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GLOBAL HEALTH MATTERS

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

NIH requests input on equity in global health research

The Fogarty International Center and seven partner Institutes and Centers request input on approaches NIH might take to promote greater equity in global health research conducted in low- and middle- income countries (LMICs).

NIH looks forward to hearing from the U.S. and the international scientific, academic, and public health communities, with a special interest in input from LMICs. Comments should be submitted no later than August 1, 2022. Questions may be sent to Blythe.Beecroft@nih.gov.

The RFI is available at https://bit.ly/EquityGlobalResearch

Photo by David Rochkind for Fogarty/NIH

NIH looks forward to hearing from the U.S. and international scientific, academic, and public health communities, with a special interest in input from LMICs.

Global Health Fellows & Scholars return with LAUNCH

In a renewal of its flagship Global Health Fellows and Scholars program, Fogarty International Center, along with partner institutes at NIH, has awarded $29 million to seven U.S. consortia and their partners in low- and middle-income (LMIC) countries to support the development of early-career global health scientists from the U.S. and LMICs over the next five years.

Fogarty has championed early-career global health scientists through its Global Health Fellows and Scholars Program for the last 20 years. This program aims to foster the next generation of global health scientists by providing these early-career trainees with a one-year mentored research training experience in global health at established institutions and project sites in LMICs. This year, the program was renamed LAUNCH or "Launching Future Leaders in Global Health Research Training Program" to better reflect its purpose.

In addition to the new name, the program is encouraging the participation of individuals from underrepresented populations in the U.S. at the graduate and postdoctoral levels and ensuring a more equitable training experience by embedding short term training in the U.S. as part of the fellowship year for trainees from LMICs, an opportunity that was not available in previous cycles.

This cycle also welcomes two new consortia, the Integrated Networks of Scholars in Global Health Research Training (INSIGHT), led by the University of Maryland, Baltimore, and ACHIEVE, which stands for Addressing the Research Capacity Gap in Global Child and Adolescent Health Disparities Utilizing Implementation and Data Sciences among Vulnerable Populations in Resource-limited Settings, led by Washington University in St. Louis. The remaining grants were awarded to existing consortia at Yale, the University of Washington, Harvard University, the University of North Carolina, and the University of California, San Francisco.

NIH partners supporting this cycle of LAUNCH include: National Institute of Neurological Disorders and Stroke

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FOCUS

The global toll of antimicrobial resistance

- The paradox of antimicrobial resistance in India
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Global Health Fellows & Scholars Return

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(NINDS); National Institute of Mental Health (NIMH); National Institute of Diabetes and Digestive and Kidney Disease (NIDDK); and NIH's Office of AIDS Research (OAR). Many NIH institutes, centers, and offices provide ad hoc funding each year for individual trainees.

Photo courtesy of Lindile Cele

Fogarty's Launching Future Leaders in Global Health Research Training Program builds on the successes and experiences of past Global Health Fellows and Scholars programs.

NIH launches new scientific data sharing website

In October of 2020, NIH announced its new Policy for Data Management and Sharing, the first new policy since 2003. Starting January 25, 2023, NIH will require all applicants to include a plan for data management in their grant applications.

In support of this policy, NIH's Office of Extramural Research (OER) launched a new NIH Scientific Data Sharing website in April of 2022 that includes content on data sharing, genomic data sharing, and related policies. The public-facing site provides a single interface for information on all NIH sharing policies and showcases data sharing-related resources across NIH.

Courtesy NCI

NCI's step-by-step instructions on how to submit genomic data.

As NIH moves to build a more efficient and equitable research environment, it is critical that data from NIH-funded research is easily accessible. NIH's commitment to making the research it funds available to the public can be seen through various data-sharing policies that increase the transparency and availability of scientific data and resources. Data sharing expedites the translation of research results into knowledge, products, procedures and, ultimately, the improvement of human health.

This new policy, which applies to research funded or conducted by NIH that results in the generation of scientific data, requires that applicants include data management and sharing plans in their proposals and funding applications. These plans must be approved by the funding NIH institute, office, or center prior to the approval of funding. It also emphasizes the importance of good data management practices and establishes the expectation for maximizing the appropriate sharing of scientific data generated from NIH-funded or conducted research.

The website provides step-by-step guides, infographics, tools, and resources to help grantees understand which policies apply to them and how to comply with them. The site covers how these policies affect clinical trials, model organisms, scientific data, genomic data, research tools, and research publications.

NIH's Office of Extramural Research is hosting a two-part webinar series, Implementation of the New NIH Data Management and Sharing Policy, to discuss details of the new policy and answer questions. Sessions take place August 11 and September 8. Registration is required and recordings will be posted on the site. OER is also posting regular updates on their Extramural Nexus blog about the data sharing policy covering everything from consent language to common data elements.

RESOURCES

https://bit.ly/NIH_Data_Sharing

Creating sustainable teen HIV care by listening more

Tasting independence for the first time, many adolescents do not seek out medical services—even when urgent health issues emerge. How, then, do health professionals reach them? "Adolescent-friendly approaches are needed," said Dr. Linda-Gail Bekker at Fogarty's sixth annual meeting of the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA) in March. "Adolescent-friendly" means tailored services with flexibility around timing and accessibility provided alongside relevant, confidential information, explained Bekker, Director of the Desmond Tutu HIV Centre at the University of Cape Town. "And where possible there are comprehensive services integrated into the mix and, when referrals are needed, they come with assistance, preferably peer navigation."

