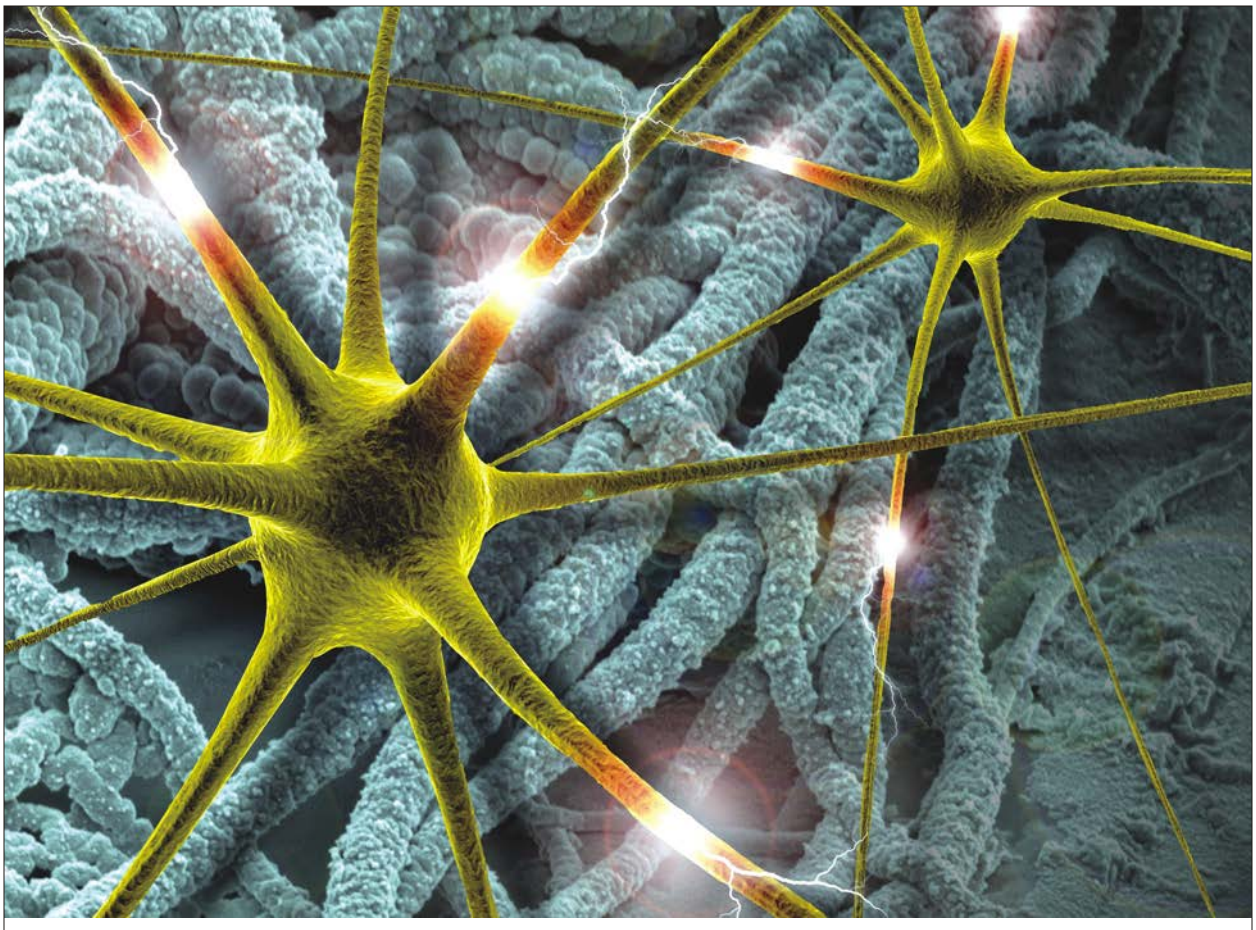

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Infant Hydrocephalus, Seasonal and Linked to Farm Animals in Uganda

Hydrocephalus in Ugandan children and other developing countries is seasonal, linked to farm animals and in part, caused by previous bacterial infection, according to an international team of researchers from Uganda and the United States, who believe that the best approach to this problem is prevention.

"Hydrocephalus in infants in developing countries is a grand medical mystery," said Steven Schiff, the Brush Chair Professor of Engineering and Director, Penn State Center for Neural Engineering.

Hydrocephalus is a build up of the fluid that normally surrounds the brain. The increased pressure causes the head to swell and damages brain tissue. Treatment includes placing a shunt to drain the fluid, but inevitably these shunts become plugged and require emergency care, not always available in rural Africa and other resource-limited regions of the developing world. Surgeons vigorously explore the use of new brain endoscopes to divert fluid buildup internally in such children, but this approach addresses the fluid and does not fix previous infection damage to the brain.

