



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

## Capacity building leads to pandemic preparedness

“Research capacity is a critical element of pandemic preparedness.” With these words, Fogarty Deputy Director Dr. Peter Kilmarx began a symposium at the annual meeting of the American Society of Tropical Medicine & Hygiene (ASTMH) in November. The panel was moderated by Kilmarx and Karen Goraleski, ASTMH CEO and a Fogarty board member, and featured speakers from Africa, South Asia, Latin America, and the Caribbean. Each speaker related how establishing research capacity before the pandemic at their respective institutions with support from Fogarty and other NIH institutes aided their national and regional response to COVID-19.

Dr. Christian Happi, Director of the African Centre of Excellence for Genomics of Infectious Diseases (ACEGID), highlighted how conducting genomic sequencing of Ebola during the 2014-2016 West African outbreak prepared them for COVID-19. “We were years ahead of the WHO because we were trying to use genomics to guide the public health response,” he said. This progressive thinking meant ACEGID, based at Redeemer’s University, Nigeria, was equipped to respond to COVID. During the pandemic, ACEGID trained more than 1,300 scientists in 42 African countries.

In Pakistan, the Aga Khan University (AKU) was able to mobilize research scientists trained in whole genome sequencing of diseases like dengue, West Nile Virus, and tuberculosis to aid in the government’s response, said Dr. Erum Khan, Professor in Microbiology at AKU Hospital. She noted, “If we hadn’t been able to move people from the research side [of the university] to the clinical side, it would not have been possible to identify COVID variants and run diagnostics” at the pace of up to 2,000 cases per day.

The Jamaican Ministry of Health wanted to use next-generation sequencing for COVID surveillance. They knew of Dr. John Lindo’s laboratory at University of the West Indies (UWI), which, through a Fogarty-funded partnership



Courtesy of ASTMH

Dr. Erum Khan, Professor in Microbiology at AKU Hospital, presents key achievements during the COVID-19 pandemic at the 2022 ASTMH meeting.

with the State University of New York at Buffalo, runs a program focused on emerging and chronic viral infections. The ministry reached out and eventually enabled UWI to set up a genomic center. Prior to that, Lindo explained, “we’d have to send samples to Trinidad and wait quite a while for results.”

Before COVID, the Centro Internacional de Entrenamiento e Investigaciones Médicas (CIDEIM) in Colombia, did not focus on virology at all but on parasitic and bacterial diseases. Yet their “know-how in diagnostic tests”—some of it developed via their Fogarty-funded training program focusing on emerging infectious diseases—allowed them to lend support for case identification and validation, according to Dr. Nancy Gore Saravia, director of CIDEIM.

Finally, Dr. Sikhulile Moyo discussed how studying HIV viral evolution prepared him for COVID. The former Fogarty Fellow and current Laboratory Director at the Botswana-Harvard AIDS Institute Partnership said that having built systems and networks in response to HIV/AIDS over the years allowed his team in Botswana to pivot and establish systematic pathogen surveillance early in the pandemic. This was critical for identifying and tracking variants, and eventually led to Moyo’s discovery of omicron.

### FOCUS



#### Konzo and the children of Kahemba

- The researchers trying to save them
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- A quest for solutions

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# Addressing mental health abroad helps US communities

As the U.S. population becomes increasingly diverse, it is more important than ever to ensure that providers can serve their patients in a culturally responsive way. A recent educational case report published in *Academic Psychiatry* highlights how global collaborations in mental health research can help providers better reach underserved communities in the United States.

The report came from a study co-funded by Fogarty and the National Institute for Mental Health (NIMH). Authors Dr. Kristina Korte, Assistant Professor of Psychology at Harvard Medical School and Clinical Psychologist at Massachusetts General Hospital, and Dr. Kimberly Hook, Research Fellow at Harvard T.H. Chan School of Public Health, described a long-standing program led by senior author, Dr. David Henderson, Chief of Psychiatry at the Boston University School of Medicine. He and his colleagues supported the Liberian Ministry of Health in developing that nation's first mental health strategic plan. They surveyed Liberians to better understand mental health needs, specifically focusing on children and adolescents and patterns of substance abuse associated with mental illness.

While in the U.S., the team enlisted the help of the Liberian immigrant community in Massachusetts through a local church congregation. These volunteers helped translate and transcribe the survey results from Liberia to ensure researchers captured linguistic nuances and cultural differences they might have otherwise missed. With the volunteers' input, researchers could identify inefficiencies, restructure their initial survey, and develop a more culturally relevant questionnaire for future study



Community-based training, such as this session in Sinoe County, Liberia, provides health practitioners with the skills to be able to recognize symptoms of mental illness.

participants in Liberia. The volunteers who helped the researchers also recognized similar mental health issues in their community in the U.S. One church member was quoted as saying, "Even though we are here in America, we are still the same Africans. We still have the same beliefs. We still handle mental and emotional health issues the same way."

