



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

NIH holds cookstove research training workshop

Simply preparing the family meal poses a deadly health hazard in much of the developing world. Household cooking and heating fires contribute to almost 2 million deaths annually, with women and children most affected by breathing in toxic smoke for hours a day.

Solving this age-old problem is surprisingly complicated, requiring many more steps than buying off-the-shelf cookstoves and distributing them. There are numerous new types of devices that use a variety of fuels, yet little is known about how much they actually improve air quality or benefit health.

To develop more expertise in indoor air pollution research, the NIH recently hosted a three-day training workshop. Faculty experts from academia,

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Photo by Jeff Gray



Scientists from around the world gathered at a recent NIH workshop to study the effectiveness of clean cookstoves and other aspects of indoor air pollution.

FDA evolves to meet global regulatory challenges

Consumers everywhere need protection from counterfeit or harmful medicines, especially in the developing world where there is often little manufacturing oversight or capacity to monitor the marketplace. The U.S. Food and Drug Administration is evolving to meet the regulatory challenges caused by surging international trade, to ensure product safety both at home and abroad.

“We live in a globalized world,” said FDA Commissioner Margaret Hamburg. “We need to create a global coalition of regulators that enables us to work together in a much more coordinated way,” she recently told a Center for Strategic and International Studies conference in Washington, D.C.

Consumers are increasingly vulnerable, she said, citing several “real-world, wake-up calls” in various countries over the past few years. These include the appearance of

contaminants in the blood-thinning drug Heparin, the industrial chemical melamine in baby formula and the solvent diethylene glycol in cough syrup.

Many developing countries, with limited funds for regulatory activities, are particularly challenged as they try to deal with fake or diluted drugs for life-threatening diseases such as malaria. “Sadly, a lot of the medications being used to treat malaria are substandard and they’re not only not treating and curing malaria, but they’re adding to the growing problem of drug resistance, because they don’t have adequate levels of the active pharmaceutical ingredient,” Hamburg said.

Improving regulatory capacity in low-resource settings brings valuable benefits in addition to consumer protection, she noted. It promotes economic development by

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The National Eye Institute

- Battling global eye diseases with research
- Helping scientists eliminate blinding trachoma
- Discovering how brains adapt if vision comes later in life

Read more on pages 7 - 13

US-Iran scientific partnerships hold promise

U.S. relations with Iran may be strained on the diplomatic front but scientific engagement between the two countries is flourishing. Attendees at a recent meeting in Tehran identified a number of promising areas for collaboration. Several Americans traveled to Iran for the country's first international and fifth annual HIV/AIDS conference. Co-organized by UNAIDS and the Iranian Research Center for HIV/AIDS—part of Tehran University Medical School—the proceedings were conducted in English. Topics ranged from the prevention of maternal-to-child transmission, to harm reduction through examination of transmission routes, to strategies to strengthen Iran's overall response to HIV/AIDS.

Iranian-born Harvard scientist Dr. Navid Madani helped organize the symposium. An NIH grantee, she said she found a warm response from the host scientific community. "Iranians place a high value on establishing international scientific collaborations and in building research capacity in their country," Madani noted.

Indeed, there are a number of longstanding research collaborations between NIH and NIH-funded researchers and their Iranian counterparts on topics including cancer, hepatitis and opiate addiction. While these types of partnerships require a license from the Office of Foreign Assets Control at the U.S. Treasury Department, obtaining one is not onerous and the benefits can be enormous, according to Fogarty's Middle East officer Judy Levin.

In the case of the HIV/AIDS, Iran's approach provides a useful model, Madani suggested. "Iran can be the beacon for all the countries around it." Iranian health officials have



Iranian-born Harvard scientist Dr. Navid Madani (left), an NIH grantee, helped organize Iran's first international and fifth annual HIV/AIDS conference.

taken measures to decrease both the HIV infection rate and the disease's stigma, she said. In addition, they offer free condoms, voluntary testing and include prison inmates in their outreach. "We can learn so much from Iran and its grassroots model of health houses in each village, not just to benefit our primary health care but also our approach to HIV prevention and care," said Madani.

The idea for the conference grew from a workshop focused on the Middle East and North Africa region held at the 2010 international AIDS meeting in Vienna, with support from the NIH Office of AIDS Research. The connections made then were strengthened in Tehran.

"The scientific interactions were quite positive," Madani observed, "In addition to this stimulating scientific dialogue, we had an absolute gold mine of people understanding each other and a unique cultural and scientific exchange." The positive response may lead to additional international scientific gatherings in Iran, a possible faculty exchange program between U.S. and Iranian institutions, as well as enhanced research collaborations.

NIGMS celebrates 50 years of scientific discovery



Many scientific advances over the past 50 years were rooted in the basic research supported by the NIH's National Institute of General Medical Sciences (NIGMS), so there was much to celebrate during its program of anniversary events.

NIGMS hosted sessions to review accomplishments in numerous scientific meetings during the year, culminating in a day-long symposium on the NIH campus, opened by NIH Director Dr. Francis S. Collins. "NIGMS has always stood for freedom of the mind in scientific inquiry," he noted, "so happy 50th anniversary!"

Over five decades, the Institute has supported research to discover how cells communicate with each other and their

environment, how genes are regulated and how proteins accomplish their varied tasks in the body. This knowledge forms the foundation for new and better ways to improve health and tackle disease. With the fourth-largest budget at the NIH of \$2.4 billion, NIGMS funds about 4,700 research grants.

"The basic research we support is a solid foundation for new and better ways to treat and prevent disease and improve health," said NIGMS Acting Director Dr. Judith H. Greenberg.

As NIGMS reflects on its progress over the past five decades, it also looks forward. "Our challenge for the future is to continue to attract and train the best minds and to champion their unfettered creativity," says Greenberg. "And if we do that, we can expect spectacular discoveries ahead."

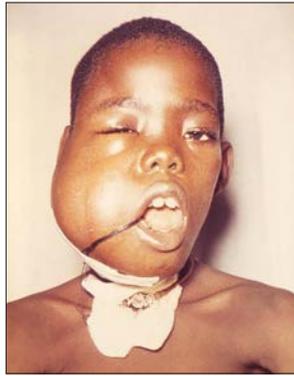
New avenues to stop Burkitt's lymphoma

Burkitt's lymphoma is a particularly cruel disease, hitting mostly children and developing aggressively. It is endemic in equatorial Africa, where chronic malaria helps weaken the immune system, and although chemotherapy can cure up to half of patients, many still die. So it was welcome news that an international team of scientists has unveiled some of the cancer's genetic secrets, making this form of non-Hodgkin's lymphoma easier to treat. Their findings were published recently in *Nature*.

