NIH accelerates clinical trials of Ebola vaccines

The NIH is helping guide two front-runner Ebola vaccine candidates through early-stage human trials and, barring safety or immunity problems, may have the vaccines ready for advanced testing in African and other volunteers as early as December, according to NIH officials.

Researchers at the National Institute of Allergy and Infectious Diseases (NIAID) are evaluating a vaccine developed by Canadian scientists, called VSV-ZEBOV, for safety and its ability to generate an immune system response in healthy adults who are given two intramuscular doses. The Walter Reed Army Institute of Research is simultaneously testing the vaccine candidate as a single dose at its Clinical Trials Center in Silver Spring, Maryland.

“The need for a vaccine to protect against Ebola infection is urgent,” said NIAID Director Anthony S. Fauci, M.D. “NIH welcomes the opportunity to collaborate with the U.S. Department of Defense to conduct human clinical tests of another promising—and hopefully, successful—Ebola vaccine candidate.”

VSV-ZEBOV, which was developed by researchers at the Public Health Agency of Canada’s National Microbiology Laboratory, has been licensed to NewLink Genetics Corporation through its wholly owned subsidiary BioProtection Systems, both based in Ames, Iowa.

Early human testing of another investigational Ebola vaccine co-developed by NIAID and GlaxoSmithKline began in early September. Initial data on safety and efficacy are expected by the end of 2014.

NIH is preparing an initial safety trial for a third vaccine candidate, from Johnson and Johnson, which could begin early next year, and is collaborating on additional vaccine projects.

NIH researchers are also moving ahead with studies of experimental treatments—including ZMapp, BCX4430, brincidofovir, lamivudine and others. In addition, NIH is collaborating on efforts to improve diagnostic tests to enable speedy and accurate identification of patients ill with Ebola, since their symptoms might initially mimic malaria or other infectious diseases.

RESOURCE
Funders urged to invest in Africa’s research capacity

Sub-Saharan Africa has made remarkable strides in strengthening its health systems—and research is integral to guiding and sustaining further progress, Fogarty Director Dr. Roger I. Glass said at the recent World Health Summit in Berlin, Germany. The summit is held annually to address global health issues.

Over the past five years, the U.S. Medical Education Partnership Initiative (MEPI) has helped transform the way African medical schools prepare trainees for careers in health care, Glass noted. MEPI institutions have revamped their medical school curricula, updated libraries and adopted technology in many aspects of education, all within an environment that values and nurtures science. He reported new research opportunities have helped attract and retain faculty, expand South-South collaborations, and build research expertise both nationally and regionally.

Fogarty’s Glass delivers Enders lecture at IDWeek

The development and global introduction of rotavirus vaccines were the subject of this year’s John F. Enders Lecture, presented by Fogarty Director Dr. Roger I. Glass during Infectious Diseases Week in Philadelphia. The annual keynote address honors the Nobel laureate who helped devise modern tissue culture techniques critical to the development of vaccines against polio, measles, rubella and rotavirus and other areas such as cancer biology. IDWeek is hosted by the Infectious Diseases Society of America and its partners.

In his talk, titled “The Global Introduction of Rotavirus Vaccines: Where will this path lead us?,” Glass reported that the number of hospitalizations for children with rotavirus has dropped more than 85 percent in the U.S. since vaccination began in 2006. Although there is a very small risk of intussusception—the telescoping of the intestine onto itself—the benefits far outweigh the risks, Glass said. With about 80 percent of U.S. children vaccinated, there have been approximately 50,000 fewer hospitalizations per year, a drop in visits to doctors or clinics, and indirect benefits including a decrease in diarrhea hospitalizations for older children and adults secondary to the protection of their younger children. An estimated one to five cases of intussusception have occurred per 100,000 vaccinated infants resulting in no fatalities in the U.S.

The WHO began recommending global use of rotavirus vaccines in 2009 to address the hundreds of thousands of diarrheal deaths that were occurring in children each year, the vast majority in developing countries. By August 2014, some 69 countries had instituted national rotavirus vaccination programs.

Many studies have documented decreased hospitalizations since implementing rotavirus vaccines, with a clear decline in rotavirus deaths in Mexico, Glass said. Several challenges remain before the full impact of rotavirus vaccines can be realized, he noted. Oral vaccines have been less effective in low-income countries in Asia and Africa for reasons that are not clearly understood.