Ultimately the project not only supported Liberia's Mental Health Policy and Strategic Plan, but in Massachusetts, the Health and Mental Health Education and Awareness for Africans in Lowell or HEAAL initiative was established between the church and the Department of Psychiatry at Boston University School of Medicine with the goal of better understanding the nature, characteristics, scope, and magnitude of health and mental health issues in this faith community of primarily immigrants and refugees.

While this global-local paradigm has clear positive implications for the patient population, this work also creates new training opportunities for mental health professionals in U.S. and global settings. As trainees work with diverse populations through global-local collaboration or community engagement, their cultural competency and humility grows, enabling providers to address potential cultural barriers to care. With the growing recognition of mental health as a global issue, it is increasingly important to help bridge the gap and provide culturally responsive care for the diverse communities of the U.S. The report notes that while this study focused on Liberia, the lessons learned can be implemented in other LMICs and their respective diaspora communities in the West.

## Save the date: Global Health Fellows & Scholars 20th Anniversary

Fogarty's flagship Global Health Fellows and Scholars program, now known as LAUNCH, will celebrate its 20th Anniversary in 2023. To mark the occasion, Fogarty invites program alumni to join us for a commemorative event at NIH in April 2023.

The event will be an opportunity to celebrate alumni accomplishments and share our hopes for future cohorts. Attendees will also have the opportunity to network and hear from directors from several NIH Institutes and Centers about the impact of Fogarty Fellows and Scholars in the global health workforce.

The Fellows and Scholars program, established in 2003, aims to foster the next generation of global health scientists by providing trainees, early in their careers, a one-year mentored research training experience at established biomedical and behavioral research institutions and project sites in low- and middle-income countries (LMICs) as well as opportunities for post-professional trainees from the U.S. and LMICs.

More information about the agenda and hybrid options for attendance will be shared in the coming months.



# Climate change accelerates outbreak frequency

The frequency of Ebola outbreaks in Uganda has been increasing due to climate change and this is likely happening in other African nations as well, according to Dr. Sam Okware, director general of the Uganda National Health Research Organization. Central Africa has suffered 28 large Ebola outbreaks, and, since 2000, Uganda has experienced seven of these, including the most recent declared in September. Managing fear and rumors is crucial to an effective outbreak response, given the negative impacts of social media seen in some places, noted Okware, who spoke at a November 25 webinar sponsored by the African Forum for Research and Education in Health (AFREHealth), an interdisciplinary group seeking to improve the quality of health care in Africa.

Lieutenant Colonel Dr. Henry Kyobe Bosa, incident commander, provided a status update for the current outbreak of *Sudan ebolavirus*, for which there is no proven vaccine. Tallies for the ninth week include 141 total cases, 55 deaths, 79 recoveries, and 22 probable cases (where samples could not be taken). The highest recovery rate has been in Kampala, where 83% of infected people have survived the illness. Lowest recovery has been seen in Mubende and Kassanda, the epicenters of illness, where 73% of infected children under age 9 have died. The movement from rural epicenter to Uganda's capital city was rapid, taking just two weeks and resulting in 10 independent clusters, Bosa noted. "Rural tools for contact tracing are ineffective in cities." Developing better response tools for an urban setting is a priority.

This current outbreak has been a disease of children and women, signaling household transmission, noted Bosa. While the initial outbreak affected children, now there is mainly illness among young adults. "Since November 12, we haven't had any new cases," stated Bosa, adding that this is considered a real "remission" given surveillance systems are running well.



An artist's rendering based on electron micrography of filamentous Ebola virus particles

Dr. Jean-Jacques Muyembe TamFum, a member of the team that investigated the first known Ebola outbreak at Yambuku Mission in 1976, recounted lessons learned from past *Zaire ebolavirus* outbreaks in the Democratic Republic of Congo (DRC). Of the 318 total infected patients, 280 died during the Yambuku outbreak, which lasted less than 11 weeks—an 88% case fatality rate (CFR). Muyembe, a microbiologist, recalls lacking even basic personal protective equipment, including gloves, so he carefully washed his hands with soap and water after handling patient samples. He credits this practice with his personal survival.

In 1995, the first outbreak after Yambuku occurred in Kikwit, also in DRC, recounted Muyembe who is now director of the country's National Institutes of Bio-Medical Research. Researchers recorded 317 total cases and 250 deaths there, a 78% CFR.

Photo courtesy of NIAID

Eight patients were treated with blood from survivors, and, in a paper published in *The Journal of Infectious Diseases*, "we concluded that Ebola antibodies were protective," said Muyembe. Yet this experiment "remained a mere anecdote for a long time" because

the observational study lacked a control arm and had a small sample size.

Still Muyembe believed in the protective qualities of antibodies, and, with help from other scientists, "the dream of my life is now a reality." That dream is EBANGA, a therapy based on a single monoclonal antibody isolated from a human survivor of the outbreak in Kikwit. Today, EBANGA is used to treat children and adults who've been infected with *Zaire ebolavirus*.

Africa needs to develop more mobile and local laboratory capacity if it is to become more effective in rapidly addressing outbreaks of the deadly hemorrhagic fever in the future, concluded Muyembe.

The webinar can be viewed on the AFREHealth website.