AHISA, a Fogarty-led alliance, comprises 26 teams of NIH-funded researchers, program implementers, and policymakers working in 11 countries in sub-Saharan Africa. AHISA aims to enhance the effective use of evidence to help overcome implementation challenges related to caring for adolescents with HIV in Africa. Bekker believes HIV services should never hinge on whether a teen's HIV test comes back positive or negative. Whatever the test result, there should be "some intervention, some process to move this young person through—a cascade of care," said Bekker. This might include mental health services and well-being modules delivered via digital options, all while taking into consideration that teens "are transitioning from pediatrics through adolescence and into adult health care."

Sustained engagement

Currently, Bekker's team is piloting "fast PrEP," a hub-and-spoke system that includes mobile clinics and pre-exposure prophylaxis (PrEP) depots situated near shops and hair salons; courier delivered PrEP; youth adherence "buddy" clubs for HIV treatment; and integrated school programs and government clinics. Bekker is applying implementation science research methods to understand whether fast PrEP can yield greater coverage of the adolescent population as measured in HIV exposure and incidence. Sustained engagement with 19-to-24-year-olds is always difficult, noted Bekker. To encourage this age group to take up health services, she has studied the effect cash incentives have on participation in an empowerment program that provides access to antiretroviral therapy and PrEP. A transfer of 360 rand (about $23) pushed into the cell phones of young women who attend the sessions made a powerful difference: 60-fold more women who received the cash "nudge" returned to the empowerment sessions compared to those who did not receive the money.

Linda-Gail Bekker, former Fogarty trainee, addressed the annual meeting of AHISA.

Photo courtesy of International AIDS Society

Considering context

Implementation science researchers also need to be heard, said Dr. Elvin Geng, Director of the HIV, Infectious Disease and Global Health Implementation Research Institute (HIGH IRI) at Washington University in St. Louis. Geng believes tensions and dynamics exist in the discipline because certain approaches have been "crystallized and systematized." Should the field be promoting standard tools like CFIR (Consolidated Framework for Implementation Research) and ERIC (Expert Recommendations for Implementing Change)? "Or do we continue to evolve and explore? There are other ways of understanding the implementation problem that could complement and extend existing approaches." His HIGH IRI program offers students —some sponsored by AHISA—a multifocal view of implementation research methodology that also honors individual experience.

Greater consideration must be paid to context, he concluded. Health systems in low resource settings that have large service gaps may not benefit from accepted, evidence-based interventions. Unique contexts may require individual strategies. "A lot of the time when you bring ideas into a cross contextual setting, you get to see the gaps in your original thinking."

For additional information: *https://bit.ly/AHISA-update*

Fogarty welcomes new board members

Fogarty recently welcomed five new members to the Center's advisory board: **Dr. Otis Brawley,** Bloomberg Distinguished Professor of Oncology and Epidemiology, Johns Hopkins University; **Dr. Wondwossen Gebreyes,** Hazel C. Youngberg Distinguished Professor in molecular epidemiology and executive directorof the Global One Health Initiative, The Ohio State University; **Dr. Jennifer Kates,** senior vice president and director of global health & HIV policy, Kaiser Family Foundation; **Dr. Maureen Lichtveld,** dean of the Graduate School of Public Health and Jonas Salk Chair in Population Health, University of Pittsburgh; and **Dr. Robert Murphy,** executive director at the Institute for Global Health and John Philip Phair Professor of Infectious Diseases, Northwestern University.

PROFILE

Fogarty fellow tackles sickle cell disease

An estimated 8,000 to 11,000 children are born with sickle cell disease (SCD) each year in Tanzania. The nation ranks fifth in the world for the highest rates of the disease, behind only Nigeria, the Democratic Republic of Congo, India, and Angola. Dr. Siana Nkya, a researcher from Tanzania, has focused her career on studying sickle cell disease and its genetic determinants in an effort to find new interventions.

Sickle cell disease causes red blood cells, which are typically round, to form more like crescent moons. Round red blood cells move quickly through the blood vessels, but these sickle-shaped cells impair blood flow and result in blood clots and poor oxygen levels, leading to chronic, acute pain syndromes, severe bacterial infections, and tissue death. Fetal hemoglobin is a major sickle cell disease modifier, meaning those with higher levels of it are more likely to experience a milder version of the disease.

Dr. Nkya, seeing the impact of sickle cell disease, chose to research the genetic factors that influence fetal hemoglobin levels in Tanzanians with the disease as part of her Ph.D. After completing her doctorate, Nkya had the opportunity to expand upon her research through a Fogarty Fellowship with the GloCal Health Fellowship at the University of California, San Francisco. There, she studied patients in Tanzania with high fetal hemoglobin levels, this time looking for specific genetic patterns that might impact their SCD.

"The way the Fogarty program is designed changed everything for me. The focus on mentored research and career development helped me become more successful as an independent researcher."