Since India has one of the highest rates of rotavirus deaths—about 80,000 per year—Glass has worked with Professor M.K. Bhan and his Indian and American colleagues for several decades to produce a safe, effective and affordable vaccine for India. The vaccine has been licensed and approved for use in India and the Prime Minister has stated that all Indian children will soon receive a rotavirus vaccine free of charge, said Glass.

This is the first new vaccine produced totally in India in a century, using an Indian rotavirus strain, an Indian company, Indian clinical trials and support directly from the government of India, he noted. “While the positive health impact of rotavirus vaccination has been enormous,” Glass concluded, “further research is essential to improve the efficacy of existing vaccines in low-income settings and develop less expensive and more effective alternatives.”
Study probes link between malnutrition, gut infection

One in five children in developing countries experiences malnutrition, which is linked to physical and cognitive impairment and greater risk of early death. Many undergo repeated bouts of diarrheal disease, but the role this plays in their development is not well understood. Scientists hypothesize that childhood gut infections cause intestinal dysfunction that negatively impacts nutrient absorption, leading to stunted growth and cognitive deficits. They also suspect that repeated infections, combined with malnutrition, can undermine the effectiveness of vaccines.

To investigate these and other related issues, an international network of scientists was formed to conduct an unprecedented study of early childhood in eight countries on three continents. They describe their approach, methodology and tools in a series of articles recently published as a supplement to the Clinical Infectious Diseases journal. The $40 million project, “Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health (MAL-ED),” is led by Fogarty and the Foundation for the NIH, with funding from the Bill and Melinda Gates Foundation.

“As a central objective of MAL-ED, untangling the complicated web of malnutrition and enteric disease is considered a crucial factor in the development of interventions that will improve child health in resource-poor environments,” the study investigators note in the overview article.

The team, which began the study in 2009, chose urban and rural communities in countries where diarrheal diseases and malnutrition are common—Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa and Tanzania—and standardized study protocols so the results could be compared. The researchers enrolled more than 200 children in each location and followed them for the first two years of life, when many developmental milestones occur.

The scientists took a holistic approach with a community-based, longitudinal design and selection of geographically, socioeconomically and culturally diverse populations. They periodically measured the children’s growth and cognitive progress and collected a wide range of data on diarrheal diseases and other potential influences such as nondiarrheal diseases, vaccines administered, micronutrient levels, diet, socioeconomic status, gut function and environment.

Surveillance was intense, with each child’s home visited twice weekly. In addition, there was monthly collection of stool samples and information on a range of potential influences on the children’s growth. Among them were early termination of breast-feeding, introduction of pathogens to the baby via solid foods, micronutrient status, inadequate diversity of foods and the state of their gut flora. Researchers also measured language development, maternal depressive symptoms, maternal reasoning abilities, child temperament and home environment. Armed with such comprehensive data, scientists can determine “individual, site-specific and general recommendations regarding the nature and timing of possible interventions,” the MAL-ED authors said.

As well as the overview article, the supplement provides descriptions of activities at each field site and data collection methodologies used. These include an analysis of a biomarker test for detecting gut absorption and permeability, the use of infectious disease histories to signal the ages when child health is most vulnerable to infectious diseases, and the reasoning behind the choice of microbiologic assays and methodologies. Researchers also described the need to collect stool samples from asymptomatic children, both to capture those infections which produce no clinical symptoms and to gauge the main causes of intestinal infection within the community. In addition, they broached the understudied topic of how children in these diverse epidemiological settings might respond poorly to vaccines, which have been proven effective in populations in high-resource countries.

The study aims to provide important guidance for policymakers considering the optimal timing and targeting of interventions to achieve the maximum benefit. “Improvements in early childhood growth and development can have a long-lasting impact, through improved school readiness, educational achievement, and ultimately, improving the economic potential for individuals and their communities,” the MAL-ED investigators concluded.

Fogarty Fellow studies sickle cell drug in Uganda

By Cathy Kristiansen

During medical school, Fogarty Fellow Dr. Juliana Anyanwu was taken aback when a Nigerian friend suddenly asked her, “Do you know your status?” She looked blank, so he explained he was referring to whether or not she had inherited a sickle cell trait, information he said was essential to have before deciding on a mate.

Anyanwu, an American pediatrician with a Nigerian father, said their conversation really made her aware of the problem of sickle cell disease in Africa and the dearth of research about it. She soon developed a passion to help change that. While having one sickle trait is benign, children inheriting it from both parents typically face a host of health problems. Without treatment, the disease kills most children before they turn five. Such deaths are common in sub-Saharan Africa, where about three-quarters of the world’s affected babies are born, according to the WHO.