# PROFILE

## Tackling tobacco, TB, and mental health in South Africa

Dr. Richard van-Zyl Smit comes from a family of physicians: His parents were physicians, his sister, who is currently practicing, married a physician, his uncle is a physician, and his aunt is a nurse. Before he applied to become a Fogarty Global Health Fellow, his cousin and fellow medical doctor, Jacqueline Firth, was accepted into the inaugural Fogarty Global Health Fellows & Scholars cohort.

A consultant pulmonologist at Groote Schuur Hospital in Cape Town, South Africa, and a deputy head of the division of pulmonology at the University of Cape Town Lung Institute, van-Zyl Smit credits his Fogarty Fellowship as the starting point for his current career. “The Fogarty program was instrumental in my career, launching me and pushing me in the direction I went. It was just a fantastic immersion into research and an opportunity I don’t think anyone should pass up,” van Zyl-Smit said.

For his Fogarty project, he exposed TB-infected macrophages to tobacco smoke and nicotine to test their immune responses. He found that this exposure significantly reduced the production of cytokines key in the defense against tuberculosis during infection. He later replicated his results using vaping products, suggesting a potential mechanism to explain the epidemiological link between tobacco smoking and the risk of TB infection.

Since his fellowship, van Zyl-Smit has been actively involved in poverty-related respiratory health issues in South Africa and has made it central to his research and career. South Africa has some of the highest rates of tuberculosis, chronic obstructive pulmonary disease (COPD) and several other chronic respiratory illnesses in the world. He has co-authored publications on TB, COPD, smoking cessation programs, and the interplay between tobacco use and diseases such as HIV/AIDS and COVID-19.

“The intersection of poverty and respiratory disease is not unique to South Africa,” said van Zyl-Smit. “However, I fear that unless we address poverty, we will be ineffective at treating all the other components related to these high rates.”



**Richard van-Zyl Smit, MD, PhD**

Fogarty Fellow:	2009-2011
U.S. institution:	Vanderbilt University
Foreign institution:	University of Cape Town
Research topic:	The interaction of tobacco smoke and pulmonary defenses against tuberculosis

Van Zyl-Smit currently serves as president of the South African Thoracic Society, co-chair of the American Thoracic Society International Health committee, and as a global ambassador for the Global Initiative for Asthma. He presented his Fogarty data at an American Thoracic Society meeting in 2008 and was awarded an international trainee scholarship from that presentation. Today he runs the American Thoracic Society’s international scholarship program.

“My Fogarty project gave me access to an entirely new network outside of my region, and I would not be in the position I am today without those connections.”

In addition to his work as a pulmonologist, in recent years van Zyl-Smit has become an advocate for mental health.

During his inaugural lecture at the University of Cape Town in 2022, van Zyl-Smit shared his personal struggles with mental health. After being diagnosed with stress-induced anxiety in 2016, he began writing his first book titled “They Don’t Award Nobel Prizes to Dead People.” The book, which helped him process his anxiety, advocates for a culture change with a stronger emphasis on work-life balance. He later went on to author another book, “Thoughts on a Saturday Morning: A collection of essays on life, work and relationships during COVID-19,” in which he wrote about the stress he and his fellow health care workers suffered at the hands of the pandemic in South Africa.

As part of the closing remarks of his inaugural lecture, he reminded his colleagues to care for themselves and each other noting, “we are of greater value alive and functional than dead or dysfunctional.”

## LOLA KOLA, PHD

*Dr. Lola Kola is a senior research fellow at University of Ibadan's WHO Collaborating Centre for Research and Training in Mental Health, Neurosciences and Drug and Alcohol Abuse. She also serves as adjunct associate professor at Lead City University, Nigeria. Prior to this, she earned master's and doctoral degrees in Medical Sociology at University of Ibadan. Kola partners on projects with the Behavioral Research in Technology and Engineering (BRiTE) Center at the University of Washington (UW) in Seattle and the Centre for Child and Adolescent Mental Health at University of Ibadan. Most recently she's a Visiting Researcher in the Centre for Global Mental Health Department of Kings College London.*



### Tell us about your work.

I developed a mobile phone app as an adjunct treatment to routine primary care for adolescent mothers with depression. In Nigeria—and in many places—young mothers don't want to go to clinics because the nurses seem unkind: "You're pregnant but not married. Your mates are in school." Because these teen mothers have depression, they may also have problems with personal care. Others shame them as "sluggish" or "lazy." Not only do they feel social stigma from family members, nurses, neighbors and friends, they've disappointed themselves and feel self-stigma. Generally, they experience very low social support.

Seeing this, I thought, How do I reach these girls? Originally, I planned in-depth interviews, but adolescents are sometimes not so trusting. They did not talk. Next, I brought them together in focus group discussions and then they couldn't stop talking! There, I noticed nine out of 10 had mobile phones and I asked what they liked to do on them. They all liked watching short videos—funny skits, you know? This struck me as a possible area for innovation for my Emerging Global Leader award, which is supported by the National Institute of Mental Health (NIMH). So, applying user-centered design, my team created 14 short videos (with music the girls chose) to help them increase their engagement with care, while teaching them how to take care of their mental and physical health.