Dr. Louis M. Staudt of the NIH's National Cancer Institute and his colleagues conducted genetic sequencing with high-capacity technology, which allowed them to quickly identify likely mutations that may cause the lymphoma. They found a surprisingly large amount of recurrent mutations compared with the number identified in other cancers. This opens many doors for improved understanding and potential treatments of Burkitt's lymphoma.

"Our job in cancer genomics is to divide cancer into precisely defined molecular categories," Staudt said. "That will enable a much more rapid understanding

Photo by Robert S. Craig/CDC



NIH-funded research recently revealed Burkitt's lymphoma has a surprisingly large number of genetic mutations, a discovery that may speed treatment for this cancer.

of essential pathways that could be responsive to drugs."

He noted that more effective treatments for Burkitt's lymphoma are needed especially in Africa. Patients there typically receive low-dose chemotherapy, rather than the high-dose therapies in the developed world where follow-up care is available for resulting infections. The low-dose regimen leaves a survival rate of below 50 percent. "That's way too low a rate," Dr. Staudt said. "So we hope that we might be able to supplement that minimal chemotherapy with some of these new targeted agents and improve the outcomes for patients there."

New therapies would also help the 15 percent of developed-world patients who are not treated adequately with current therapies, he noted. This includes the elderly, who are more vulnerable to infections after high-dose chemotherapy, even with ample supportive care.

RESOURCES

NCI report: <http://bit.ly/cancerSP6Z>

HPV vaccine can protect women with HIV

Women with HIV can benefit from receiving a vaccine against another sexually transmitted pathogen, the human papilloma virus (HPV), although they commonly do not receive the inoculation, according to an NIH-funded study.

The vaccine, which protects against four common types of HPV, is designed to trigger an immune response before exposure to the virus, which typically spreads without immediate symptoms.

"Even among women who test positive for one type of HPV, the vaccine may effectively prevent infection with others—especially high-risk forms that cause cancer," said Dr. Jessica A. Kahn, of the University of Cincinnati, who led the study. "It's important that doctors don't withhold the vaccine in these cases, thinking that it's too late for a vaccine to be effective."

The study, published in the *Journal of Acquired Immune Deficiency Syndromes*, found nearly three-quarters of the women had an existing HPV infection, but only about half tested positive for a high-risk HPV type that causes cervical cancer or genital warts.

Cervical cancer disproportionately arises in developing countries, where it is the most common cause of cancer

deaths in women, killing more than 200,000 each year and on the rise. To counteract this, the nonprofit GAVI Alliance plans to bring HPV vaccines to health authorities in developing countries at greatly reduced price, reaching 28 million women and girls by 2020.

Women in developing countries are especially vulnerable to cervical cancer, given the lack of access to care and high rates of HIV infection, which increases the risk for cancer.

"Cervical cancer screening for sexually active young women is an important clinical priority, but our findings suggest it is especially so for women at risk of HIV," said study co-author Dr. Bill G. Kapogiannis of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

NIH agencies also supporting the study were the National Institute on Drug Abuse, National Institute of Mental Health, National Institute of Allergy and Infectious Diseases, National Cancer Institute and National Center for Research Resources.

RESOURCES

Abstract: <http://1.usa.gov/MMG4ew>

Press release: <http://1.usa.gov/YQtorM>

NIH holds cookstove research training workshop

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nongovernmental organizations, the NIH and other government agencies gave lectures and hands-on demonstrations of cookstoves and emissions testing to about 20 trainee scientists from the U.S. and seven developing countries.

“Most people are still unaware of what an important issue this is,” NIH Director Dr. Francis S. Collins said at the workshop’s opening session. “Yet here is a situation that we can do something about, not that it’s going to be easy. We clearly have a path going forward to make a difference and save many lives.”

Traditional cookstoves and open fires used in cooking food, boiling water and heating homes burn dung, wood, charcoal, rice husks or other cheap fuels. The resulting smoke, often intensified by poorly ventilated rooms, can cause the same risk for disease as a lifetime of smoking and is blamed for lung cancer, acute pneumonia and chronic obstructive pulmonary disease. Scientists suspect exposure plays a role in many other health problems, ranging from low birth weight and asthma to cataracts and burns, but more research is needed on linkages. Women and children can also face physical threat while out alone gathering fuel.

The workshop’s sessions examined technical issues such as combustion efficiency, proper ventilation and accurate emissions measurement, as well as behavioral aspects involved in encouraging households to adopt clean-burning stoves. The appliance must be easy to use and reliable, or it might be abandoned in frustration. The design must also incorporate cultural preferences, for instance if the stove is to be used for rice or tortillas, or for cooking one dish at a time or several. People need to be educated about the

NIH director Dr. Francis Collins (center) discusses indoor air pollution with Dr. Bill Martin of NICHD, while Fogarty director Dr. Roger Glass (far right) observes a cookstove demonstration with guests.



Photo by Michael Spencer/NIH

health benefits and trained in correct operation. The fuel choice is also important since it must be inexpensive and readily accessible. Chimneys, fans, location of the stove and safety issues require evaluation as well.

“Research is going to be essential and this is where NIH has a critical role to play,” Collins told the workshop. “You have to understand the whole host of issues that relate to the acceptability of new kinds of cookstoves in place of the open fires. And that means we have to understand communities and cultures and we have to be able to understand engineering. We need to measure a reduction in exposures so we have confidence that it’s going to result in a better health outcome.”

Clean cookstoves not only offer health benefits but can also free up women and children’s time for education and other activities, improve the environment with reduced emissions and bring economic benefit through local industry involvement.

Workshop participants were able to study 20 various types of stoves on display and observe a number of them in operation. Sessions included discussions of research design approaches, data needs and the challenges posed by intervention studies. Participants then applied the information by working in small groups with faculty mentors to develop study designs that could help fill existing research gaps.

The NIH has supported studies on the health risks of indoor air pollution for several decades. In 2010, it joined the Global Alliance for Clean Cookstoves, a public-private partnership launched by Secretary of State Hillary Clinton. The Alliance plans to have 100 million homes adopt clean and efficient stoves and fuels by 2020. The U.S. government has committed more than \$50 million to the effort, including about \$25 million in NIH-funded research projects.

The workshop was organized and hosted by Fogarty’s Center for Global Health Studies, a trans-NIH incubator for crosscutting global health projects. The event’s partners included the National Institute of Environmental Health Sciences, National Institute of Child Health and Human Development, National Heart, Lung and Blood Institute, USAID, Environmental Protection Agency and Global Alliance for Clean Cookstoves.

RESOURCES

Website: http://bit.ly/NIH_indoorairpollution

FDA evolves to meet global regulatory challenges

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creating stable, more reliable industries, from local farming to generic drug manufacturing. It also improves the health and well-being of citizens and, in turn, can influence a country's political system. "On many levels, your investment in regulatory capacity is fulfilling health needs, economic development needs and, in some cases, political stability," Hamburg said.