Anyanwu successfully applied for a Fogarty fellowship to help run a clinical trial in Uganda to study the safety of a treatment for sickle cell disease—hydroxyurea. The drug is commonly used in developed countries, but because it can curb the immune system it poses a potential concern for patients in countries with a heavy burden of malaria and other infectious diseases, combined with extremely limited health services. Children with sickle cell disease are known to be at particular risk for serious complications if they develop malaria, so it is important to know if hydroxyurea exacerbates this vulnerability. Uganda has a high level of both diseases.

The trial, funded by the Doris Duke Charitable Foundation and collaborators, is randomizing 200 children to receive hydroxyurea or a placebo. The principal investigators are Drs. Chandy John at the University of Minnesota and Christopher Ndugwa of Mulago Hospital in Uganda; both serve as Anyanwu’s mentors.

Their sage advice has been crucial to her success. You can’t expect everything to go A-B-D-C-E and F,” Anyanwu said. “There will be challenges and you learn from these challenges. It’s good to have someone who’s been there, done that, wisdom from someone else who has been through the experience you are trying to go through.”

After arriving in Uganda, Anyanwu became immersed in overseeing management of the trial, which enrolled its first patient in September 2014. She ensured appropriate documents were in place, examined lab processes that would be required and prepared and edited an operations manual. She also needed to confirm everyone was on the same page. “I wanted to make sure that trust was in place, that everyone understood the goal of the trial and would work toward it as a team,” she said.

The experience has helped her develop new skills and gain valuable insights. “It’s been a real eye-opening opportunity. You’re thrown into a new environment, a slightly different work culture, and you’re trying to learn so many things,” she noted. “I know that international health is what I am meant to do.”

The study’s results may have great implications and cause a paradigm shift in sickle cell disease management in Africa, Anyanwu said. If the trial shows hydroxyurea’s benefits far outweigh the risks for children, the evidence could help persuade health officials to make it available, which could save lives and reduce pain and other symptoms. “I’m also hoping this trial will be a catalyst for other interventions for the disease and that this will emphasize the need for newborn screening here,” she said. “And I hope it will also shed light on the need for more sickle cell research in sub-Saharan Africa, because it’s immense.”
What was it like to be on the ground for the first Ebola outbreak?
When our international investigation team of five arrived deep in the Zairian jungle at the epicenter of the first outbreak in 1976, we were scared out of our wits. We were working with the most basic protective equipment in the sweltering heat, sand flies were biting us, we developed rashes and didn’t know if we would catch the virus too. But as I listened to witnesses describe what had happened, it was clear to me that the disease might have been spread by hospital procedures, which it had in part, through use of unsterilized injections. It also became clear that infection spread by close contact with infected body fluids.

How was it different from today’s epidemic?
Many factors went into limiting the 1976 epidemic. Early on, a local doctor recognized it was a very different illness and within a few weeks, someone was out there taking a look. When our team arrived, the government had already cordoned off the area and quarantined 275,000 people—and they paid attention to the quarantine. The villages were isolated, both by the river and poor roads. But the current epidemic wasn’t reported for several months and control efforts were meager; people fled into the forest and spread disease there or headed for the main roads that led them right to the cities and to neighboring countries.

On arriving in the villages back then, we worked hard to earn people’s trust, showing community leaders an electron microscopic photo of the virus and saying we’d come to stop the disease spreading, treat patients and talk with their families. Our most important tool was house-by-house visits. And we reopened the hospital, which had been closed in response to staff deaths, to offer normal outpatient services and restore trust in the health system. In this epidemic, people were initially running away and not cooperating with the health care providers. The outbreak spread fast, moved to urban areas and belated attempts to contain it didn’t work. In Liberia, for instance, quarantined people were short of food, unaware of how to protect themselves and increasingly distrustful. And there were not enough health workers to handle those who sought help.

What did you learn about Ebola in 1976?
We found it essential to have a group able to lead efforts overall, to organize and coordinate with others and form partnerships with community leaders. For instance, we delegated a scientist to do serology, a communications officer, a physician managing the clinical care and I was in charge of epidemiology and surveillance. For every step, it’s important to ensure transparency and to communicate extensively about what’s going on. Then you need infrastructure for the teams to carry out effective logistics, transport and identification of patients.