Following her fellowship, Dr. Nkya helped develop a newborn screening pilot program at the Temeke and Muhimbili hospitals, based in Dar Es Salaam, the first ever in Tanzania. In the United States a nationwide newborn screening program for sickle cell disease was implemented in 2006 and has reduced the under-5 mortality rate by up to 94%. There are no nationwide programs like this in any African country today, despite sub-Saharan Africa carrying most of the global SCD burden.

In 2019, Dr. Nkya was awarded an Emerging Global Leader Award to continue her research, specifically looking at the role of fetal hemoglobin decline and its determinants on sickle cell disease expression in the first three years of a child's life.

Siana Nkya, Ph.D.

Fogarty Fellow:	2016–2017
US Institution:	University of California, San Francisco
Foreign Institutions:	Muhimbili University, Tanzania
Research topic:	Sickle cell disease

This study, now in its fourth year, examines the correlation between the age a child presents with sickle cell disease, how high fetal hemoglobin levels impact the severity of the disease, and the rate of fetal hemoglobin decline—all with the goal of developing interventions for sickle cell disease. So far, over 250 children have enrolled and participated in the study.

In addition to her time researching and lecturing, Dr. Nkya, along with her colleague Dr. Mohamed Zahir Alimohamed, founded the Tanzanian Human Genetics Organization (THGO) to advocate for research and training, increased awareness, and diagnostics in human genetics and related fields across the country. They came to the idea after attending an annual conference in Ethiopia in 2018. "We noticed that we were the only Tanzanians there, which made us realize that Tanzania was behind in human genetics research and unable to contribute to these ongoing efforts in Africa." THGO hosted the African Society of Human Genetics conference in August 2021, the first time the annual conference was held in Tanzania.

In the future, Dr. Nkya hopes that her research will help identify genes and genetic variants in patients with sickle cell disease that will open the door for new interventions and therapeutics. "It has made me hopeful to see that we have more scientists that can do research in Africa, in the context of Africa," said Nkya. "I hope that we make Fogarty and NIH proud by doing meaningful research that will have an impact for generations to come."

RESOURCES

https://bit.ly/SianaNkya

Q&A

MOHAMED SEIF EL-DIN, MB.BCH, MPH

Mohamed Seif El-din is the Director of Poison Control and Burn Care Administration and Vice Head of the Central Administration of Critical and Urgent Care of Egypt's Ministry of Health. Following medical training at Ain Shams University, he received certification in research methods for guideline policy development and a master's in public health. He's served as a representative for the European Union Twinning project on road safety, a member of the National Road Safety Council, and Egypt's lead representative to the WHO's road safety projects. He is currently pursuing a doctorate in public health.

What inspired your interest in research?

My first work experience after graduation was as a health officer in the Cairo ambulance service. I observed that calls about injuries were more frequent than any other emergency. Yet there were no studies conducted around this valuable data. I wrote a proposal to develop a database information evaluation system for road traffic injuries and the American University in Cairo awarded me a budget. Later, my masters' thesis was based on data collected from the system I'd created.

Eventually, I was promoted to Director of the Information and Decision Support Center in the Critical Care and Urgent Department in the Ministry of Health. One of my accomplishments was a systematic review of different types of injuries at the national level. The outcomes of this research formed the basis of Egypt's national ambulance reform plan. My interest in injury prevention research is sustained by the many opportunities for collaboration with academia, local and international government agencies, NGOs, and nonprofit organizations. In addition, my research has helped me gain skills across many disciplines, including psychology, engineering, and urban planning.

Tell us about your Fogarty trainee experience.

Fogarty selected my application to participate in a two-month training program to enhance my injury epidemiological knowledge, skills, and experience. The program strengthened my ability to write proposals including how to pose research questions, formulate hypotheses, construct methodologies, gather reliable data, and analyze outcomes.

Through Fogarty, I worked with colleagues from different specialties. This cross-discipline collaboration allows you to learn from others. I developed an appetite for acquiring knowledge in fields parallel to my own research. For example, I now have a diploma in advanced hospital management, which enables me to translate scientific evidence and outcomes into action plans.

My program mentors didn't spare any effort when offering help during or after the course… and always with a friendly attitude! Because of Fogarty, I finalized my doctorate dissertation and published three independent scientific papers, and this led to steady progress at the Ministry of Health.

Why study injury epidemiology?

Injury epidemiology helps me integrate the research of different specialties within my three administrative areas: road traffic injuries, burn injuries, and poison toxicology. For example, I've explored the links between drug abuse/addiction and traumatic brain injury severity prognostic assessment. That said, road traffic injuries are the primary injury issue in Egypt—and across the globe. Road traffic collisions cause health, social, and economic effects that outweigh even war and conflicts. Effective road safety interventions require: Integration between different stakeholders; coordinated collaboration; and evaluation of context — there is no one size fits all. Local context matters.

Tell us about your current role.