Although the FDA is not a development agency, its efforts have an impact on public health activities. For example, by ensuring the quality of drugs and devices delivered to developing country patients with HIV/AIDS, the FDA is protecting the investments made by the President's Emergency Plan for AIDS Relief. Similarly, stronger regulatory systems and deeper knowledge about global supply chains can help regulatory authorities collectively to better ensure the safety and quality of products for patients and consumers around the globe.

As the FDA is expanding its reach to colleagues in the development community, including the WHO, it is assisting others in building global regulatory capacity. It's also in-

creasing partnerships with industry, which has a stake in improving the quality and integrity of products it wants to sell.

In a recent study focused on Africa, the FDA and USAID investigated pharmaceutical quality and monitoring, suggesting ways to fill the gaps.

And the Institute of Medicine recently pro-

duced a study identifying the steps needed to develop regulatory systems in developing countries and how the FDA and other regulators can contribute.

The FDA's increased global perspective came out of necessity. About 24 million product lines come into the U.S. each year, quadruple the number of a decade ago. In the area of drugs, four-fifths of active pharmaceutical ingredients come from abroad, as do two-fifths of shelf-ready drugs consumed by U.S. consumers.

"We no longer view ourselves as a domestic agency; we believe that we have to be a global agency with a global mission," Hamburg said. "We simply have to have new models [that] build on the notion of partnership both with

Photo courtesy of the FDA



The U.S. Food and Drug Administration is evolving to provide global leadership to combat production and shipment of poor-quality drugs and other products.

other regulatory authorities and with industry to raise standards and also share information in new ways."

Regulators should form new coalitions and develop systems for working together, including technology that enhances data sharing and facilitates risk-based analyses. "We need to be able to use the best science, the best experience and expertise, to target the highest risk products and to use our resources in ways that will make the greatest difference," she said.

To make the most of limited funds, regulators should be strategic in where they direct resources, for instance, by focusing on vulnerabilities in a product's supply chain or scrutinizing drugs intrinsically at elevated risk of being falsified, Hamburg said.

Meanwhile, the NIH and FDA have pledged to work more closely to speed research discoveries. They are collaborating on an initiative to fast-track scientific breakthroughs to the public and developing a chip that can more quickly gauge if a new drug compound has potential to improve health. The two agencies have also awarded more than \$10 million for studies of nanoparticles, a heart-lung model to test drug safety and effectiveness, an innovative clinical trial design and a new strategy to predict eye irritation.

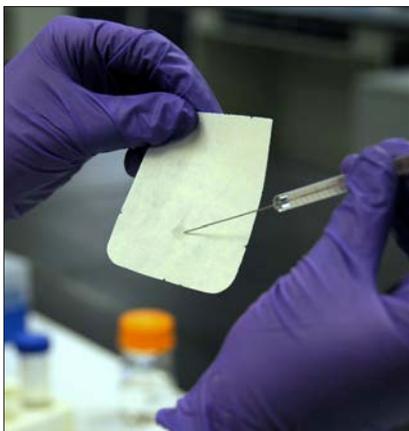
Increased cooperation around the world is in the best interests of everyone, including the U.S. "It means that those products that are coming from outside our borders will be of higher quality," she said. And, she added, the U.S. benefits by finding ways to "effectively share the workload."

Hamburg concluded that the FDA is committed to tackling the challenges of its global mission. "Anyone who's working at the FDA, whether it's working on the science, inspection or compliance side, feels the tug and pressures of globalization."

RESOURCES

FDA global website: <http://1.usa.gov/RC0k78>
 FDA's Hamburg at CSIS: <http://bit.ly/HambXX4>
 IOM report: <http://bit.ly/NAPreport>

Photo courtesy of the FDA



The FDA is working to increase scientific capacity in developing countries to improve drug safety.

PROFILE

Fogarty fellow tackles inherited childhood glaucoma in Nigeria

In the ophthalmology practice, one patient stood out: a young man diagnosed with glaucoma who doggedly pursued a career as an accountant until he could no longer see. He had a hereditary form of glaucoma that typically develops much earlier in life than the well-known adult-onset type, and that currently is resistant to medical and surgical treatment.

“You are seeing a 15-, 17-, 20-year-old who has his life mapped out before him and you discover he is going blind from juvenile-onset glaucoma,” said Dr. Oluwatoyin F. Fafowora, a former ophthalmology clinical practitioner, who was moved by her patient. “Because it affects the younger generation, I found it rather painful to be treating it. I very much prefer research. It’s more meaningful.”

Oluwatoyin F. Fafowora, M.D., M.P.H.

Fogarty Fellow:	2008-2010
Fellowship at:	University of Ibadan, Nigeria
Research focus:	juvenile-onset glaucoma
Website:	http://1.usa.gov/STgSpz

The door to research opened when she received a Fogarty fellowship in 2008 to engage in global health studies. Fogarty’s Global Health Program for Fellows and Scholars offers postdoctoral and doctoral students the opportunity to spend a year collaborating with a mentor at an established research site in a developing country. The experience is intended to encourage early-career scientists to pursue global health research, provide a training resource to the host institutions and nurture international research partnerships.

Under her fellowship, managed by the University of California, Los Angeles (UCLA), Fafowora returned to her native Nigeria to investigate potential genes behind the specific condition that had struck her young patient—juvenile-onset open-angle glaucoma. This form of glaucoma is prevalent throughout West Africa, allowing her to tap into a larger pool of patients than would be possible in the U.S. Fafowora led a team at University College Hospital



Photo courtesy of Dr. Fafowora

Former Fogarty Fellow Dr. Oluwatoyin Fafowora is studying the genetic basis for juvenile-onset glaucoma, which is prevalent in West Africa.

in Ibadan that tracked down families with a history of the disease and collected samples of their DNA.

Earlier research identified about seven candidate genes and Fafowora sought to confirm their involvement and identify additional genes. Her project showed such promise, her fellowship was extended for a second year.

She says she discovered research is very different from clinical work and she had to quickly learn a range of new skills during her fellowship. “You have to decide the importance of the disease, the feasibility of studying that disease, the usefulness of the outcome. And also what is important to you and to the funding institute,” she said. “Then writing the proposal itself was a good experience.”

For her project to succeed, she needed help on the ground in Nigeria. “My collaborator and I have been able to work together almost seamlessly and that helps open up a new vista. You can achieve more than if you were working individually.” In addition, advice from her Nigerian and UCLA mentors kept her project on track. “They could see further down the road than I could, so they could help to iron wrinkles out before they arose,” Fafowora said.

She’s still working to complete analysis of the data to pinpoint genes that bring a high risk for this type of glaucoma and then hopes to publish her findings. Once the relevant genes have been identified, children can be screened for them. “Then you have a much better chance of preserving vision.” Fafowora said. “We hope our findings will contribute to the development of gene therapy for glaucoma.”