What role can scientists play?
In Zaire, we conducted surveillance and epidemiology. We collected information on the clinical spectrum, incubation period and transmission routes, and instituted control measures that seemed to work, such as quarantine and rapid burial of corpses. We did lab diagnosis and some virology in the field. It is essential to share the information that has been collected. In this outbreak, there is so little scientific information in regard to what we need to know, such as age of patients, sex, types of contact the patients had and mode of acquisition. We also want details on the clinical presentation and results of treatment.

Further research should include many different kinds of specialists. We never identified the animal source of the virus so we need ecologists and naturalists to do longitudinal studies on fruit bats, great apes and other species. We need social scientists and anthropologists to study how best to talk with local leaders, educators and villagers, and to study socially acceptable but safe ways to conduct burials and have workable isolation and quarantine. And health systems everywhere in the region need to be strengthened. There will be new microbes that arise where you have animals in contact with humans. We have to be prepared to not only detect and respond to them but to prevent them from taking hold.


Dr. Breman, pictured on far right, was part of the international team that in 1976 identified and described the disease caused by a new, deadly virus in the Democratic Republic of the Congo: Ebola. Breman was with the CDC, where he spent much of his long career in global health, focusing on numerous infectious diseases that burden African populations. He has also worked for the WHO, certifying global eradication of smallpox and, more recently, guinea worm. He joined Fogarty in 1995 to direct institutional strengthening and research training programs. He retired in 2010, but continues to consult on topics such as malaria as Fogarty scientist emeritus.
Most children with sickle cell disease in Africa suffer relentless pain, experience numerous infections and die before their fifth birthday. Although treatments exist, they are not widely available in sub-Saharan Africa, where 70 percent of the world’s children with sickle cell disease are born, according to the WHO. NIH is funding a number of efforts to develop low-cost methods to diagnose the condition and investigate affordable treatments to help reduce the suffering.

Most of the interventions used today for sickle cell disease were produced for wealthy countries with higher health budgets and patients already protected by better nutrition and vaccines against infectious diseases.

“Supporting sickle cell research in sub-Saharan Africa and other low-resource settings can make a difference,” said Dr. George Mensah, who focuses on global health research at NIH’s National Heart, Lung and Blood Institute. “We cannot be paralyzed by the enormity of the challenges.”

A global movement is growing to address the inequity in sickle cell disease treatment. The WHO named it a public health priority in 2006, followed by the UN in 2008. “There’s a total sea change in interest and what’s being done for sickle cell disease patients and the understanding of our moral and scientific relationship with them,” said Fogarty grantee Dr. Richard S. Cooper, of Loyola University in Chicago. “Investors and scientific institutions have begun to take the issue much more seriously,” he added.

**Sickle cell causes pain, early death**

Sickle cell disease, one of the world’s most common genetic disorders, occurs when a child inherits a trait from each parent that causes most of their red blood cells to form into crescents, rather than discs. Affected blood is less able to carry oxygen and flow smoothly, which causes a host of health problems and a shorter lifespan. Children who inherit only one trait are protected against severe malaria, which is why the disease is most prevalent in malaria-endemic parts of the ancient world, primarily Africa, the Middle East and Southeast Asia. Countries in Equatorial Africa bear the greatest burden (see chart above right).

With population migration, the disease has spread widely, including to the U.S., where the disease affects roughly 100,000 people, according to the CDC.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>SICKLE CELL BIRTHS/YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigeria</td>
<td>91,011</td>
</tr>
<tr>
<td>Tanzania</td>
<td>11,877</td>
</tr>
<tr>
<td>Uganda</td>
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<td>Angola</td>
<td>9,017</td>
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<tr>
<td>Cameroon</td>
<td>7,172</td>
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<td>Zambia</td>
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<tr>
<td>Ghana</td>
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</tr>
<tr>
<td>Guinea</td>
<td>5,402</td>
</tr>
<tr>
<td>Niger</td>
<td>5,310</td>
</tr>
<tr>
<td>Sub-Saharan Africa Total</td>
<td>242,187</td>
</tr>
<tr>
<td>Worldwide Total</td>
<td>305,773</td>
</tr>
</tbody>
</table>

Due to the paucity of accurate data for most countries in sub-Saharan Africa, researchers have estimated the number of sickle cell births in 2010, based on population surveys, sickle cell trait frequencies and statistical modeling.

countries include strong pain relief medications, the drug hydroxyurea and blood transfusions. Several preventive steps are also available, such as genetic testing and counseling, assisted reproductive technology, and vaccines and prophylactic antibiotics to avert infections. Most patients receiving these interventions reach their 40s or 50s, before they face potentially fatal conditions like pulmonary hypertension and organ failure.