As a director and vice head at Egypt's Ministry of Health, I manage the central administration of all urgent and critical care. I oversee information systems and conduct research for road traffic injuries, poison control, and burn care. As a member of the National Road Safety Council in Egypt, I interact with different stakeholders, including the ministries of education, interior, environment, and infrastructure, to decrease the burden of road traffic injuries. I also lead the ministry of health partnership team in an international collaboration among four Egyptian universities and three European universities: Malta University, University of New Castle, and Sweden Royal Institute of Technology. This project developed an IT diploma and a professional certificate in clinical toxicology, which is currently lacking in Egypt. In ways this is similar to a previous EU project I participated in where we constructed a uniform GPS-coordinated accident registration system in Egypt. As a result, we can now share safety and post-crash investigation to come up with reliable safety recommendations for decision making.

RESOURCES

https://bit.ly/MohamedSeifEl-din

The global toll of antimicrobial resistance

Following his 1928 discovery of penicillin, biologist Alexander Fleming warned that overuse of the drug could lead to resistant bacteria. Nearly 100 years later, the world is grappling with this reality. Resistance develops when bacteria acquire, through genetic mutation or genetic transfer, new characteristics rendering them impervious to the drugs meant to kill them. Ranked by the WHO as one of the top 10 global health threats, antimicrobial resistance (AMR)—when not only antibiotics but also antivirals, antifungals, and antiparasitics lose power—makes infections difficult or impossible to treat and raises the risk of disease severity and spread.

Resistant pathogens end more lives than HIV/AIDS or malaria: 1.27 million people died in 2019 as a direct result of AMR, as estimated by an international team of scientists in a report published earlier this year by *The Lancet*. The team calculated an additional 4.95 million AMR-associated deaths.

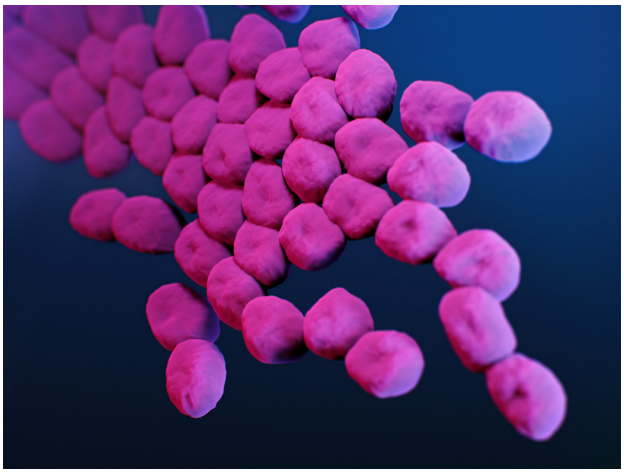


Photo courtesy of CDC Antibiotic Resistance Coordination and Strategy Unit

Acinetobacter bacteria *causes pneumonia and wound, bloodstream, and urinary tract infections. Nearly all infections happen in patients who recently received care in a healthcare facility.*

"One of the most sobering findings in our study was that AMR disproportionately affects young children," the study's lead author, Dr. Chris Murray of the Institute for Health Metrics and Evaluation, University of Washington, told Fogarty in an email. Children under 5 represent roughly one in every five AMR-linked deaths.

LMIC burden

The researchers estimated disease burden for 23 pathogens and 88 pathogen-drug combinations in 204 countries and territories in 2019. No nation is immune to AMR, yet it is low- and middle-income countries (LMICs), home to nearly 85% of the world's population, that shoulder the highest burden. The magnitude of the problem is difficult to assess given the lack of rigorous surveillance and data in LMICs. Western sub-Saharan Africa (SSA) had the highest estimated death rates: 27.3 deaths per 100,000 people attributable to AMR and 114.8 per 100,000 associated with AMR. Five regions— south Asia and all four SSA regions —had AMR-associated death rates higher than 75 per 100,000. By comparison, high-income regions had a direct AMR death rate of 13 per 100,000 and an associated death rate of 55.7 per 100,000.

Three types of infections accounted for 78.8% of AMR deaths in 2019, the report found: lower respiratory and thorax, bloodstream, and intra-abdominal. Of the deaths directly attributable to AMR, an estimated 73% (929,000) were caused by six pathogens: *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. These six pathogens also accounted for nearly three-quarters of the total AMR-associated deaths.

"What is important to emphasize is that out of the seven deadliest bacteria resistant to antibiotics, vaccines are currently only available for two (*Streptococcus pneumoniae* and *Mycobacterium tuberculosis*)," stated Murray. "One of the aims of such breadth and novelty in our approach was to help clinicians make faster, life-saving choices and reduce the use of antimicrobial agents where expectations of effectiveness are low."

Murray concluded, "Future work should combine data from humans, animals, and environment within the framework of 'One Health' to accurately reflect the intertwined nature of AMR. This means multisectoral partnership between the research community and other experts (such as physicians, pharmacists, public health and veterinary specialists) is needed."

Within Fogarty's One Health portfolio is a Redeemer's University project supported by the National Institute of Allergy and Infectious Diseases and the NIH Office of the Director. Helmed by Dr. Christian Happi, the research will examine AMR trends and dynamics of transmission in Eastern and Western Africa; create a portable screening tool for clinical care; and explore potential benefits of enhancing antibiotic efficacy against multidrug-resistant bacteria.

Resources: https://bit.ly/GlobalTollAMR

The paradox of antimicrobial resistance in India

Indian medical staff care for a patient with multi-drug resistant tuberculosis. India has one of the highest rates of antimicrobial resistance (AMR) in the world.