My evaluations showed that this adjunct treatment (adjunct to face-to-face clinical care) delivered through a mobile phone app helped the young mothers overcome problems related to stigma and improved treatment outcomes. We also found that relatives played an important role in supporting teen mothers' uptake of digital tools.

### What is Nigeria's most urgent health issue?

Nigeria has an outdated mental health law known as the Lunacy Act of 1958. First enacted in 1916, this legislation was later amended in 1958, but it hasn't been updated since then, despite several attempts by the mental health community. It is archaic! It uses the derogatory term "lunatics" to refer to mentally ill patients and it only acknowledges asylum-type care—it does not include rehabilitation of mentally ill patients within communities. I would go so far as to say that Nigeria faces a human rights emergency in mental health.

### What's ahead?

I worked with the WHO country office in Abuja, Nigeria, from 2011-2014 as a National Consultant for mental health and I coordinated the rollout of the WHO's Mental Health Gap Action Programme (mhGAP) in the country. The mhGAP provides a framework for scaling up health interventions in non-specialist settings and this informs my own research today. I focus on developing digital psychosocial tools to increase patient access and to strengthen health systems. I'm currently designing (with help from young mothers) an electronic magazine to provide health education to address the impact of climate change on mental health in pregnancy. I'm also part of a new project, supported by NIMH and co-led by my mentor, UW Professor Dror Ben-Zeev. WADMA or the West Africa Digital Mental Health Alliance aims to grow the next generation of regional researchers and clinicians designing tools for mental health care. Finally, I'm building my own team and increasing my international collaborative network so that I can move deeper into public health and apply for more competitive grants.

## Konzo and the children of Kahemba

All researchers of konzo, a paralyzing disease that can occur in impoverished regions where bitter cassava is a food staple, share at least one thing in common: utter shock when first encountering the disease. Dr. Desire Tshala, who grew up in a modern, urban area of the Democratic Republic of Congo (DRC), said, “I couldn’t believe that in my own country, just 600 miles from the capital city, Kinshasa, people were living in such a high degree of poverty and malnutrition. In the villages in and near Kahemba, DRC, about two out of 10 people” are affected.

The Yaka tribe’s word “konzo,” referring to an antelope tethered at its knees, was used to describe cases seen in the Belgian Congo in 1928. Later, this term was adopted by Dr. Hans Rosling, the late Swedish physician and epidemiologist, who began characterizing the disease in 1989. At that time, no one understood what caused konzo: Was it a virus? Mutations? Rosling identified the cassava plant, a tuberous root containing toxic cyanide that also happens to be the world’s fourth most consumed food staple.

Specifically, Rosling showed that cyanide poisoning from cassava, when it coincides with a diet lacking in sulfur-based amino acids, can damage upper motor neuron pathways within an individual’s brain. The result is sudden,

*Kahemba residents gather near the health center. Even as Dr. Desire Tshala worked in the lab to find answers to konzo, the people of Kahemba remained foremost in his thoughts.*

non-progressive and non-reversible paralysis of the lower and/or upper extremities in severely affected people. So a child—usually those affected are malnourished children or mothers of child-bearing age—who has been eating cassava lifelong will wake up one morning either limping or needing a stick to walk or only able to crawl. This condition will remain unchanged throughout the child’s life. (In rare cases, another meal of improperly processed, toxic cassava will worsen the paralysis.)

Because konzo happens in isolated, rural areas, the exact number of cases remains unknown, though scientists estimate hundreds of thousands of affected people, most of them living in the DRC. The disease usually occurs as an outbreak triggered by crisis situations, such as drought, civil wars or famine.

Dr. Julie Cliff, a physician and epidemiologist who worked with Rosling in Mozambique, explained, “Everybody says, ‘Once you’ve seen konzo, you have to do something, you cannot stop.’ It’s just a horrifying sight to see so many people paralyzed. And in rural areas, paralyzed people cannot walk to their fields, yet they still crawl. I find that particularly moving.”

Dr. Matthew Bramble, a genetic medicine researcher who is exploring connections between konzo and the gut microbiome, said, “You can read all you like about cassava-associated paralysis, but when you go to the village and the kids are greeting you on all fours and people have canes and, later, the person you’re eating with is on the ground, well.... The community is completely used to it, and that is the most unusual component of konzo.”

Dr. Michael Boivin, a neuropsychology specialist whose research in the Democratic Republic of Congo began in the 1980s, credits one man as the driving force behind much of the konzo research happening today: “Desire Tshala. He’s at the center of it all.”

### Spearheading prevention

Dr. Desire Tshala was 31 when he first confronted konzo. Dr. Thorkild Tylleskar, a former Rosling student, suggested

Photo courtesy of Neeraj Vashist



Tshala work with him in the field. That was 1996. Tshala's neuro-epidemiological characterization of konzo, a project for his Ph.D. thesis, involved transporting villagers in remote, konzo-affected areas to cities and conducting "electrophysiology investigations with equipment brought from Sweden." This early research sparked his passion and resulted in a logical progression towards increasing scientific understanding of konzo's effects.