Today, Fafowora is a research fellow at UCLA’s Jules Stein Eye Institute, studying for a doctoral degree in epidemiology. She hopes that ultimately, with her strong clinical background and expanding research skills, she’ll contribute to a wave of discoveries that will end blindness from inherited glaucoma. “I’m in research now and I like it. I want to work to find new knowledge, to make a difference.”

DR. GYAN ("JOHN") PRAKASH, PH.D., M.B.A.

As associate director at the National Eye Institute's Office of International Programs—Office of Global Health, Dr. John Prakash plays a key role in overseeing his Institute's international involvement in eye disease research and training. He previously held senior positions at AMAR International and Pfizer Pharmaceuticals' International Division. He earned a Ph.D. in microbiology from the University of Illinois at Urbana-Champaign, and received postdoctoral training in biotechnology at the University of California, Los Angeles, Medical School and the CDC. He earned an M.B.A. in pharmaceutical management at St. Joseph's University in Philadelphia.



What is your perspective on the need for global health research into eye conditions?

Eye conditions affect so much of the population at some point in our lives, whether at birth; as we age, as with macular degeneration; or as a condition brought on by another disease, such as diabetes. That's what makes the research we conduct and support so essential. And we at NEI are committed to taking a global approach. The vision research community is very active in many parts of the world—such as China, India, Brazil, the U.K., Germany and many other countries—and we are looking for discoveries from wherever they may arise. International research can inform us about diseases that are prevalent in many different parts of the world.

Overall, we are emphasizing high-quality science, including molecular biology, genetics and clinical research programs, where we can collaborate and learn from the scientists who are driving the research advances. For many years, NEI has fostered an active interest in international research, collaboration and training, managed through a special office within the Institute. Today, one of our main goals is to sustain a vigorous international research environment, expand collaborations in vision research among different countries and support international partnerships that are providing scientific value to the NEI programs.

How does NEI research address the enormous disease burden in low- and middle-income countries?

Eye diseases are prevalent around the world. No area is free from blindness, although most blindness occurs in developing countries. What's more, up to 80 percent of blindness is preventable. We want to work with the global research and health care communities to stop vision loss before it happens. Much of what we learn about eye health comes from performing global research and from studying specific patient populations, such as pediatric or elderly patients. Country- or region-specific research might provide more in-depth answers to the causes of blindness.

What is the makeup of NEI's international and global portfolio?

We have underway more than 50 international collaborations, projects, affiliations and other engagements on all six continents. The heaviest concentration of our collaborative engagements is in Asia, which accounts for about 40 percent, while 35 percent of our global initiatives are in Europe and the rest are elsewhere. In India, for example, the Aravind Eye Hospital is working with the U.S. Cleveland Clinic to identify primary open-angle glaucoma biomarkers. And Harvard University is collaborating with the L.V. Prasad Eye Institute to develop pluripotent stem cells for eye diseases and with Sankara Nethralaya in genetic studies. It's a very exciting time to be working in this area.

How does NEI plan to foster the next generation of global health scientists?

One of NEI's key global health goals is to develop human capital in the U.S., so we're ready to meet whatever needs arise in vision research and training. This means supporting excellent mentors to train the next generation of scientists and professionals. In fact, the NEI has a record of training numerous scientists in our intramural labs who have returned to their original countries. Several have become leaders there. We are currently training 66 international scientists and fellows in NEI's intramural labs, generally one or two from a given country, but 16 from China, 15 from India and 8 from Korea. In the past two years, 18 trainees have completed their studies and returned to their homes to continue their careers in global health and vision research.

We also manage an NIH-wide effort, the Khorana-Nirenberg Scholars Program, to train scientists of exceptional ability and potential as leaders in their countries. The training is in any field, not necessarily eye research. Once they are established in their countries, there is a high probability they will continue to conduct research, train others at home, and create long-term partnerships, including many with colleagues in the U.S.

FOCUS

Battling global blindness, eye disease through research

Blindness is tragic wherever it strikes. For many in the developing world, it condemns them to a life of poverty with little chance to live independently. As much as 90 percent of the global burden of eye disease is shouldered by developing countries, where treatable diseases often go undiagnosed. About 39 million people around the world are blind and a further 246 million are unable to see properly, according to the WHO.

To help combat visual impairment and eye disease globally, as well as in the U.S., the National Eye Institute at the NIH supports a wide range of research studies. The NEI recently developed a new strategic plan to guide its activities in international research and global health. Its goals include establishing a full-time office devoted to the issue, fostering a sustainable research environment globally, expanding collaborations to advance vision research and supporting partnerships that add scientific value to NEI programs. In addition, the NEI intends to develop scientific capacity in the U.S. through training and mentoring to meet global health challenges and support vision research in the future.

NEI currently funds more than two dozen grants at 36 foreign sites in 15 countries. A number of these research projects focus on eye diseases prevalent in low-resource

The National Eye Institute currently funds more than two dozen grants in 15 non-U.S. countries, supporting global health research in genetic, infectious and environmental eye diseases.

Photo by Ray Whittin/World Bank



About 39 million people in the world are blind, yet 80 percent of blindness is considered preventable. The National Eye Institute at NIH supports research into eye diseases that hit the world's poor the hardest, including trachoma, cataracts and other conditions.

About the NEI

THE NATIONAL EYE INSTITUTE is one of the 27 institutes and centers that constitute the NIH. Its director is Dr. Paul A. Sieving. NEI has the mission to conduct and support research, training, health information dissemination and other programs with respect to blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight and the special health problems and requirements of the blind.

Established by Congress in 1968, the NEI supports approximately 1,600 research grants and training awards made to scientists at more than 250 medical centers, hospitals, universities and other institutions across the country and around the world. The NEI also conducts laboratory and patient-oriented research at its own facilities located on the NIH campus in Bethesda, Maryland.

settings such as trachoma in Ethiopia and Tanzania, glaucoma in Ghana and corneal ulcers in India. Meanwhile, scientific collaborations in developed countries are probing a wide range of specialities from retinal stem cells in Canada, to diabetic retinopathy in Denmark, to pediatric eye disorders in the U.K.