"Brains of children with hydrocephalus can be completely or mostly destroyed either by the scarring from the disease or by the pressure of the cerebrospinal fluid that cannot escape," said Schiff. "Many of these children with the worst aftereffects of infection will be mentally deficient and survive only as long as their mothers can adequately care for them. Understanding the causes could eliminate or prevent the enormous costs to lives and families that hydrocephalus brings."

Hydrocephalus in infants in sub-Saharan Africa is thought to be caused most often by meningitis-type infections during the first month of life. The U.S. and Ugandan researchers looked at the fluid from the brains of three sets of 25 consecutive infant hydrocephalus patients during January, July and October to try to determine the cause of the disease. By the time parents bring infants with rapidly growing heads to the CURE Children's Hospital in Mbale, Uganda, the underlying infection is gone. The researchers were unable to culture any bacteria from the samples.

To identify traces of previous bacterial infection, the researchers used DNA sequencing to look for 16S ribosomal DNA that exists in all bacteria. They reported their findings in the current issue of the Journal of Neurosurgery: Pediatrics, showing that 94 percent of the samples contained bacterial remnants. The researchers found a seasonal difference between samples representing infection during the dry season that were predominantly Betaproteobacteria and Gammaproteobacteria, that resulted from rainy season infection. Acinetobacter appeared in the majority of patients following rainy season infection.

Some sequences that appeared in the DNA analysis were from unknown bacteria and in many cases the bacterial fragments were not identifiable as to the type of Acinetobacter they represented.

In the United States and other industrialized countries, infant hydrocephalus is usually due to either a congenital anomaly or, in low birthweight premature infants, due to brain hemorrhages from immature blood vessels. At one time, Group B Streptococcus was a common cause of postinfectious hydrocephalus in infants in industrialized countries, but now physicians test mothers for the infection and treat with antibiotics before they give birth and the infections are rare. Surprisingly, according to Schiff, in Uganda, none of the remnant DNA in the infants was from Group B Streptococcus.

Looking for the source of the neonatal infections, the researchers targeted the living environment from infants with evidence of prior acinetobacter infection and located patients' homes. What they found were villages of huts where cow dung was pounded into the hut floors to keep water and ants out and used in patios around the huts where vegetation is cleared to protect against snakes. Newborns enter an environment where they not only live near animals, but also are surrounded by their material.

The researchers sampled both the cow dung floors and excrement from cattle, goats and chickens. They found similar genetic sequences from the bacteria retrieved from the infants as in the hut floors and nearby dung.

"It is really hard to keep infants to an adequate standard of cleanliness in this environment," said Schiff. "The bacteria we found reflects, I think, a significant environmental influence."

While the researchers have not yet proven that these bacterial infections are the cause of the devastating hydrocephalus occurrences, they believe that in part, bacterial infections from animals are the cause.

Historically, certain East African peoples have applied cow dung to stem bleeding in umbilical cord stumps, which caused newborn infections. Although such infections are now rare, the scope of newborn bacterial infections related to living in close proximity to domestic animals remains poorly categorized.

"As far as we can tell, these types of environmental newborn infections are the dominant cause of hydrocephalus on the planet," said Schiff. "We may be dealing with bacteria that we can't culture, viruses or parasites, and we may be dealing with different organisms in different locations"

The researchers are continuing their work and forming an African Hydrocephalus Consortium with Rwanda, Kenya, Tanzania and Zambia. They are conducting follow-up clinical trials at the Mbarara University of Science and Technology in southwest Uganda on mother-infant pairs with new neonatal infections, and at the CURE Children's Hospital of Uganda on older infants with postinfectious hydrocephalus. These trials use next generation technologies and high quality microbiology to sort out the causative agents affecting these infants. They are also continuing to explore the environmental connection so that public health strategies toward preventing the initial infections might be found.

Other Penn State researchers on the project include Linguine Li, Postdoctoral Fellow, veterinary and biomedical sciences; Abinash Padhi, Postdoctoral Fellow, biology; and Sylvia L. Ranjeva, undergraduate, engineering science and mechanics, who were first authors on the paper; Bhushan Jayaro, director, Animal Diagnostic Lab and Professor of veterinary and biomedical sciences; Vivek Kapur, head and professor, veterinary and biomedical sciences; Mary Poss, professor, biology and veterinary and biomedical sciences, all at Penn State .

Also part of the project were Benjamin C. Warf, Associate Professor of Surgery, Harvard Medical School, Children's Hospital Boston and Derek Johnson, Executive Director; John Mugamba, Medical Director and Zephania Opio, laboratory director, CURE Children's Hospital of Uganda.

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