UCSF Department of Medicine
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PROTECTING HEALTH WORLDWIDE

Tackling a Major Killer

Tuberculosis (TB) is the world's most deadly infectious disease, claiming 1.7 million lives in 2016. Yet with proper treatment, most forms of TB are curable. "TB is associated with impoverished settings and highly vulnerable populations and, sadly, it's a disease that's largely ignored," said Payam Nahid, MD, MPH, Professor of Medicine in the ZSFG Division of Pulmonary and Critical Care, who strives to develop better TB treatments.

Dr. Nahid has collaborated with partners in Vietnam to establish a clinical trials unit in Hanoi as part of the TB Trials Consortium, an international network funded by the U.S. Centers for Disease Control and Prevention. Current projects include:

Reducing treatment time: Most patients with drug-susceptible TB receive a standard six-month course of treatment. Dr. Nahid launched an international trial to test the efficacy of administering higher doses of an antibiotic derivative of rifampin for four months. "If it's successful, patients could complete treatment sooner, are more likely to stay adherent, and we might even be able to reduce transmission," he said.

Preventing drug tolerance: "TB is a wily pathogen, and can adapt itself to drug pressure by going into a drug-tolerant dormant phase," said Dr. Nahid. "Then it becomes very difficult to clear." He is using a novel transcriptional profiling assay to discover which TB genes switch on once a patient starts taking medications. "That could provide us with new targets for drug development," he said.

Developing tailored treatments: It's likely that based on severity of disease, patients need durations other than the standard six months of treatment to be cured. Dr. Nahid developed a trial to identify patients who are easy, moderate and hard to treat, and customized treatment length and composition for each group. "We want to pursue more stratified approaches, where our objective is curing everybody by getting the right regimen to the right patient," he said.

Training workshop conducted by Anne Purfield, CDC lab coordinator (left), with Vietnam National Reference Lab staff. Dr. Payam Nahid (right and inset) reviews chest X-ray of a patient suspected of having TB in Hanoi Lung Hospital

Dr. Nahid and collaborators also opened a research unit in Ho Chi Minh City to study the feasibility of screening U.S.-bound immigrants for latent infection and offering them treatment before they leave Vietnam. He also has helped develop practice guidelines in the U.S. as well as for the World Health Organization.

"It's exciting to look at TB all the way from the bench to patient and finally to policy level," said Dr. Nahid. "It's also a beautiful thing working at UCSF, because of the collective of experts…. The potential impact on TB is large."

Linking Rural Sickle Cell Patients to Care

More than fifteen percent of the world's babies with sickle cell disease (SCD) are born in India. "The disease is almost exclusively concentrated in tribal populations, which are among the most vulnerable populations in India," said Reena Gupta, MD, Associate Professor in the ZSFG Division of General Internal Medicine.

Since 2013, she has partnered with SEWA Rural, a nonprofit in the western Indian state of Gujarat, to improve the health of SCD patients. "SEWA Rural has had an amazing impact on reducing maternal and under five child mortality but they hadn't really been able to touch maternal mortality among women with SCD" said Dr. Gupta. "They said, 'We haven't figured out how to crack this nut, and would love to partner to address this problem.'"

Dr. Gupta applied an approach similar to her work in improving population health across the San Francisco Health Network. In India, she and colleagues worked to universally screen all pregnant women, newborns and their family members for SCD. Then they developed a demonstration project, creating a chronic disease registry and

seeing SCD patients every three months in a dedicated sickle cell clinic. An outreach counselor contacts patients who miss appointments and is available by phone if patients have any symptoms or concerns.

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"Because of the lack of diagnosis and access to care, it's estimated that up to 20 percent of kids born with SCD die in childhood from conditions like sepsis and severe anemia, which are highly preventable with low-cost interventions," said Dr. Gupta. She has worked to administer evidence-based preventive treatments, such as providing daily antibiotics to children until age five to prevent life-threatening infections. All SCD patients are offered pneumococcal vaccination and folic acid supplements. Those with severe anemia or multiple pain crises in one year received blood transfusions and hydroxyurea.

Dr. Reena Gupta
ZSFG Associate Professor of Medicine

Dr. Gupta is exploring ways to scale up this approach. "It's so exciting to create care models that use continuity of primary care and proven interventions to have a robust, low-cost impact," she said. "It's been a tremendous opportunity to work with our partners to promote health equity and advance care for vulnerable populations in rural areas of India."