Without treatment, the disease takes its toll early, as children are battered by chronic pain, anemia, repeated infections, stroke, leg ulcers or breathing difficulties. This affects not only the child, but the entire family of caretakers, bringing major social and economic consequences, including missed school and work days and income loss.

Budget-constrained health authorities in Africa commonly fund treatment of infectious diseases that threaten high death tolls, such as malaria, tuberculosis and HIV/AIDS, or those covered by childhood vaccinations, rather than relatively rare conditions that are expensive to diagnose and treat. At most, some patients with sickle cell disease might receive a handful of vaccinations, antibiotics when bacterial infections erupt, medication for severe pain and, especially if they supply money and suitable donors, blood transfusions to lessen physical crises.

Researchers are working to change that, however, with several studies currently underway in developing countries aimed at providing sound evidence to convince policymakers of the feasibility and benefits of offering programs to diagnose and treat sickle cell disease. Scientists agree that children with a double trait derive clear advantages from the pneumococcal vaccine—not universally administered in sub-Saharan Africa—and protective antibiotics during the early years of life. The decision to invest in hydroxyurea is less clear-cut.

Two key projects were recently launched in Nigeria and Uganda to study the safety and effectiveness of the drug, the main intervention used in wealthy countries. Hydroxyurea, designed as a cancer treatment, has proved remarkably effective at spurring production of normal-shaped fetal hemoglobin, which relieves symptoms in sickle cell disease. It was approved in 1998 to treat adults in the U.S., more recently for use in children. A daily pill, mixed into food if need be, it markedly cuts the frequency of severe pain episodes, hospitalizations, lung damage and blood transfusions.

But the drug’s main side effect is to depress infection-fighting white blood cell counts—a matter of particular relevance in Africa, with its heavy burden of immune system challenges from pathogens and malnutrition. For instance, studies have shown that children with two sickle cell traits are more vulnerable to death from malaria than other infected children, so it is important to gauge if hydroxyurea’s immune system depression adds to this risk in malaria-endemic areas.

“In some places, the position of the government and the experts has been that hydroxyurea should not be used in Africa,” according to Cooper. “There has been great concern that you would expose these children to a higher risk from infection.” One of the scientists Cooper trained with support from his Fogarty International Research Collaboration Award is leading the drug study in Nigeria. Dr. Bamidele Tayo, a Loyola University investigator, is conducting a pilot to examine whether a low, fixed dose of the drug will benefit patients without also harming them. The project is funded by the Doris Duke Charitable Foundation.

To raise the dose to higher levels would require frequent monitoring, which is unrealistic given the setting. Before achieving widespread use, it’s important to determine the trade-off between maximum efficacy and what strapped health systems might be convinced to provide, Cooper said. . . . continued on p. 8

Researchers in Uganda and Nigeria are testing a drug that alleviates sickle cell disease symptoms—but can also depress the immune system—to ensure it is safe for children in malaria zones.
The drug costs about $1 per day in the U.S. and half that for its cheapest generic form available elsewhere. “It’s an old drug, off patent,” Cooper noted. “But even 50 cents a day can be too much for a family in Africa.”

Meanwhile, a Ugandan study is looking specifically at hydroxyurea’s interplay with malaria. Researchers recently launched a phase 3 clinical trial of the drug in children aged one to four, who live in a malaria-prone area of Uganda—where sickle cell trait prevalence reaches 45 percent in some pockets. The NOHARM study is led by Dr. Chandy C. John of the University of Minnesota and Dr. Christopher Ndugwa of Makerere University. Funded by the Doris Duke Charitable Foundation, its goal is to examine whether the drug elevates the risk of fatal complications from malaria. “It’s possible that kids on hydroxyurea, once they get malaria, could be at higher risk for more severe malaria, but we are hoping to show otherwise,” John explained. Participants in Fogarty’s Global Health Program for Fellows and Scholars have helped to get the study up and running (see related story on page 4).

The Ugandan health ministry is very interested in the study’s outcome, John noted. If hydroxyurea is determined to be both safe and effective, it might become part of routine care for all children with sickle cell disease in the country. “Identifying young children early, before the disease has had a chance to damage their organs, and treating them early is the key to a better life for these kids,” John said.