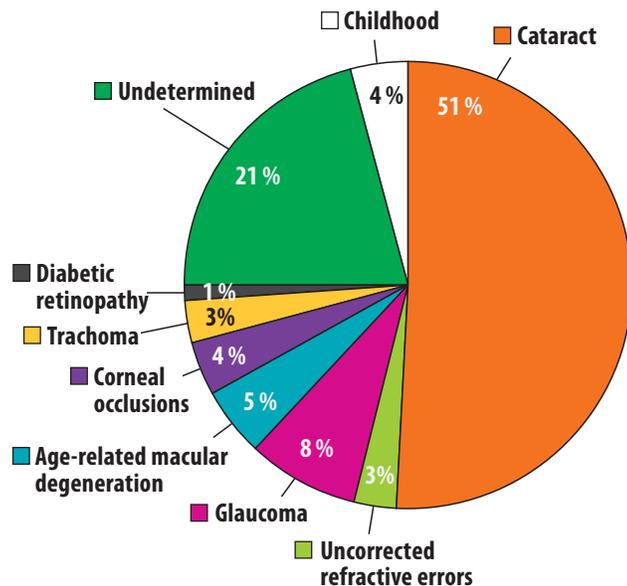
Photo by Alan Gignoux/World Bank



This section was produced by Cathy Kristiansen, with contributions from Christopher G. Thomas, Tom Hoglund and Richard S. Fisher.

In addition, the NEI has been collaborating with the WHO since 1979 to build research capacity by pairing experienced investigators with local scientists to study an eye health problem in that country. This collaboration has produced some 30 scientific publications about topics such as visual impairment in school-age children in developing countries and the evaluation of eye care services and the burden of poor vision and blindness in Brazil.

Global eye disease



Source: The WHO



Photo by Chris de Bode/WHO

India and China suffer high numbers of blindness. The National Eye Institute supports collaborations, partnerships and training programs with these countries and several others in research to prevent blindness.

Turmeric improves eyes



Photo by Jeff Gray

Retinitis pigmentosa is a group of degenerative eye diseases caused by genetic mutations that lead to severe vision loss and blindness. Worldwide, more than one person in 4,000 is affected. Current experimental gene therapy involves injecting

healthy copies of the culprit gene into patients' eyes. Although early clinical trials are promising, this approach is expensive and challenging, with more than 45 genetic mutations identified.

Recently, NEI-funded researchers found that curcumin, the active ingredient in the spice turmeric, may treat some forms of retinitis pigmentosa. A study led by Dr. Radha Ayyagari, associate professor of ophthalmology at the University of California, San Diego, showed that curcumin prevented the abnormal and damaging protein build-up usually caused by a mutant gene.

The researchers investigated the P23H gene governing the protein rhodopsin, which eye rod cells need to detect light. With this mutation, the protein accumulates and eventually kills the cells. Previous research showed that curcumin inhibits build-up of the protein amyloid beta, thought to contribute to Alzheimer's disease.

The team found curcumin prevented mutant P23H rhodopsin from abnormally clustering in laboratory-cultured cells, so they fed the compound to rats genetically engineered to have the mutation. These rats, unlike control animals, showed reduced protein accumulation, which in turn preserved the number of retinal rods and cones and increased the light-induced electrical response in the rats' eyes.

Another benefit of curcumin is that unlike many drugs, it crosses the blood-retinal barrier, a protective meshwork of cells surrounding the retina. The researchers found curcumin had reached the rats' retinas after only two days of feeding. This suggests that patients with retinitis pigmentosa could simply take curcumin pills or include turmeric in their diet, rather than have a drug or a gene surgically injected into their eyes.

Unusual protein clustering may also be linked to eye diseases that affect other cells in the retina. The results reported by Ayyagari and her colleagues suggest that curcumin could treat all of these cases. But further work is needed to back up these preliminary findings and test which curcumin dosages are most effective.

RESOURCES

Full article: <http://1.usa.gov/RDmd3u>

Research shows path toward trachoma elimination

Repeated mass treatments with antibiotics can greatly reduce the occurrence of trachoma, a bacterial eye infection that causes blindness in millions of people, NIH-supported research has shown. In addition to paving the way to eliminate the disease, which largely strikes developing countries, studies indicate the therapy also protects communities from other infections, reducing child deaths from pneumonia, diarrhea and malaria by 50 percent.

After years of targeted funding and research, trachoma has been wiped out in some regions and the WHO aims to vanquish it in remaining places by 2020. Research funded by the NIH's National Eye Institute (NEI) is playing a crucial role by identifying effective antibiotic regimens to combat the scourge. These include determining how often to administer treatment, what portion of a community must be reached and how to prevent re-infection.

The main treatment for active trachoma, caused by the *Chlamydia trachomatis* bacterium, is the antibiotic azithromycin. Mass treatment became economically feasible only in 1998 when the International Trachoma Initiative began making substantial quantities of azithromycin available at no cost. "We now had a single-dose antibiotic, which provided the impetus to fight this disease," recalls Dr. Sheila K. West, NEI grantee and professor at Johns Hopkins University.

The National Eye Institute at the NIH supports research to determine the most effective ways to deploy antibiotics to eliminate trachoma, which currently affects about 40 million people, mostly in the developing world.

The idea of treating entire communities at once is similar to vaccination programs against diseases such as polio and typhoid. Both infected and non-infected individuals in a community are inoculated, to reduce the pool of infection and prevent the eruption of new cases. Unlike vaccinations, though, mass treatments with antibiotics typically need to be repeated numerous times.

Studying ways to prevent infection

This raised questions of how frequently and for how many years treatments should be administered to keep infection at bay. It might be impossible to reach every person in a community, so how widespread did the treatment need to be to produce "herd immunity," as in vaccination programs? Should only children receive the antibiotic or also adults? Would periodic mass treatments with antibiotics increase the risk of drug resistance?

NEI focused on these important issues, funding researchers to conduct several large community-based studies in different locations with widespread trachoma infection. Early results showed a single mass treatment with

"Elimination (of trachoma) will be an enormous task, but the treatment and prevention approaches needed for success are now more clearly defined."



Photo by Raúl Vasequez/ORBIS

azithromycin reduced disease prevalence in a community, but infection returned within a year in the most severely affected areas. Another study tested the impact of multiple mass treatment rounds and found communities needed more than seven—and perhaps as many as 10—annual mass treatments to conquer trachoma. Subsequent trials confirmed that long-term reduction and even elimination of the disease is possible with repeated mass antibiotic treatments involving most residents of a community over several years.

"By giving treatment on an annual basis, you eventually catch up and prevent the disease from flourishing," West said. "The question now is not so much how frequently you do it, but whether you can get away with treating just kids versus treating everybody."

Meanwhile in Ethiopia, NEI-funded researcher Dr. Thomas M. Lietman led a clinical trial involving 24 communities to determine whether mass treatment of children younger than 11 would protect the entire population. Working in collaboration with the Carter Center and the health ministry, Lietman discovered after one year that trachoma occurrences among children given azithromycin had plunged from 48 percent to less than 4 percent. Infection also dropped significantly in older, untreated children and adults, suggesting that repeatedly treating younger children might be a cost-effective strategy to control infection throughout a community.

Not only did the antibiotic ward off eye disease, but Lietman and his colleagues discovered another benefit—child deaths dropped by half in treated communities, suggesting that azithromycin helps mitigate potentially lethal infections such as pneumonia, diarrhea and malaria.