Photo courtesy of Tony Fredrick/CDC

India, home to one in every six people on the planet, has one of the highest rates of antimicrobial resistance (AMR) in the world. As a Fogarty Global Health Fellow, Dr. Matt Robinson worked in Pune, India, to characterize the burden of antimicrobial resistance among hospitalized patients with fever illnesses. "Fever is the most common reason why people in India seek medical care and we found that almost every patient hospitalized with fever received antibiotics — despite mosquito-borne diseases, which are not treated by antibiotics, being the cause of most of these illnesses," said Robinson.

There's a perception that Indian doctors over-prescribe antibiotics, yet that is not entirely true, said Robinson. In resource limited settings, where patients might not be seen by a nurse for 24 hours, options are limited. "So sometimes you provide treatment for the worst possible scenario," like prescribing antibiotics before identifying the cause of illness.

Other challenges faced by Indian doctors include the many different drivers of AMR. First, there's limited access to safe water, sanitation, and hygiene. Second, many Indians self-medicate without knowing how to use the drugs appropriately. Third, resistant organisms and infections circulate more freely, said Robinson. "Carbapenem-resistant organisms are about 20 times as common in India as they are in the U.S. while about two-thirds of all carbapenem-resistant *Klebsiella* and *E. Coli* bloodstream infections occur in India." The Drug Resistance Index, a measure of efficacy of antibiotic treatments across nations, records generally higher rates of resistance for priority pathogens in LMICs, with India showing the highest rate of all.

"Are more patients in India dying from AMR infections or from lack of access to antibiotics? The answer is lack of access to antibiotics," said Robinson. "In one place you have this weird paradox, where overall you have insufficient access to antibiotics, yet some patients receive antibiotics inappropriately."

Multipronged approach needed

The country has reached a "certain tipping point" where antimicrobial resistance is rampant, so Indian doctors prescribe last line antibiotics to everyone and this in turn makes resistance even worse, explained Robinson. "It becomes this horrible spiral where AMR is increasing, so clinicians begin to prescribe ever-broader spectrum antibiotics."

Perhaps ironically, India is the world's top producer of antibiotics, supplying over 40% of the global market, according to a report published by the not-for-profit Stockholm International Water Institute. This, too, contributes to the nation's AMR problem with high concentrations of antibiotics measured in water bodies surrounding pharmaceutical works and significant contamination of air and soil within manufacturing zones. Along with poor management of pharmaceutical waste, the widespread use of antibiotics in animals and crops also contributes to high AMR rates in India. Human health is affected when antibiotic-resistant bacteria are transmitted between people and animals through contact, food products, and the environment.

Multiple drivers of AMR means solving this problem requires a "multipronged approach," said Robinson. "The government of India is working very hard to improve infection prevention and control in health care facilities, while making general improvements in sanitation." Enhanced healthcare systems are also required so patients have access to trained medical professionals and not just the pharmacy counter. Increased access to diagnostics would help doctors become better stewards of antimicrobials. Most importantly, new antibiotics are needed, said Robinson. In the past few years, novel drugs have become available, but they only work against resistance commonly seen in the U.S. "None of them target the mechanisms of resistance common in India."

Discovering sepsis, tracking antimalarial drug resistance in Africa

Nearly 85% of an estimated 30 million annual cases of sepsis occur in low- and middle-income countries (LMICs). Sepsis—a life-threatening condition which develops when a patient's immune system responds in an extreme way to an infection—can lead to tissue damage, organ failure, even death. In developed countries, sepsis usually results from severe bacterial infections in older people with multiple medical problems. No single effective therapy for sepsis exists, yet decades of studies in the U.S., Europe, and Asia have led to unified treatment guidelines.

Not so in Africa.

"In sub-Saharan Africa (SSA), we have a poor understanding of the pathophysiology of sepsis since, essentially, every conceptual model reflects host and pathogen features relevant to the Global North," said Dr. Matthew Cummings of Columbia University. To start, sepsis is more common in SSA because there's no shortage of pathogen diversity. "Bacteria, mycobacteria, parasites (most commonly malaria), viruses… a wide variety of pathogens cause sepsis in Africa," said Cummings. Meanwhile most sepsis patients are younger and have HIV or another co-infection not frequently seen in high-income countries.

Antimicrobial resistance adds one more challenge. Considerable resources are needed to run conventional laboratory tests to identify pathogens and appropriate antibiotic treatments, Cummings explained. In addition, the antibiotics for treating resistant bacteria are more expensive than traditional ones.

How, then, can Africa reduce its burden of sepsis? First, increase recognition of the syndrome to improve emergency care, said Cummings. Second, untangle different biological features of the syndrome to develop precision treatments. "We recently published a paper in *Critical Care*, showing for the first time that biological sepsis subtypes exist in Uganda that have distinct profiles associated with unique features and outcomes." Finally, address the role played by HIV-associated tuberculosis.