Eventually, his projects received funding from Fogarty, the National Institute of Environmental Health Sciences (NIEHS), and the National Institute of Neurological Disorders and Stroke (NINDS), enabling him to develop an experimental lab model and explore his most pressing questions. "In the same village or family, you'd see that some children are more susceptible than others, so I was looking for a biomarker." By 2016, his experiments on rodents had suggested that cyanate, a chemical relative of cassava cyanide, may be associated with konzo.

The value of konzo research extends far beyond African villages, he explained. "Our models and what we are learning from the various studies—including epigenetic, microbiome, and toxicology studies—is very helpful in terms of understanding all motor neuron diseases, including ALS." His research is also relevant in terms of studying the toxicity itself. "We work on cyanide, an important toxin in chemical warfare, and our understanding of it benefits the counterterrorism program at NINDS."

### The wetting method

Though his research grew more sophisticated, the villagers of Kahemba remained foremost in Tshala's thoughts. Seeing the prevalence of paralysis, he decided his team could no longer continue observational studies. "We needed to start an intervention to prevent the disease." He collaborated with Dr. James Howard Bradbury's team to introduce the wetting method in Kahemba (with added help from the DRC's National Nutrition Program at the Ministry of Health).

The wetting method removes the toxic components of cassava from cassava flour, according to a study co-authored by Bradbury and Cliff. A food preparer mixes cassava flour with water and creates a thin layer of mixture which is left to dry in the sun for two hours or five in the shade. During this time, the chemicals break down, producing hydrogen cyanide gas, which harmlessly dissipates into the atmosphere.

Dr. Julie Cliff helped field-test the wetting method in Mozambique. "It should work to prevent konzo, it doesn't take too long, and the rural women find it easy to use."

Though hopeful, Tshala knows he faces an uphill battle.



*A child who has been eating cassava lifelong will wake up one morning either limping or needing a stick to walk or only able to crawl. This condition will remain unchanged throughout the child's life.*

Photo courtesy of Michael Bovin

"While the wetting method works, it's difficult for people to change the way they've been processing food." Also, Tshala expects that natural catastrophes, like droughts or flooding, and climate variations, will likely increase the prevalence of konzo in the African countries already affected: DRC, Angola, Zambia, Tanzania, Mozambique, Uganda, Cameroon, and Nigeria.

### The poorest of the poor

Cliff's own global health career stretches back to the 1970s. After a stint in Tanzania, the Australian native began working in Mozambique, where, in 1981, she faced her first konzo epidemic as a Ministry of Health physician. "We had a huge epidemic—hundreds of cases of paralyzed children, women of reproductive age and a few men. It was overwhelming." Rosling, who had been working in the district, and Anders Molin, a Swedish doctor, investigated. This led to subsequent publications and a landmark epidemiological case history.

In the years following, Cliff continued to research konzo and the wetting method, while making significant contributions to the development of the Mozambique health system. She also contributed to a data report on konzo sponsored by the WHO. While the UN health agency has shown some interest, it hasn't been enough, she explained. "We, the konzo workers, have felt continually frustrated because we've never managed to get this issue onto the agenda of the big organizations."

This is because konzo is a problem among the poorest of the poor, she said. "The solution is development. Put resources into these poor, rural areas. Give them agricultural support."

# Bitter cassava, bitter irony

To get to Kahemba, site of Dr. Michael Boivin's konzo research program in the Democratic Republic of Congo (DRC), you begin in Kinshasa, DRC's capital city, and drive for two days until you reach a rural region near the Angolan border. Over the years, depending on economic and political conditions, people have moved back and forth between the two countries, Boivin explained: "It's with this movement and instability, if you will, that people fail to ferment, dry and process cassava sufficiently to eliminate the cyanide contained within it."

Failure to detoxify cassava places children at risk of konzo; malnourishment escalates the danger. "It's the perfect storm of toxic cassava flour as a food staple and no beans or animal protein sources for sulfur-based amino acids so that, if cyanide levels build up sufficiently within a short period of time, the poison penetrates the blood-brain barrier, causing permanent and irreversible neurological injury," said Boivin.

Damage to the upper motor neuron pathways in the brain results in paralysis. Boivin's recent research reveals that konzo has more extensive, if less visible, cognitive effects.

## Colonial legacy

"Bitter cassava is not indigenous to the Congo basin. The Portuguese brought it from the Amazon in 1558 and it just thrived in Congolese soil," explained Boivin. "And, today, what's the option for millions of poor people who face famine due to drought or war? Starve... or eat bitter cassava and risk konzo."

Boivin has witnessed the effects of konzo since 1990, when a Fulbright scholarship brought him to DRC. He later revisited the country to complete an ecological analysis of konzo. "Then in May of 1993, I planned to return to the DRC for an assignment with Thorchild Tylleskar, Hans Rosling, and their colleagues from Uppsala University in Sweden." At that time, the WHO

Nutritionist Dr. Nicole Mashukano (right) teaches the wetting method to village women in Kahemba.

described konzo as an upper motor neuron disease that did not affect cognition. "We suspected otherwise," said Boivin. The team set out to prove it, but before they could begin, civil conflict in the region forced them to evacuate. Boivin turned his attention to cerebral malaria. Sometime later, at a scientific conference, he presented his research of school-age children affected by that disease, when "a tall, formidable Congolese neurologist came up to me and said, 'We need this kind of work on our konzo project, would you write up a grant with me?'"