However, the potential for drug resistance to antibiotics is a key concern. Studies have shown the bacterium *Streptococcus pneumoniae* is capable of building resistance, but the risk diminishes several months after treatment. The long-term effect of administering multiple rounds of azithromycin is still unknown.

Preventing blindness and re-infection

Repeated trachoma infections often lead to trichiasis, a condition of turned-in eyelashes that scratch the eyeballs to the point of blindness. In such cases, mass antibiotic treatment does not prevent vision loss, although surgery can. Yet, trichiasis recurs in half of post-surgical cases. To improve outcomes, the NEI funded the Surgery for Trichiasis, Antibiotics to Prevent Recurrence (STAR) trial. West and her colleagues in Ethiopia randomized one group of patients with trichiasis to receive azithromycin after surgery; the other group received standard postsurgical care, which involved topical tetracycline ointment. Azithromycin reduced overall trichiasis recurrence by one-third and severe trichiasis recurrence by almost half, compared with standard treatment.

NEI-funded research over the past decade has answered these and other scientific questions necessary to tackle trachoma, laying the groundwork for other organizations to become involved in elimination efforts. For example, the Bill and Melinda Gates Foundation has awarded \$12 million to Johns Hopkins University to continue its work. With more than 40 million people suffering from trachoma throughout the developing world, elimination will be an enormous task, but the treatment and prevention approaches needed for success are now more clearly defined.

“NEI stepped up to the plate early on by funding trachoma research, hoping that would lead to other partners to come in and fill in the gaps, and that has now happened,” West said. “The goal of elimination of blinding trachoma by

Photo by Kieran Riley/CORBIS



Trachoma is the leading cause of preventable blindness. It spreads through contact with hands, clothing or flies.

2020 will be a challenge. Research to inform programs on strategies to achieve that goal will be a key component to success.”

Blindness from trachoma and trichiasis



Trachoma is currently the leading infectious cause of preventable blindness worldwide. Repeated, untreated infections over years build scarring on the inside of the eyelids and make the eyelashes turn in—a condition known as trichiasis. This scrapes and irritates the cornea, compromises vision and eventually causes blindness.

Trachoma remains a significant public health concern in many developing countries, especially in regions that suffer from overcrowding, water shortages and poor hygiene. Infection spreads from person to person, usually among children, through contact from hands, clothes, or flies that carry discharge from the eyes. Due to their close contact with children, women suffer three times more infections than men.

The WHO estimates that 40.6 million people suffer from active trachoma and 8.2 million have trichiasis. Hardest hit areas are in the Middle East, North and sub-Saharan Africa, India, Southern Asia and China. To tackle this misery, the WHO launched a trachoma elimination strategy, called “SAFE,” involving trichiasis surgery, antibiotics and improved hygiene, which it hopes will succeed by 2020.

RESOURCES

Article: <http://1.usa.gov/RThmKc>

Website: www.vision2020.org

Vision research leads to new theories on brain plasticity

A baby was born blind in a small Indian village. His parents assumed he was just another victim of the family curse, destined to a life without sight like his sister, father and grandmother before him. Blindness is all too common in India, striking one in 100 people.

The parents, resigned to his fate, sent the boy to an institution for the blind when he was four years old. His world changed inexorably a few years later, when health workers visited his school to conduct screening tests and determined his eyes were treatable. He soon underwent surgery and at last began to see. The scientists monitoring him were astonished to observe his post-surgery vision develop in ways that earlier research had deemed impossible. This discovery not only challenged established views on brain plasticity but may also lead to new approaches for children with deafness or autism.

The boy's screening and surgery were provided at no cost by Project Prakash, a nonprofit organization established in India to diagnose and treat people with curable blindness. It was founded by Massachusetts Institute of Technology neuroscientist Dr. Pawan Sinha, who was moved to act by a chance encounter with a blind person during a visit to his native India. Begun as a humanitarian program, Project Prakash led Sinha to make surprising discoveries about how the brain develops and humans learn to see. "Prakash," the Sanskrit word for light, signifies both bringing sight to children and illuminating scientists' understanding of brain development.

By treating children and young adults, allowing them to see for the first time in their lives, Sinha has had a unique opportunity to study how the brain learns to process color, shape and movement. "The population of individuals who are blind from birth and who have treatable conditions—these are extremely rare cases in the West," Sinha noted. His patients provide a unique window into the process of visual learning, enabling him to monitor the entire process from day one. Babies are not good research subjects because by the time they can communicate, they've already passed key developmental milestones. Project Prakash patients can verbalize their experience and remain still for brain scans, so scientists can observe how different parts of the brain engage during vision tests.

What Sinha and his colleagues have discovered has turned earlier scientific notions on their head. For many years, researchers believed there was a developmental window for



Photo courtesy of Dr. Pawan Sinha/Project Prakash

With research funding from the NIH's National Eye Institute, Project Prakash has made discoveries about brain plasticity that may lead to new approaches to treat deafness and autism.

vision that closed at around six years of age. They thought anyone blind from birth would not be able to acquire much visual proficiency if they gained sight later in life. Sinha's patients have forced reconsideration of those theories.

"Project Prakash is not just benefiting the children who are being treated, but it's likely to have far greater consequences," Sinha said in a recent interview. "That one can directly combine a medical humanitarian intervention with basic science, it's a powerful idea."

Since 2006, the NIH's National Eye Institute has provided research funding to Project Prakash, which has been "critical" to its success, Sinha noted. Based at the Shroff Charity Eye Hospital in New Delhi, the venture has so far screened more than 20,000 children and surgically treated at least 400 with curable conditions. Many more have received non-surgical care, including glasses. Its findings have also led to a petition in India's Supreme Court to ensure that every child in the country must be examined by an ophthalmologist before admission to a school for the blind.

Children encountered by Project Prakash have not previously undergone screening or treatment for a variety of reasons, including limited family finances, religious beliefs, distance to hospitals and old theories that sight cannot be recovered after a certain age. "Many parents really don't know whether the blindness that their child has is a treatable condition or not. Some of them believe it is just fate," Sinha said.

Project Prakash research has revealed the brain has significant capacity to "catch up" in interpreting color and light signals to recognize objects, regardless of whether the



Courtesy of Dr. Pawan Sinha/Project Prakash

By studying how previously blind children in India learn to see, MIT's Dr. Pawan Sinha has discovered the brain is more adaptable than previously thought.

window was dark during the early stages of development. For example, Sinha led one study on object recognition involving three participants, all of whom had gained vision after the age of six. They tried to identify a variety of simple objects displayed on a computer screen. For three months after treatment, they could recognize some objects displayed separately, such as a triangle or a circle, but tended to identify a third object when the shapes overlapped.

Additional tests showed that motion aids the brain's ability to distinguish individual objects, which was a key finding in the science of blindness. For example, the participants could see a triangle displayed among scattered lines more readily when it constantly moved than when it was stationary.