Antimalarial resistance in Africa

Malaria is an everyday reality for many people: 219 million cases are tallied each year. Across Africa, the parasitic infection transmitted by mosquitoes is commonly treated with artemether, a derivative of the drug artemisinin, combined with a second antiparasitic, often lumefantrine. The regimen works by delivering a one-two punch, explained Dr. Melissa Conrad, an assistant professor at University of California, San Francisco. Artemisinin kills parasites quickly but has a short half-life, disappearing from the blood stream within two days. Here the second drug takes up the fight. "Recent research has shown *ex vivo* and clinical evidence of emerging artemisinin resistance in Uganda," said Conrad. *Ex vivo* refers to laboratory studies performed on tissues or cells removed from a living organism.

Many rural hospitals in Africa lack the resources to conduct necessary lab tests.

Photo courtesy of Staff Sgt. Andrea Merritt, U.S. Army Africa

When one drug in a combination regimen begins to fail it leaves more parasites to be killed by the second drug, increasing the probability that the second drug will become ineffective. "From *ex vivo* drug sensitivity studies we see some evidence of what we think is decreased sensitivity to lumefantrine in the same region of Uganda where we are seeing artemisinin resistance," said Conrad. The U.S. President's Malaria Initiative and the Uganda Ministry of Health are planning to conduct clinical therapeutic efficacy studies, in which tests are done on human volunteers, to verify this trend. Urgency is needed; malaria claims more than 400,000 lives annually, most of them children younger than 5.

Meanwhile, there are reasons for hope, including new drugs in the pipeline, though none are "as close to being readily available as we wish," Conrad said. "We can work with the existing drugs to get people treated but it's going to take a lot of really good clinical work." This means using appropriate drugs and educating patients to use them correctly. Given evidence that there is not yet full-scale resistance to artemisinin— "it's more of a tolerance" —prolonged treatment with existing drugs may help overcome the current problem. Scientists are also studying triple combination therapies, where parasites must cope with three drugs simultaneously.

HIV & TB, two paths to antimicrobial resistance

HIV and Tuberculosis are both very prone to developing antimicrobial resistance, yet they adopt opposite strategies for doing so, said Dr. Patrick Cudahy. The virus that causes AIDS makes a "billion" copies of itself, most of which don't work. "But a few of them might actually be impervious to treatment and that's how HIV drives resistance," said the Yale School of Medicine instructor. By contrast, TB doesn't mutate much and instead "just hunkers down, waits you out, and takes six months to treat, which is very unique for a bacterial infection," said Cudahy. In that time, TB seizes every opportunity —inappropriate medication or missed doses of medication—to grow resilient.

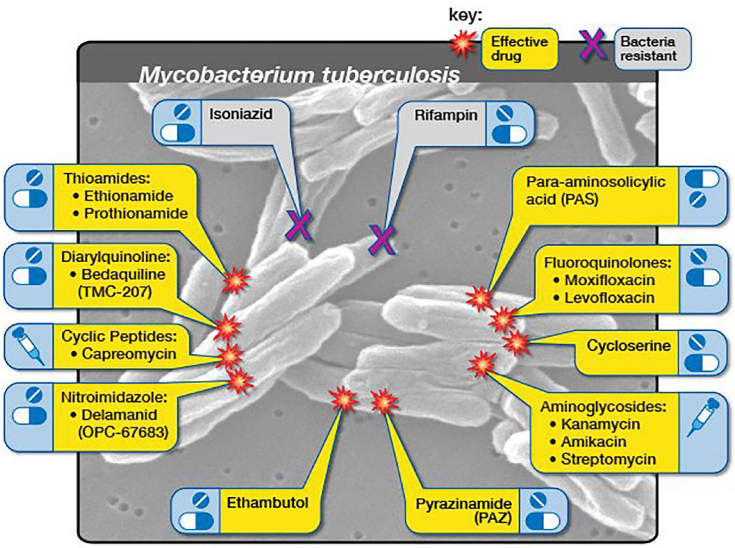
Cudahy's earliest medical training in South Africa took place in "big open wards of TB patients." Many patients were co-infected with HIV and some undoubtedly had multidrug-resistant tuberculosis (MDR-TB). Even experienced doctors found it difficult to measure treatment response. "That's how I got interested in developing a biomarker—a very early signal—that can tell us if a patient with MDR-TB is responding to therapy," said Cudahy, describing his Fogarty-funded project. Study results will help reduce development of new resistance and further transmission of TB by ensuring that patients are on effective medications.

About a quarter of patients with MDR-TB and HIV do not survive. "If a person is exposed to drug-resistant TB—or develops resistance due to being given the wrong drugs or being unable to take their drugs reliably—then they need second line medications," said Cudahy. Until very recently, this meant several pills and daily injections for up to two years with drugs that had "profound" side effects—deafness and kidney injury. "The new WHO drug regimen for MDR-TB is four oral drugs for six months—so that's fantastic progress," he said. Meanwhile, a new genetic test can detect "the vast majority of MDR-TB. That's a game-changer since we now know what we're dealing with from the beginning."

Characterizing epidemic spread

Dr. Karen Jacobson trained in Cape Town, South Africa, not long after scientists had first sequenced the TB genome and begun to recognize mutations predicting resistance to first line drugs (isoniazid, rifapentine, and rifampin). "As sequencing became a standard part of diagnostics, I wondered: Could we use this routinely collected data to better understand disease spread and evolution of disease?" Her project, funded by Fogarty and completed in 2017, identified regions of the Western Cape Province with a high burden of drug-resistant TB. "Even after adjusting for TB burden, we found communities differentially impacted—not every community with a lot of TB also had a lot of MDR-TB."