And so began Boivin's collaboration with Desire Tshala.

## Developmental delays

In 2011, parts of DRC became stable enough for the pair to begin "a multi-faceted research program" in Kahemba. Through 2017, Tshala and Boivin's team documented konzo's effects on development, constructing a portrait of affected, school-aged children.

Continuing work in the region pioneered by Jean-Pierre Banea in the DRC Ministry of Health and Nutrition, Tshala and Boivin's team, in partnership with Esperance Kashala-Abotnes at the University of Bergen in Norway, was the first to document overall cognitive delays in addition to motor delays from poorly processed cassava in infants and very young children.

These disturbing results raised an urgent question: How can konzo be prevented? "The only practical way is the wetting method," said Boivin. It was clear, though, that mothers who learned the method only practiced it for a time before returning to familiar tradition.

## Caregiver intervention

Previously, with funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, Boivin's team had adapted a caregiver training intervention for Ugandan mothers living with HIV. The Mediation Intervention for Sensitizing Caregivers (MISC) teaches mothers how to better care for their children, leading to improved developmental outcomes and survival rates for the children.

Boivin hypothesized that it might encourage mothers towards sustainable use of the wetting method. Preliminary results show the program is making a difference.

"We're preventing konzo, a permanent, irreversible neurological disease, in the most abject impoverished setting you can imagine," said Boivin. If some mothers become peer leaders-trainers for the wetting method with MISC, the benefits could extend exponentially—to her family, her community, and beyond.



# A quest for solutions to prevent konzo

While working on an Ebola project in the Democratic Republic of Congo (DRC), Dr. Matthew Bramble—a staff scientist at Children’s National Medical Center—met Dr. Desire Tshala, who convinced him to work on konzo, a disease he’d never heard of. Over the next two years, Bramble helped analyze data collected by Tshala’s team without once meeting anyone affected by the disease. Eventually, Bramble found time to make the long trek to Kahemba. “You get to know the kids, and, well, the story changes. It’s no longer just interesting science. Now I’d like to solve it.”

Bramble’s Fogarty-funded project aims to reveal connections between konzo and the gut microbiome—the trillions of bacteria and other microbes living in our gastrointestinal tracts. The human body cannot metabolize linamarin (a toxic, cyanide-related chemical in cassava), so it eliminates it instead. “If linamarin is going through you, it’s still got to be acted on by intestinal microflora,” explained Bramble. The gut microbiome, then, may play a significant role in konzo’s genesis.

## Big data applications

In Kahemba, there are many households where one sibling gets konzo but another doesn’t, despite sharing the same lifestyle and food, said Bramble. “Why that exists we still don’t know.” To find answers, his team assembled a hundred sibling pairs—one hundred konzo-affected children plus a hundred unaffected siblings—collected samples, and then performed 50 million DNA reads. Data analysis is not yet complete, but early findings have shown “some very interesting metabolic differences between affected and unaffected children.”

**“It’s likely that not all answers will be found in hard molecular science.”**

Neerja Vashist, co-author and a graduate student researcher in the Department of Genomics and Precision Medicine at George Washington University, said they knew a “big data component” would be needed to answer the most pressing questions about konzo. “Big data allows you to get a lot of information out, and the data we get from the gut microbiome can possibly be applied, in a laboratory setting, to test other hypotheses.”



*Dr. Matthew Bramble spends time with the children of Kahemba. “You get to know the kids, and, well, the story changes. It’s no longer just interesting science.”*

Photo courtesy of Matthew Bramble

Historically, the villagers have seen konzo as random and sporadic, said Bramble. “But I don’t think it’s either. There is a variable enabling this to happen to some but not all the kids. This is what the newest konzo research is trying to identify.” Bramble noted that outbreaks of konzo always follow an environmental stressor that interferes with the processing of cassava. He hopes his research elucidates the factors determining which children are affected.

## Introducing a new strain

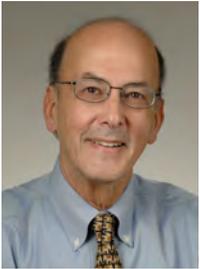
It’s likely that not all answers will be found in hard molecular science, said Bramble, who also conducts research in the Philippines. There, he discussed konzo with Professor Vivian Topor, an agricultural expert. “Over her 30-year career, she’s bred various strains of cassava and, based on the color, you can estimate the cyanide content in some varieties.” He plans to introduce cassava from the Philippines to DRC, monitoring the crop to see how it behaves. “Cassava toxicity is very dependent on the environment. So poor soil and/or low water can make the plant more poisonous, but this new strain doesn’t fluctuate nearly as much as others.”