Whether blind people can, on gaining sight, immediately learn to visually recognize objects they previously knew by touch has been a mystery. Sinha and his colleague Dr. Richard Held conducted a series of experiments that showed the brain rapidly—even within a week of surgery to repair the eyes—starts mapping information across the senses about how an object looks and feels.

Project Prakash also uses functional brain imaging pre- and post-operatively to see how children's brains are organized and function in the weeks and months after surgery, Sinha said. Project Prakash studies "are giving us unprecedented and extremely valuable information about how the scaffolding of vision gets set up. They inform our conceptions of basic neuroscience and may be relevant for how we can tackle some neurological problems, conditions that require an understanding of brain mechanisms of plasticity."

Sinha has studied 40 children with autism, testing their visual and auditory patterns, and identified deficits in temporal integration. "Even though superficially autism has very little to do with congenital blindness, it can benefit from the same kind of model as Project Prakash, merging the provision of medical care with the opportunity to learn more through research," he added.

Another potential application is with deaf children. "Exactly the same sort of idea would apply to deafness as to blindness: Would the brain of a child who has been deaf from birth be able to acquire auditory processing capabilities, would he be able to acquire spoken language even if he is treated several years after his birth?," Sinha wonders.

As for the children who are currently untreatable because of damaged eye structures, Sinha dreams that one day they will gain eyesight as well. "Having cortical prostheses is way down the road, but at least conceptually, one can imagine feeding information derived from a camera directly to the cortical regions of the brain and enabling vision."

The light shining from Project Prakash is reaching other developing countries with high numbers of blind children—such as Brazil, Pakistan and China—where officials are studying Project Prakash so they can replicate its success.

For the blind boy who had cataract surgery at age seven, his eyesight now measures 20/100. Within ten months of his operation, he'd learned to see and identify static objects. For him, and a growing number of Project Prakash patients, the light now glows brightly.

Object recognition test	
<p>Separated</p>	<p>Overlapping</p>
<p>Stationary</p>	<p>Moving</p>

Among the other fields of science taking a cue from Project Prakash findings is autism. "Some of the visual impairments that have been reported in the domain of autism are very similar to the kinds of impairments we find in the Prakash children soon after they gain sight," Sinha said. "We are trying to find out whether this is a superficial or coincidental similarity or something deeper."

RESOURCES

Project Prakash website: <http://bit.ly/PPrakash>

NEI article: <http://bit.ly/SsPpEr>

ITC Bookman Std NIH lecture: <http://1.usa.gov/Q2YKM>

OPINION

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

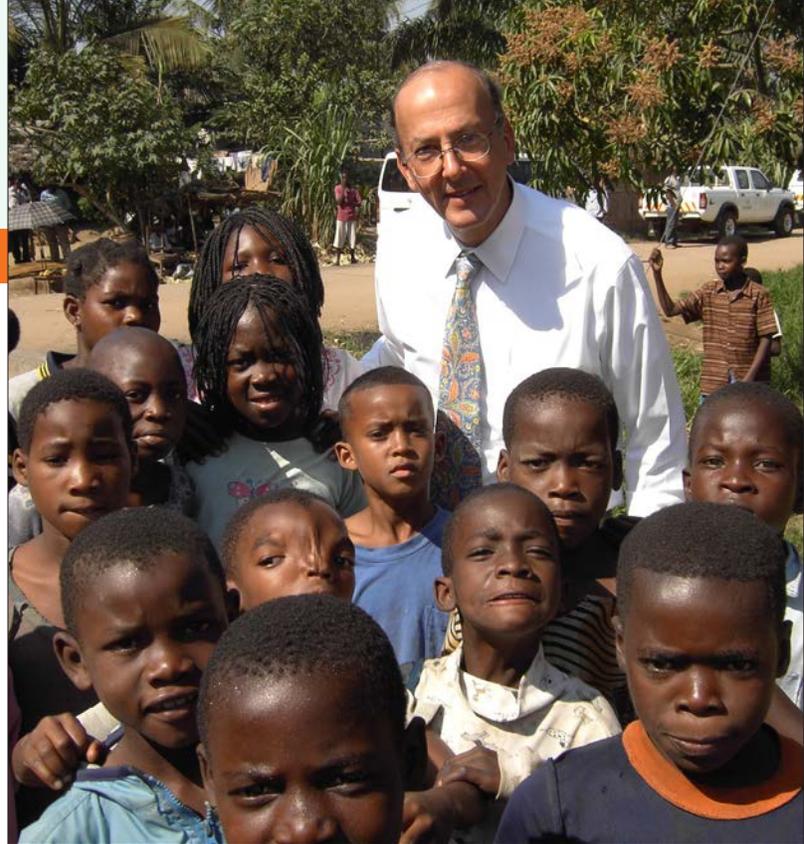
H3Africa begins building Africa's genomics expertise

Humans evolved in Africa and, today, populations in Africa carry the world's richest genetic diversity. However, the field of genomics has barely touched the continent, concentrating instead on developed countries with their ready supply of scientists, sophisticated equipment and study populations.

It's heartening to see that this is now changing, thanks in large part to the efforts of the NIH and Wellcome Trust to establish H3Africa—the Human Heredity and Health in Africa Consortium. This bold initiative is intended to build genomics-related research expertise and infrastructure across Africa. Deepening the understanding of genomic variations in its many populations promises to improve health by enabling more accurate disease identification and diagnosis and—as the world moves toward personalized medicine—tailored treatments based on an individual's genomic profile.

H3Africa's funds, targeted to be \$38 million over the first five years, have begun flowing through nine initial awards to African genomics scientists. These grantees will collaborate with researchers across the continent and around the globe to study illnesses of particular interest in Africa, such as sleeping sickness and rheumatic heart disease. Many studies will inform disease research in other parts of the world as well. For instance, a grant to South African researchers focuses on genomic and environmental factors that raise the risk of cardiovascular disease, a big killer everywhere.

H3Africa is also supporting an effort to establish an African biorepository to store and distribute biological samples from populations on the continent. To facilitate the sharing of the enormous genomic data sets that will result, H3Africa is supporting a bioinformatics network, initially with nodes of computational expertise in at least 15 countries. The vision for H3Africa has been shaped by NIH director Dr. Francis S. Collins—whose work in Africa led to the discovery of the first gene for diabetes—together with National Human Genome Research Institute director Dr. Eric Green and NHGRI senior investigator Dr. Charles Rotimi, who also leads the trans-NIH Center for Research on Genomics and Global Health.



Fogarty, along with several other NIH Institutes and Centers, is pleased to have a role in this remarkable goal of expanding African genomics capacity. Indeed, many of our programs support training directly relevant to genomics research, bioethics and population studies and data analysis. Our informatics training program has nurtured critical expertise needed to chip out discoveries from mountains of genetic sequencing data.