The social context allowing TB to spread is well-known, said Jacobson who is an associate professor at Boston University School of Medicine. Overcrowding, malnutrition, and poverty all contribute to its prevalence. But understanding rifampin-resistant TB is another question. "We've come to see in South Africa…that most of the resistant TB is actually transmitted. People catch it in that form," said Jacobson. With the newest diagnostics, doctors can prescribe the correct drug regimen faster and so break the chain of transmission. "But there still are a lot of questions about why in certain communities the rifampin resistance can become so successful," said Jacobson. One hypothesis is that people with HIV may serve as incubators for resistance evolution resulting in a strain capable of transmitting in the community.



MDR-TB occurs when a tuberculosis strain is resistant to first-line drugs. To cure MDR-TB, healthcare providers must turn to a combination of second-line drugs, which may cost 100 times more than first-line therapy.

Illustration courtesy of NIAID

To prevent spread of MDR-TB, funding and support of ongoing sequencing and early detection of cases is needed. "If resistance to the newer drugs begins, then we need to ask: Where is this occurring? Under what circumstances? Can we add other drugs to the regimen?" said Jacobson. "Tuberculosis, although an ancient disease, is one that's really been understudied and underfunded. Yet it remains a leading killer globally."

OPINION

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

To improve global health, invest in people

The World Health Organization estimates an additional 18 million health workers are needed to achieve functional health systems across the globe by 2030. Currently, programs such as the U.S. President's Emergency Plan for AIDS Relief and the U.S. President's Malaria Initiative contribute $1.56 billion annually to support the global health workforce. Now, President Biden is calling on Congress to approve an additional $1 billion to fund the Global Health Worker Initiative. This program would serve as a framework to guide investments while strengthening coordination among our partners, including other nations, regional organizations, and the private sector.

The initiative rests on four pillars: protection of health workers; expansion of the workforce; advancement of equity and inclusion; and promotion of technological solutions. These pillars have long been familiar to Fogarty. Our unique mission includes fostering the workforce of early-stage researchers and building research capacity in low- and middle-income countries (LMICs). Since 1989, more than 7,500 individuals from over 130 countries have been trained through our many programs including our AIDS International Research Training Program and Medical Education Partnership Initiative.

New technologies play an important role in addressing workforce issues and the future of health care itself. One of our most novel programs with the greatest numbers of grant submissions is Fogarty's Mobile Health (mHealth) initiative. In Africa, it has been said that more people have cell phones than toilets. Mobile health solutions can fill gaps by empowering community health workers to perform medical tasks, connect patients with resources, or arrange access to clinics or medical facilities.

Fogarty mHealth projects have included cell phone-based solutions that link high-risk pregnant women to birthing centers; screen people with poor vision; monitor patients to ensure adherence to their medications, (e.g., drugs for tuberculosis, HIV, and high blood pressure); identify new cases of leishmaniasis; diagnose cervical cancer; and connect oncology professionals to patients in need of palliative care. Technology—both the digital tools carried in health workers' hands and the enterprise level systems supporting these tools—can train professionals, extend a worker's reach, and drive innovation.

I must add that Fogarty focuses on developing a research workforce because the delivery of health care is ever-changing and driven by data science and innovation. It is researchers who create new ways to deliver care, monitor adherence to treatment, and document recovery or failure. Fogarty seeks research leaders who can anticipate what's ahead and understand how to become the agents of change we need.

Fogarty also prizes equity and inclusion because we understand that patients respond best to health workers who look like themselves, whether ethnic minorities, women, the disabled, or rural inhabitants. Given that women represent 70% of the health care workforce worldwide, we need to address issues of unpaid labor, unequal salaries, and lack of maternity leave, and how these impact quality of care. We also need to ensure girls can complete their education since many drop out when they start their period because their schools don't have appropriate sanitation facilities.

When I first worked in Bangladesh more than three decades ago, our field teams were composed exclusively of men, while women were hired as part-time contractors so they could not rise into positions of leadership. Today, I can happily report that these old traditions have changed. Women have entered the workforce, and this has led to an upgrade of status and paying jobs.

The spectrum of health worker occupations is vast and includes not only community health workers, nurses, and physicians, but researchers, laboratory scientists, pharmacists, public health workers, supply chain experts, and future leaders. Spending on these skilled workers provides, on average, a nine-to-one return on investment, said economic advisor Daleep Singh at the May launch of the Global Health Worker Initiative. I, too, believe that when we invest in worthy people and encourage them in research, we never go wrong.

RESOURCES

https://bit.ly/ImproveGlobalHealth

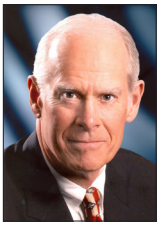
PEOPLE

Nkengasong confirmed as PEPFAR lead

Dr. John Nkengasong was confirmed as the Director of the President's Emergency Plan for AIDS Relief (PEPFAR). Nkengasong previously led the Africa CDC. Originally from Cameroon, he is an esteemed virologist with over 30 years of experience in global health and will be the first person of African origin to lead the PEPFAR program.

