’s Miller on detail to global health nonprofit
Dr. Mark Miller, Fogarty’s Associate Director for Research, is serving a detail to the French nonprofit, Agence de Medicine Preventive (AMP), which promotes preventive medicine and public health in low- and middle-income countries. Miller’s posting will give Fogarty the opportunity to pursue new research collaborations on influenza, Ebola and other topics.

Sina shares Fogarty expertise with Wellcome Trust
Dr. Barbara Sina, bioethics program officer in Fogarty’s Division of International Training and Research, recently spent six weeks at the Wellcome Trust in London, collaborating on activities related to the Global Forum on Bioethics in Research.

Researchers produce map showing Zika risk
Scientists have created a detailed global map of countries most at risk of Zika virus transmission. The modelers took into account both environmental and socioeconomic factors to predict Zika’s spread. More than 2.7 billion people live in at-risk areas. Article: http://bit.ly/ZikaMapping

Experts warn of disease resurgence
Diseases such as chikungunya, dengue and Zika are undergoing a global resurgence, in part because the number of scientists trained to study these vector-borne diseases is shrinking, experts warn in a report issued by the Forum on Microbial Threats. Report: http://bit.ly/1S1XW8s

World’s aging population poses challenges
The portion of the world’s population aged 65 and older is expected to nearly double to around 17 percent – 1.6 billion people – by 2050, a recent NIH-funded report says. This demographic trend presents policymakers with challenges, including how to reconfigure social and health support systems to maximize well-being in an aging population. Report: http://1.usa.gov/1SAJnTF

Study examines global research funding
An independent study of the world’s key health research funders, what they support and how they make decisions was recently published in the open-access journal, Health Research Policy and Systems. Together, the 10 largest funders provide $37.1 billion annually for research. Report: http://bit.ly/1REIhtN

Global bioethics forum issues report
Bioethics issues related to conducting research during the recent Ebola outbreak and other emerging epidemics were discussed by representatives from 35 countries during the 2015 Global Forum on Bioethics in Research. The final meeting report and presentations are now online. Website: http://bit.ly/GFbioethics

Evaluation training courses posted
Free online courses on monitoring and evaluation are available to help health care systems in low-income settings maximize the impact of their programs. The courses—developed by MEASURE Evaluation with funding from USAID—were produced in English, French, Spanish, Portuguese and Vietnamese. Website: http://unclive/1S2OaCZ
Zika virus

For the latest information on Zika virus research and related NIH funding opportunities, visit: http://bit.ly/ZikaInfo

Cuban delegation makes historic visit to NIH

Fogarty International Center Director Roger I. Glass (right) welcomes Cuban Vice Minister of Public Health, Dr. José Angel Portal Miranda, at the start of a historic visit to NIH on Wednesday, March 30, 2016. The highest level Cuban official ever to visit NIH, Portal Miranda held talks with NIH Director Dr. Francis S. Collins and several institute directors, and toured the NIH Vaccine Research Center.

The discussions focused on ways to strengthen scientific exchange between the two countries and expand research collaborations in areas of mutual interest, including cancer and infectious diseases such as chikungunya, dengue, flu and Zika. The visit occurred nine days after President Barack Obama visited Cuba—the first by an American President in nearly a century.


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