Include in HIV treatment platform

Existing health systems developed to diagnose and treat HIV/AIDS, as part of the U.S. President’s Emergency Plan for AIDS Relief, could easily be expanded to also check infant blood samples for sickle cell disease. “I think the time has come to think of how you bundle and leverage resources to maximize the benefits from infrastructure that’s already there,” Mensah observed.

However, there would have to be a commitment to also provide some level of treatment, said Dr. Julie Makani of Muhimbili University and the Wellcome Trust, who is collaborating with NIH. “Ethically, you can’t diagnose them and say, ‘Sorry, we have nothing for you.’ You do need a level of service to be present before you can screen.”

That’s why researchers like Cooper and John are working to produce data they hope will demonstrate that the existing interventions for sickle cell disease can bring clear benefits for sub-Saharan Africa. Positive results may also motivate stakeholders to negotiate affordable pricing for the region so that diagnostics, vaccines and drugs can be added to existing patient services.

Even if treatment were inexpensive and widely available, more research would be required, according to Mensah, who asked, “Would it be acceptable to the community? Do they know enough about the benefits and the harm? And what have we done in terms of providing health education and communication to make sure there’s acceptance of the effective interventions?” The NIH can play an important role in helping to answer these and other scientific questions, he said.

Lessons learned in Jamaica

Sickle cell disease has been studied in Jamaica for more than 40 years and has produced some findings that may apply in Africa. Funded by the Wellcome Trust and the UK Medical Research Council, the work was led for more than three decades by Dr. Graham Serjeant. A high proportion of Jamaicans have African ancestry; about 10 percent carry the sickle cell trait and one of every 300 children born has the burden of two traits.
In a recent talk at NIH, Serjeant shared some lessons learned in Jamaica. As in other low-resource settings, pneumococcal infection puts Jamaican children at great risk, he said. Penicillin prophylaxis offers some protection, but patients often have difficulty taking the medication consistently. Researchers tested whether a monthly injection would encourage more compliance than pill-taking, and they found that not only did it reach almost 90 percent, but it was also associated with less invasive pneumococcal disease. Another study showed additional protection is provided from the pneumococcal vaccine—providing policymakers with evidence they could use in deciding how to allocate funding for the greatest impact.

Another intervention studied in Jamaica concerns acute spleen sequestration, in which sickled red blood cells become trapped in the spleen, enlarging it and causing a life-threatening emergency. Researchers taught caretakers how to palpate a child’s spleen, recognize when it is swollen and immediately seek help at a clinic. “The message is, you can teach your mothers to diagnose this complication,” Serjeant said. “In Jamaica the death rate from this cause dropped from 28 percent to 3 percent.”

Cooper has been establishing a research collaboration among his Loyola colleagues, Jamaican scientists and their Nigerian counterparts to build capacity for genetic and clinical studies of sickle cell disease at the University College Hospital in Ibadan. With Fogarty support, the investigators have held training sessions, and compared data and lessons learned to enhance patient care in Nigeria. The South-South collaboration provides an excellent opportunity to transfer advances in clinical care that are appropriate for low-resource settings, Cooper said.

Among the urgent research priorities is to investigate the genetic variety of double sickle cell trait carriers. About 5 percent of them show few symptoms throughout their lives. By studying them, scientists may discover a clue that could lead to new treatments or even a cure.

Jamaica currently only has the resources to check about 40 percent of its newborns for sickle cell disease, but it is working to expand screening to cover all babies. It is trying to reduce the number born with the disease, by offering genotyping to 16,000 high school students so they can discover if they have the trait before they select a mate. It’s too early to know the outcome but researchers hope it will have an impact. Sickle cell trait screening has reportedly been very successful in Saudi Arabia and Bahrain but may be difficult to replicate in settings with different cultural practices and levels of health resources.

**Genomics may hold key to cure**

Genomics is another area that holds promise for advancements in sickle cell disease. The Human Heredity and Health in Africa initiative, known as H3Africa, was recently established by the NIH and Wellcome Trust to train a cadre of African geneticists and establish genomic biorepositories on the continent.

H3Africa recently convened a gathering of sickle cell disease experts in Tanzania, including scientists, clinicians, policymakers, educators and others. They discussed the accumulated global research, considered how to build more evidence and capacity, and agreed to form an information-sharing network.

Sickle cell disease is caused by a single genetic mutation, yet patients can have mild, moderate or severe forms of the disease. Studies could focus on both the genetic and environmental factors. Among other urgent research priorities is to investigate the genetic variety of double sickle cell trait carriers. About 5 percent of them show few symptoms throughout their lives. By studying them, scientists may discover a clue that could lead to new treatments or even a cure.