An agricultural solution to prevent konzo “inherently makes sense,” said Vashist. “Change the crop, fix the problem permanently.” Yet, research conducted by Tshala, Cliff, and others show proven benefits when using the wetting method and nutritional rehabilitation. Until scientists gather evidence-based results for a new crop-swap solution, these older methods may best protect the children against konzo.

# OPINION

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

## Let's not forget our pandemic achievements as we prepare for a new year



It's not yet time to declare victory over COVID-19, even if most nations have learned to live side-by-side with the pandemic. Still, events over the past two years reveal how global health impacts individual well-being and national security. As you know, the Fogarty International Center helps each of the other

institutes at NIH become engaged with global health research. For more than 50 years, Fogarty has been building partnerships between institutions in the U.S. and abroad, while training the next generation of scientists focused on universal health needs. These collaborative ventures include investigations of the dual burden of infectious and noncommunicable diseases, while encompassing data science, economics, genetics, climate change science, and many other disciplines.

### Contributions made by Fogarty trainees

Throughout the pandemic, researchers trained by our programs have made scientific discoveries that have contributed to international security. Take Dr. Jessica Manning, a former Fogarty fellow who now conducts malaria research in Phnom Penh. Her team at the Ministry of Health sequenced the viral strain infecting the first Cambodian COVID-19 patient and documented early spread of pandemic disease outside of China.

Similarly, Dr. Christian Happi, director of the African Centre of Excellence for Genomics of Infectious Diseases, sequenced the first SARS-CoV-2 genome in Africa by adapting sequencing and analytical pipelines he'd created back when he was a Fogarty grantee studying Ebola. In Botswana, Dr. Sikhulile Moyo leveraged the skills he'd acquired while supported by a Fogarty HIV research training grant to track COVID-19 mutations for his country's Ministry of Health. Last November, he alerted the world of a new omicron variant, which within six weeks became the dominant global strain, challenging the ability of COVID vaccines to control its spread. In the Dominican Republic, Dr. William Duke, a national commission member, used what he'd learned as a Fogarty trainee to help create a COVID-19 intervention plan to prevent and control the disease.

### An enduring legacy

As we prepare to begin 2023, I want to share additional news about Fogarty's Global Brain and Nervous System Disorders Research across the Lifespan program. In 2023, this "brainchild" of Dr. Kathy Michels, a Fogarty veteran who retired earlier this year, will be 20 years old! The program's exploratory and developmental research grants help investigators build research capacity, research collaborations and research networks within institutions, countries and regions.

Global Brain studies address a range of conditions. I'd like to bring two unique projects, both targeting fetal alcohol spectrum disorders, to your attention. Psychologist Tatiana Balachova of the University of Oklahoma has designed an intervention for women in Russia, while Drs. Sandra and Joseph Jacobson, a research team from Wayne State University, conducted the first-ever prospective longitudinal study of the syndrome in South Africa. Findings from both projects are ripe for translation within an American context.

Other examples of Global Brain program investigations with broad implications in our own country include a psychobiological study of early psychosis in China; schizophrenia research capacity building in Macedonia; a planning grant to reduce the burden of chronic psychotic disorders in Tanzania; an exploration of the family consequences of Zika in Brazil; an investigation of maternal traumatic stress and child development in South Africa; a study of internet-based treatment for common mental disorders in Latin America; an exploration of the genetics of psychosis in Africa; and a study on dementia and related health and social challenges in Lebanon. The program has supported collaborating scientists working in Shanghai Mental Health Center in China, Macedonia Academy of Sciences and Arts, Muhimbili University of Health and Allied Sciences in Tanzania, Altino Ventura Foundation in Brazil, the National Institute of Psychiatry in Mexico City, and Addis Ababa University in Egypt, among many other institutes.

Once again, I thank Kathy Michels for generously endowing Fogarty with a substantial legacy. Best wishes to her and to each of you in 2023.



## University of Lagos names first female vice-chancellor

Dr. Folasade Ogunsola was named Vice Chancellor of the University of Lagos, the first woman to hold the position. A principal investigator on the MEPI Jr project, Ogunsola was a founding member of the Nigerian Society for Infection Control and served as team lead for Infection Prevention and Control during the 2014-2016 Ebola outbreak.



## Infectious disease leader Lee Riley passes away

Dr. Lee W. Riley, a pioneer in global health, died on October 19, 2022, at 73. An expert in molecular epidemiology, Riley was director of the Global Health Equity Scholars Program at UC Berkeley School of Public Health, one of the consortia in Fogarty's Global Health Fellows & Scholars/LAUNCH program.



## RAPIDD program co-founder awarded Kyoto Prize

Dr. Brian Grenfell, co-founder of Fogarty's Research and Policy for Infectious Disease Dynamics (RAPIDD) modeling program, was awarded the 2022 Kyoto prize in basic sciences for his research in phylodynamics, a methodology that predicts the dynamics of RNA viruses in wildlife.



## Fogarty grantees elected to National Academy

Three Fogarty grantees were recently named to the National Academy of Medicine.