Former Fellow, DS-I Africa grantee named to TIME100

TIME has named former Fogarty fellow, Dr. Sikhulile Moyo of the Botswana Harvard AIDS Institute Partnership, and DS-I Africa grantee, Professor Tulio de Oliviera of the Stellenbosch University and the University of KwaZulu-Natal, to its annual list of the most influential people in the world for their discovery of the Omicron variant of SARS-CoV-2.



Former congressman, Fogarty advocate, dies

The Honorable John Edward Porter died on June 3, 2022. He was 87 years old. He founded and co-chaired the Congressional Human Rights Caucus, co-authored legislation creating Radio Free Asia, and served as chairman of the Global Legislators Organized for a Balanced Environment, known as GLOBE USA. Most recently, Edwards served as Research!America's chair emeritus.

Global health community mourns loss of Stephen Blount

A former director of the CDC Office of Global Health, Blount's work included the Polio Plus Initiative which reduced the number of polio-endemic countries from 41 in 1997 to four in 2010 and the Global Measles Partnership, an effort that reduced measles mortality worldwide by 39 percent between 1999 and 2010.

Virologist responsible for rotavirus discovery has died

Australian virologist Dr. Ruth Bishop, credited with discovering rotavirus in 1973, passed away on May 12. Her discovery led to widespread rotavirus vaccination, saving the lives of thousands of children globally. Bishop chaired several WHO committees and is cited as a significant influence on Bill and Melinda Gates in establishing their foundation.

Fogarty staff receive HHS Distinguished Service Award

Two Fogarty staff members received the HHS Secretary Award for Distinguished Service for their work with the Rapid Acceleration of Diagnostics (RADx) Initiative group. Dr. Nalini Anand, Director of the Center for Global Health Studies and the Division of International Science Policy, Planning and Evaluation, oversees scholarship in global health science and policy.

Dr. Marya Levintova, Program Director for the Division of International Training and Research, oversees grants in several of Fogarty's programs including NCD-Lifespan and the Global Trauma and Injury Research Training Program. RADx, an NIH initiative, speeds innovation in the development and implementation of COVID-19 testing technologies.

Global HEALTH Briefs

NIAAA launches alcohol resource

Helping Your Patients with Alcohol-Related Problems from the National Institute on Alcohol Abuse and Alcoholism is a free resource on alcohol and health covering screening through recovery. Physicians, physician assistants, nurses, psychologists, and pharmacists can earn CE/CME credits.
Resource: https://bit.ly/AlcholResource

Action needed on cancer in sub-Saharan Africa

A recent *Lancet Oncology* commission stresses the need for an Afro-centric approach and proposes actions, such as developing or updating national cancer control plans in each country, that must be taken urgently to address the escalating catastrophe.
Report: https://bit.ly/LancetCancerAfrica

Change from within needed for decolonization progress

The premise of this special collection from the *Annals of Global Health* is the understanding that meaningful progress toward decolonization must come from within the institutions that built the field of global health. Doing so will also require deep reflection on the role different disciplines have in advancing decolonization.
Collection: https://bit.ly/DecolonizationCollection

WHO calls for increased investment in IPC

The first-of-its-kind report from WHO provides a global situation analysis of how infection prevention and control (IPC) programs are being implemented in countries around the world. The report identifies gaps, offers guidance, and highlights the importance of integrating interventions with water, sanitation, and hygiene strategies.
Full report: https://bit.ly/WHO_IPC

Global roadmap promotes healthy longevity

Released in early June, the roadmap uses evidence-based recommendations on ways to ensure that all people of all ages can achieve healthy longevity equity. The report includes goals, structures, and recommendations across four domains: the longevity dividend, social infrastructure, physical environment, and health systems.
Roadmap: http://bit.ly/38rZIt6

Funding Opportunity Announcement	Deadline	Details
Chronic, Noncommunicable Diseases and Disorders Research Training D43 Clinical Trials Optional	Jul 13, 2022	https://bit.ly/NCD_ResearchTraining
Global Infectious Diseases (GID) Research Training Program D43 Clinical Trials Optional	Aug 3, 2022	https://bit.ly/InfectiousDiseasesResearch
Fogarty HIV Research Training G11 Clinical Trials Not Allowed D71 Clinical Trials Not Allowed D43 Clinical Trials Optional	Aug 22, 2022	http://bit.ly/NIHGlobalHIV
Emerging Global Leader K43 Independent Clinical Trials Required K43 Independent Clinical Trials Not Allowed	Nov 3, 2022	http://bit.ly/E_Lead

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

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NIH systems that use ORCID iDs

eRA Commons allows applicants and grantees to track applications through the entire grant process. Applications to many NIH grant programs will not be accepted if no ORCID iD is linked to an applicant's eRA profile.

PubMed is NIH's repository of biomedical and life sciences literature. Linking your ORCID iD to your PubMed bibliography allows for clear identification of authorship. This is especially important if you've changed names or have a similar name to other authors. If your previously published work has not been associated with your ORCID iD, contact the publisher(s) so they can update past publications.

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RESOURCE

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