

Statement of Steven J. Schiff

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August 2, 2011

**House Committee on Foreign
Affairs, Subcommittee on Africa, Global Health, and Human
Rights**

Chairman Smith and Congressman Payne, thank you for the invitation to testify today.

I am a pediatric neurosurgeon who started my career practicing at the Children's hospital here in Washington, DC. I now direct the Center for Neural Engineering at Penn State University, seeking solutions to problems that lie at the intersection of medicine, engineering, and science.

I have known Dr. Warf for many years, and hearing of his efforts to address childhood illnesses in Uganda, I visited him in 2006 to see how our engineering center might help his patients. It was readily apparent that he and his colleague Dr. Mugamba were inundated with cases of postinfectious hydrocephalus. At that time, they had treated over 1000 patients, without being able to culture any of the causative organisms in their laboratory. I asked Dr. Warf what the single most important problem was that he faced at the hospital, and he said finding out what causes these cases of postinfectious hydrocephalus. I have since devoted much of my professional effort towards seeking those answers.

We began by bringing specimens from Ugandan infants back to Penn State and 'threw the book at them' in terms of advanced ways of growing organisms. We grew nothing.

We then turned to DNA collection tools police use at crime scenes and set up a small forensics lab at the CURE hospital. We gathered DNA from the brain fluid of infants at the time of surgery to sequence the bacterial genes that might be present. My Penn State colleagues, Vivek Kapur and Mary Poss, and I found evidence of bacteria within the brain fluid in nearly all of the children. The bacterial types appeared consistent with those found on a farm with animals. The bacterial spectrum changed during rainy seasons.

The most prevalent bacteria was *Acinetobacter*, a notorious organism that has caused terrible wound infections in our military personnel in both the Vietnam and the Iraq-Afghanistan conflicts.

We then undertook fieldwork to track down the infants in which we found evidence of *Acinetobacter* infection. Environmental samples from huts, dung and water supplies yielded very close genetic matches for the organisms that we had previously retrieved from the infants' brains.*

Our findings were significant but did not determine what initially made the infants sick. Most of them developed serious infections within the first month of life, called neonatal sepsis. The World Health Organization estimates that infections lead to the death of 1.6 million infants each year, the majority in sub-Saharan Africa and southern Asia. The causal bacteria in the developing world appear different from those we see in the US. And most of the culture results from septic African neonates have failed to grow out organisms in any laboratory.

With funding from the Penn State Clinical and Translational Sciences Institute, and the endowment funds of Harvey F. Brush, we began a study of neonatal sepsis at one of Uganda's major referral hospitals at the Mbarara University of Science and Technology. Last year we recruited 80 mother-infant pairs, and in partnership with their head pediatrician Dr. Julius Kiwanuka, collecting spinal fluid and blood from the babies and birth canal specimens from the mothers.

We cultured the specimens on site at Mbarara and shipped the DNA samples to the U.S. We also collected specimens for viral RNA analysis, to ensure that we did not overlook any important viral role in this syndrome.

We were able to culture bacteria from the blood and spinal fluid of only a minority of the infants, and we found no evidence of significant transmission of maternal bacteria to them or any relationship to HIV infection in the mothers.

We are now collaborating with the J. Craig Venter Institute near Washington, DC, to perform an exhaustive sequencing of the bacterial and viral content of these samples. We have further received clearance from the Mbarara hospital, and the government agency that oversees human research in Uganda, along with Penn State and Harvard human investigations oversight committees, to proceed with extensive additional sampling.

Since CURE treats all of the hydrocephalus that develops in Mbarara patients, once we have studied a sufficient number of infants with neonatal sepsis from Mbarara, we will know which infections lead to hydrocephalus treated at the CURE hospital. Once we have identified the organisms, we can determine the routes of infection.

Recently, by fusing Dr. Warf's case data with US NOAA satellite data, we demonstrated a strong link between climate and postinfectious hydrocephalus. Infants get sick at intermediate levels of rainfall, emphasizing the role of the environment and consistent with our bacterial DNA findings. Our work demonstrates that in fully unraveling the mystery of postinfectious hydrocephalus we are benefitting from US technology in ways we had not anticipated.

We are committed to optimally surgically treat the large numbers of children who have hydrocephalus. However, we will never operate our way out of this problem. A critical long-term goal is more effective treatment of children with neonatal sepsis to decrease the brain complications in the survivors. And most importantly, once we understand the root causes, we need public health measures to prevent these infections.

Hydrocephalus is a thus global health issue well beyond the specifics raised by a small, very fine African hospital, a great U.S. charitable organization that brings the highest quality medical care to children around the world, and the finest physician I have ever met, Dr. Warf. Of the 130 million children born around the world each year, we are inadequately addressing the million and a half who die of preventable newborn infection.

As a physician and scientist, I am struck by how much we do not know about newborn infections in developing countries. I am concerned that one reason is that the newborn infants who die there have no political voice.

What we learn in Uganda needs to be replicated in other countries, such as Kenya, Tanzania, Rwanda, Zambia, Sudan and South Africa. All of them have similar cases.

We need to create inexpensive technologies that can be used indigenously to reduce the costs of identifying the microorganisms, determining their resistance to drugs and developing environmental and public health strategies.

I offer 3 conclusions:

- 1) We have not paid sufficient attention to the massive loss of human life from newborn infections in the developing world;
- 2) We now have the technology to shed new light on the causes of a substantial fraction of these deaths; and
- 3) We can now develop sustainable strategies and scalable technologies to more effectively prevent the deaths and tragic survivals from these devastating illnesses.

The fate of millions of lives depends upon our actions.

Thank you.

* Li L, Padhi A, Ranjeva SL, Donaldson SC, Warf BC, Mugamba J, Johnson D, Opio Z, Jayarao B, Kapur V, Poss M, Schiff SJ, Association of Bacteria with Hydrocephalus in Ugandan Infants, Journal of Neurosurgery: Pediatrics, 7:73-87, 2011.