Dr. Marleen Temmerman, principal investigator on a Fogarty Global Infectious Diseases grant, was recognized for being a penholder of the U.N. Global Strategy for Women's, Children's, and Adolescents' Health and founding director of the International Center for Reproductive Health at Ghent University.



Dr. Gagandeep Kang, a professor in the Division of Gastrointestinal Sciences at Christian Medical College in Vellore, India, and recipient of multiple Fogarty grants, was recognized for her contributions to understanding and improving child health during the SARS-CoV-2 pandemic.



Dr. Wafaie Fawzi, principal investigator for the Fogarty-funded Partnership for Global Health Research Training Program, was recognized for advancing the science of safety and efficacy of nutritional interventions in the prevention and management of major global health threats.

## Dashboard aims to aid food crisis response

The Global Alliance for Food Security (GAFS), convened by the Group of Seven (G7) and the World Bank, launched the Global Food and Nutrition Security Dashboard in early November. The dashboard includes global and country-level data on food crisis severity, global food security financing, and innovative research to strengthen crisis response and resilience.

## GMU launches public health college

George Mason University has renamed its College of Health and Human Services to the College of Public Health, a first for Virginia according to the university. The college includes the School of Nursing and the Departments of Global and Community Health, Health Administration and Policy, Nutrition and Food Studies, and Social Work.

## White House expands global health security partnerships

The Biden Administration announced new and enhanced health security partnerships with six countries and a strengthening of existing partnerships in 19 more, with a goal of directly supporting at least 50 countries, by 2025. The administration hopes to strengthen and achieve capacity in five critical areas in order to prevent, detect, and respond to infectious disease threats.

## TDR releases research skills curriculum

The Special Programme for Research and Training in Tropical Diseases (TDR) and the Global Health Network (TGHN) have developed a curriculum to provide knowledge and skills in health research to those with limited or no previous experience in order to deliver a safe, ethical, and accurate study.

## WHO holds school on refugee health

The third annual Global School on Refugee and Migrant Health was held in Dhaka, Bangladesh, in late November/early December. The virtual program focused on capacity-building for health systems response, addressing gender, culturally pertinent health care, the role of universities, and global and regional cooperation.

Funding Opportunity Announcement	Deadline	Details
Interventions for Stigma Reduction to Improve HIV/AIDS Prevention, Treatment and Care in LMIC Countries R01 Clinical Trial Optional	Dec 20, 2022	<a href="https://bit.ly/HIV_AIDS_StigmaReduction">https://bit.ly/HIV_AIDS_StigmaReduction</a>
Japanese Research Fellowships (JSPS)	Feb 17, 2023	<a href="http://bit.ly/JSPSforUS">http://bit.ly/JSPSforUS</a>
International Research Scientist Development Award (IRSDA) K01 Independent Clinical Trial Required K01 Independent Clinical Trial Not Allowed	Mar 8, 2023	<a href="http://bit.ly/IRSDAK01">http://bit.ly/IRSDAK01</a>
International Bioethics Training D43 Clinical Trial Optional R25 Clinical Trial Not Allowed	Jun 6, 2023	<a href="http://bit.ly/BioethicsTraining">http://bit.ly/BioethicsTraining</a>

For more information, visit [www.fic.nih.gov/funding](http://www.fic.nih.gov/funding)

## Global Health Matters

November/December 2022

Volume 21, No. 6 ISSN: 1938-5935

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## Revised NIH data requirements start Jan 25

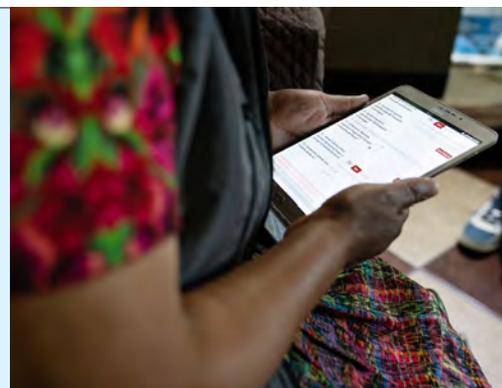
Starting January 25, 2023, NIH will require a data management plan in grant applications. The NIH Data Management & Sharing (DMS) Policy applies to all research, funded or conducted in whole or in part by NIH, that results in the generation of scientific data, regardless of funding level.

Scientific data is defined as data commonly accepted in the scientific community as of sufficient quality to validate and replicate research findings, regardless of whether the data are used to support scholarly publications.

Refer to the Funding Opportunity Announcement to determine if the DMS Policy applies to your application. NIH has also compiled a complete list of NIH activity codes subject to the DMS Policy.

Current NIH policies specific to certain types of research (e.g., clinical trials, research generating large-scale genomic data) continue to apply. In the event that another applicable policy has more detailed expectations than that of the DMS Policy, those expectations should be followed in addition to the DMS Policy.

Policies related to data sharing vary across countries. Investigators from foreign institutions and U.S. investigators collecting data in other countries should familiarize themselves with the policies governing data sharing in the countries in which they plan to work and address any specific limitations in the data sharing plan in their application.



*The revised policy applies to all research that generates scientific data.*

Photo courtesy of CDC / Nicholas S. Tenorio