Building Trust, Fighting Malaria

"If you're a sustenance farmer in Uganda with five kids, every month one of them has malaria, and you have to miss work and pay to bring them to the doctor," said Grant Dorsey, MD, PhD, MPH, a malaria epidemiologist and Professor in the Division of HIV, Infectious Diseases and Global Medicine. "This disease keeps people in poverty."

He has worked to improve malaria treatments in collaboration with Philip Rosenthal, MD, Professor of Medicine and Moses Kamya, MMed, MPH, PhD, now Chair of the Department Medicine at Makerere University in Kampala, Uganda. Together they started the Infectious Diseases Research Collaboration, a nonprofit which employs 500 people. Current investigations include:

Reducing malaria risk: PROMOTE-II evaluates interventions to prevent malaria in pregnant women who are immune themselves, but whose placentas become a target for the malarial parasite – often resulting in miscarriage, preterm labor and stillbirth. Randomized trials demonstrated that giving expectant mothers a new malaria drug is highly effective at preventing malaria during pregnancy, and that administering chemoprevention to children during their first two years of life – before they have developed immunity and are most in danger – dramatically reduces malaria risk.

Investigating malaria epidemiology: "Just because you have malaria parasite in your bloodstream doesn't mean you're infectious," said Dr. Dorsey. "We're trying to understand who we should be targeting and how to reduce reservoirs of infection." In collaboration with European partners, the PRISM project built an insectary in rural Uganda – a sealed shipping container housing thousands of mosquitoes. Researchers feed the mosquitoes blood meals from adult volunteers to better understand transmission dynamics from human to mosquito. They hope to test targeted interventions for reducing malaria in entire communities.

Dr. Grant Dorsey (inset) cofounded the Infectious Diseases Research Collaboration, a Ugandan nonprofit which conducts research on malaria and other diseases

Global FOCI

Adithya Cattamanchi – Uganda, Vietnam; **Gabriel Chamie** – Uganda, Kenya; **Elizabeth Fair** – India, Uganda, Madagascar, Tanzania, Indonesia, Mozambique; **Maggie Feeney** – Uganda; **Elvin Geng** – Zambia, Uganda, Kenya; **Eric Goosby** – Africa; **Bryan Greenhouse** – Asia, Uganda, South Africa; **Reena Gupta** - India; **Judith Hahn** – Uganda; **Diane Havlir** – Uganda, Kenya; **Laurence Huang** – Uganda; **Peter Hunt** – Uganda; **Vivek Jain** – Uganda; **Ari Johnson** – Mali; **Midori Kato-Maeda** - Tanzania, Uganda, Philippines; **Dhruv Kazi** – Inida, China, Mexico, South Africa; **Sarah Kim** – Philippines; **Catherine Koss** – Uganda, Kenya; **Paul Krezanoski** – Madagascar; **Sulggi Lee** – Uganda; **Teri Liegler** – South Africa, Kenya, Uganda, China, Peru; **Carina Marquez** – Uganda, Kenya; **John Metcalf** – Zimbabwe; **Elizabeth Murphy** – Philippines; **Payim Nahid** - Vietnam; **Kartika Palar** – Latin America; **Patrick Phillips** - Vietnam; **Monika Roy** – Zambia; **Isabel Rodriguez-Barraquer** – Asia, Latin America; **Phil Rosenthal** – Uganda; **Dean Schillinger** – Mexico; **Priya Shete** – Uganda, South Africa, Vietnam; **Sheri Weiser** – Kenya, Uganda, South Africa; **Christina Yoon** – Uganda

Collecting high-quality data: Because Uganda lacks the resources to monitor the effectiveness of interventions, Dr. Dorsey and his partners created a surveillance network among 21 government health clinics. They drilled boreholes to provide access to water and installed solar panels to generate electricity, then provided microscopes and trained clinic staff how to diagnose malaria and report data via cell phone. "The system has become our eyes and ears for what's going on in Uganda," he said. "We've used it to detect epidemics in certain parts of the country, and to look at the impact of population-level interventions."

"It takes a long time to build trust and infrastructure," said Dr. Dorsey. "Now Uganda has become a major site for many UCSF investigators. There's a lot of talent in Uganda, and a lot of trainees there have become our collaborators. We're really committed to Uganda and this partnership."

Elizabeth Chur
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