We're also identifying ways to form linkages between H3Africa and the Medical Education Partnership Initiative that Fogarty co-manages. In both cases, funding goes directly to African institutions, empowering them to develop medical and research education as they see fit. We anticipate synergies will develop between the two groups, further propelling cutting-edge science in Africa. These programs that establish meaningful collaborations and training opportunities on the continent can perhaps decrease, or even reverse, the brain drain of scientists and accelerate the pace of discovery and capacity building at home.

As H3Africa takes root, I anticipate additional funders will add their support and we'll see scientific research in Africa blossom in unprecedented ways. As the momentum builds, so will the likelihood that the health of populations on the continent will improve steadily and bring relief to those who have suffered the world's heaviest disease burden for far too long. And for science in general, unlocking the secrets of African genomes will reveal much about the genetic roots from which we all came.

RESOURCES

H3Africa website: www.H3Africa.org

Article: <http://bit.ly/H3AfrGN>



Dybul to be Global Fund's executive director

Amb. Mark R. Dybul has been appointed executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria, beginning early in 2013. Previously of the NIH's National Institute of Allergy and Infectious Diseases, Dybul helped create, and then led, the President's Emergency Program for AIDS Relief, PEPFAR.



Etienne to direct PAHO

Dr. Carissa F. Etienne has been elected director of the Pan American Health Organization, for a five-year term beginning in February 2013. She is currently assistant director general of health systems and services at the WHO. Originally from Dominica, she holds degrees in medicine and surgery from the University of the West Indies.



Abdool Karim recognized for HIV, women's health

Dr. Quarraisha Abdool Karim has been named by the Academy of Sciences for the Developing World to receive its 2012 Prize for Medical Sciences in honor of her contributions to HIV prevention and women's health. A Fogarty grantee, Abdool Karim is on the faculty of Columbia University and at the Centre for the AIDS Programme of Research in South Africa.



DelVecchio Good receives Silver Magnolia Award

The Shanghai Municipal Government has honored Fogarty co-principal investigator Dr. Mary-Jo DelVecchio Good with its Silver Magnolia Award. She was chosen for her contributions to mental health education, especially of women. A professor at Harvard University Medical School, she has furthered mental health research training in China.



Warf receives MacArthur Award

Fogarty grantee Dr. Benjamin C. Warf has been named a 2012 MacArthur fellow for his work in intracranial diseases in children. Currently at Boston Children's Hospital, he previously was medical director at CURE Children's Hospital in eastern Uganda, where he pioneered a low-cost treatment for hydrocephalus.



Merson receives Kentucky Colonel Award

Dr. Michael H. Merson has been named a Kentucky Colonel for his contributions to global health and HIV/AIDS. Merson, founding director of the Duke Global Health Institute, is a Fogarty grantee and serves on the Center's advisory board.



Eckhart to receive award for history contributions

The Foundation for the History of Women in Medicine has named Dr. N. Lynn Eckhart as a recipient of its 2012 Alma Dea Morani, M.D. Renaissance Woman Award. Eckhart directs academic programs at Partners Healthcare International and is interim dean of the Lebanese American University. She has helped lead the selection of Fogarty scholars.

Assessing global pollution

Lead, mercury, pesticides and other industrial pollutants are risking the health of 125 million people globally, making it as dangerous as malaria or tuberculosis, according to a new report, "2012 World's Worst Pollution Problems," from the Blacksmith Institute and Green Cross Switzerland. Full report: <http://bit.ly/SXh4Uf>

Global TB cases decline slightly

About 8.7 million new cases of tuberculosis were diagnosed worldwide in 2011, down 2.2 percent from the previous year. The disease remained a heavy global burden, killing 1.4 million people, the WHO says. Full report: <http://bit.ly/TeeBee66>

Global health spending database offered

The WHO is making freely available its "Global Health Expenditure Atlas," a database on health spending by regional, national and continent-wide formats. Full report: <http://bit.ly/TqnDBt>

Depression is common, although treatable

Depression affects about 350 million people around the world and contributes to the 3,000 suicides that occur daily. Effective treatments exist, but those most in need do not receive them, according to the WHO's report, "Depression: a global public health concern." Full report: <http://bit.ly/DepGlobal>

Making quality research easier to find

A university in Chile has created a non-commercial database of health research to make relevant, high-quality health research easier to find. The PDQ-Evidence database will be systematically updated through searches of PubMed and other databases. Website: <http://bit.ly/Sss9Aa>

mHealth to tackle chronic diseases

The WHO and International Telecommunications Union have established evidence-based and operational guidance for governments and others seeking to tackle noncommunicable diseases using mobile technology, especially text-messaging and apps. Announcement: <http://bit.ly/mHealthUD7>

US defense body active in global health

The U.S. defense department's impact on global health is substantial and more prominent now than before 9/11, including a focus on HIV/AIDS, concerns about emerging disease threats, and U.S. nation-building activities in Iraq and Afghanistan, a Kaiser Family Foundation analysis shows. Full report: <http://bit.ly/USGlobalKF>

Funding Opportunities

Funding Opportunity Announcement	Details	Deadline
Limited Competition: Brain Disorders in the Developing World (R01) - Non-AIDS (R21) - Non-AIDS	http://1.usa.gov/L6UUfk http://1.usa.gov/JjpxKs	February 14, 2013
Limited Competition: Brain Disorders in the Developing World (R01) - AIDS (R21) - AIDS	http://1.usa.gov/L6UUfk http://1.usa.gov/JjpxKs	April 11, 2013
Chronic, Non-Communicable Diseases and Disorders Across the Lifespan Training Award (D43) Planning Award (D71)	http://1.usa.gov/Hj3YfL http://1.usa.gov/GW4LyT	April 17, 2013
Global Infectious Disease Research Training Program Training Award (D43) Planning Award (D71)	http://1.usa.gov/H0U3Gq http://1.usa.gov/GZ22uc	May 21, 2013
International Research Ethics Education and Curriculum Development Award (R25)	http://bit.ly/EXmay22	May 22, 2013
Fogarty HIV Research Training Program for Low- and Middle-Income Country Institutions International Training Grant (D43) Extramural Associate Research Development Award (G11) Planning Grant (D71)	http://bit.ly/FOGjly24 http://bit.ly/FOGjly242 http://bit.ly/FOGjly243	July 24, 2013

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

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GLOBAL HEALTH

From John Snow to Genome Science



Sir Mark Walport

Director, The Wellcome Trust
Appointed UK's chief science adviser

THE DAVID E. BARMES GLOBAL HEALTH LECTURE

Wed. January 30, 2013

11 a.m.

Masur Auditorium, Building 10

Event will be videocast <http://videocast.nih.gov>

Sponsored by the Fogarty International Center and the National Institute of Dental and Craniofacial Research