For now, policymakers need to reassess how resources are allocated in Africa with a focus on reducing preventable deaths and disabilities, maintains the NIH’s Mensah. “When children don’t have the opportunity to make it to age 5, that should be a national priority.”
It has been heartbreaking to see the images and learn of the horrific details emerging from the Ebola outbreak in West Africa, where the health systems are fragile and medical research capacity is lacking. With health care workers on the front lines, many have become infected themselves. Liberia has lost 96 already, according to a recent Washington Post op-ed by that country’s leader, President Ellen Johnson Sirleaf. “This is a huge hit for a country that had barely 50 doctors to care for a population of 4.4 million at the start of this outbreak,” she observed.

In the 24 previous occurrences of Ebola, the virus was controlled early by rapid response, active surveillance and quarantine. This time, the outbreak is occurring in countries recovering from conflict, without the health infrastructure or quantity of trained personnel to effectively deal with the problem.

With health officials and care providers overwhelmed by the sheer number of people stricken by this terrible virus, it’s no wonder that little attention is being given to studying the outbreak in any detail. There is barely time to count the dead. Without trained epidemiologists tracking the epidemic, studying its transmission, noting what care is provided, how many recover and how many succumb—we are losing the opportunity to learn vital information that could help us discover new and better ways to contain this or future outbreaks.

It is imperative that the international community provide Liberia, Sierra Leone and Guinea with not only the immediate assistance it so desperately needs, but also an investment in long-term capacity building to improve medical education, increase the quantity and quality of doctors and health care workers, and develop scientific expertise and disease surveillance skills.

As none other than smallpox veteran Dr. D. A. Henderson recently noted, it is distressing that there is still such an utter lack of epidemiological data—months after the alarm was sounded and the world began taking notice.

As he pointed out, there is so much that can be learned from age distribution curves, intervals between dates of onset of patients in households, viral load and other information from lab tests and more.

It’s just this kind of scientific capacity the NIH’s Fogarty International Center has been working to develop in low- and middle-income countries for more than a quarter century. Four years ago, we began a partnership aimed at revitalizing African medical education. Known as the Medical Education Partnership Initiative (MEPI), the program is funded by the President’s Emergency Plan for AIDS Relief (PEPFAR) and NIH, and is administered jointly by Fogarty and our sister agency, the Health Resources and Services Administration.

With MEPI support, African medical schools are dramatically increasing enrollment, broadening curricula, upgrading Internet access and providing cutting-edge skills labs and other technologies. Where students used to fight to use shared text books, they are now each issued notebook computers loaded with the latest instructional materials and equipped to access current journal articles. The pace of change is astonishing and we hope will result in sustainable health improvements across the continent. Sadly, the countries hardest hit by Ebola did not submit successful proposals to receive MEPI awards. And yet we must join together to share information and resources to help them recover and move forward.

A modest investment in health infrastructure—including training health care workers, doctors and researchers—could provide the tools countries like Liberia need to halt disease outbreaks in their tracks and prevent the need for large-scale emergency efforts like the one we’re assembling to fight Ebola.

The U.N. is calling on the international community to provide $1 billion to stop this epidemic. I join Liberia’s president in encouraging some funds be directed to strengthen medical education and research training in Western Africa to prevent a future disaster on this scale. In her words, “We owe it to the thousands of citizens and health workers who have so far lost their lives to be prepared.”
HEALTH Briefs

More TB cases than expected, WHO says
Improved data collection reveals about a half million more tuberculosis cases exist than previously estimated, according to the WHO’s annual global TB report. About 1.5 million people died of TB last year and 9 million became newly infected, WHO says. People with HIV accounted for nearly a quarter of the deaths and 1.1 million of the new infections.

NIH, Gates expand global collaboration
The NIH and Bill and Melinda Gates Foundation have announced they are expanding their collaboration to improve health in developing countries, for instance on vaccines against viral diseases, new tuberculosis drugs and ways to improve maternal and infant nutrition.
Website: http://bit.ly/NIHandGates

WHO sees deaths rising with climate shift
Climate change will cause about 250,000 deaths globally each year from 2030-2050, via heat exposure in the elderly, diarrhea, malaria, childhood undernutrition and other impacts, according to a new WHO risk assessment study.

Africa doubles scientific output
African scientists more than doubled their output of research papers during 2003-2012, with most focusing on the health sciences and agriculture, according to an analysis by the World Bank and publisher Elsevier. However, Africans produced only 1 percent of total global research, the report said.

Study details African research capacity
The volume of research funding for poverty-related and neglected infectious diseases has grown but sub-Saharan African countries are still heavily dependent on external support. A study commissioned by the European and Developing Countries Clinical Trials Partnership provides a landscape analysis of research capacity.

Scientists reveal four new cancer hazards
Researchers have added four substances to the list of cancer-causing metals, pesticides, drugs and natural and synthetic chemicals found in the environment, bringing the total to 243, a U.S. toxicology report showed.

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Obama honors two NIH scientists, Fogarty grantee
In his annual recognition of top U.S. scientists and innovators, President Barack Obama honored two NIH scientists and one Fogarty grantee for their esteemed work. He presented the National Medal of Technology and Innovation to Drs. Douglas Lowy and John Schiller of the National Cancer Institute for their work on the human papilloma virus, which led to vaccines against the most prevalent strains causing cervical cancer.

Lowy and Schiller are working with colleagues at the WHO and other organizations to find ways to distribute HPV vaccines to those in need. In other work, they have partnered with pharmaceutical manufacturers in emerging countries in efforts to produce several second generation HPV vaccines that may be cheaper to manufacture and easier to deliver to underserved populations.

Obama awarded the National Medal of Science to Dr. Jerrold Meinwald, a professor emeritus at Cornell University. Meinwald was a Fogarty Scholar in residence from 1983-85 and an investigator on one of Fogarty’s first biodiversity grants, which supported chemical prospecting research and training in Costa Rica.

Wolfe is named to US global health affairs post
Dr. Mitchell I. Wolfe has been selected as the new U.S. Deputy Assistant Secretary for Global Affairs in the Department of Health and Human Services. He previously served for 16 years at the CDC, both domestically and directing its Thailand and Vietnam offices.

Earhart is new US health attaché in China
Dr. Kenneth C. Earhart has been appointed as U.S. health attaché in Beijing. Earhart, a Navy veteran, previously directed the CDC’s Global Disease Detection Regional Center in New Delhi. He has researched diseases such as dengue fever, influenza and Rift Valley Fever.

CDC taps Hader to head its global AIDS division
The U.S. CDC has selected Dr. Shannon L. Hader, an infectious diseases physician and pediatrician, to lead its Division of Global HIV/AIDS. She was previously a director at the international development firm, Futures Group, and before that was CDC Country Director in Zimbabwe.

Fogarty grantee is recognized for parasite research
The Washington Global Health Alliance has presented Fogarty investigator Dr. Kenneth D. Stuart with its Impact Award. Stuart, a University of Washington professor and founder of Seattle BioMed, is an expert in trypanosomatids—parasites that cause sleeping sickness, Chagas disease and leishmaniasis.
Malnutrition in all its forms, particularly childhood obesity, is growing at an alarming rate among children in Latin America. Researchers, policymakers and implementers must work together to identify evidence-based strategies to turn the tide, according to participants in a recent workshop organized by Fogarty’s Center for Global Health Studies.

Designed to connect stakeholders from the Americas, the meeting was co-sponsored by NIH’s National Heart, Lung and Blood Institute, Office of Behavioral and Social Sciences Research, National Institute of Child Health and Human Development, National Institute of Diabetes and Digestive and Kidney Diseases, the CDC, Pan American Health Organization and Office of Global Affairs at the U.S. Department of Health and Human Services. The 50 conference participants represented more than a dozen countries and came from academia, civil society, international organizations and government—including lawmakers from Chile and Peru. The combination of unhealthy diets, physical inactivity, and lack of access to healthy food and environments conducive to physical activity pose a serious health burden in many Central and South American countries. According to workshop co-chair Dr. Juan Rivera Dommarco of Mexico’s Institute of Medicine, about a quarter of adolescents in the region are overweight or obese, “and the problem is growing.”

Obesity research conducted elsewhere is not always applicable to Latin America’s different populations, cultures and environments, according to co-chair Dr. Benjamin Caballero of Johns Hopkins School of Public Health, who obtained his medical degree in Argentina. “Obesity is a much more complex problem in developing countries,” he said, noting that programs to alleviate poverty can under certain conditions spur chronic diseases such as obesity and diabetes when they boost caloric intake, rather than promote healthy eating and physical activity.

Conference participants are developing a series of articles that will identify the future research agenda, define policy and implementation issues, and describe capacity building needs required to move the field of obesity prevention forward in Latin America.