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Blackflies May Be Responsible for Spreading Nodding Syndrome

New Transmission Theory May Offer Important Clues to Guide New Research, Reports *International Journal of Infectious Diseases*

London, United Kingdom, October 2, 2014 – Despite decades of research, scientists have yet to pinpoint the exact cause of nodding syndrome (NS), a disabling disease affecting African children. A new report suggests that blackflies infected with the parasite *Onchocerca volvulus* may be capable of passing on a secondary pathogen that is to blame for the spread of the disease. New research is presented in the *International Journal of Infectious Diseases*.

Concentrated in South Sudan, Northern Uganda, and Tanzania, NS is a debilitating and deadly disease that affects young children between the ages of 5 and 15. When present, the first indication of the disease is an involuntary nodding of the head, followed by epileptic seizures. The condition can cause cognitive deterioration, stunted growth, and in some cases, death.

There is an acknowledged link between NS and onchocerciasis, an infection by a small worm commonly known as river blindness. NS is only present in areas where onchocerciasis is endemic and other studies have shown that there is a high rate of onchocerciasis infections in children with NS. Despite this apparent connection, investigators have been unable to link the two concretely. *Onchocerca volvulus*—the parasite that causes river blindness--has not been shown to affect brain function, which would be required if the parasite were also directly responsible for causing NS.

This new study from the Institute of Tropical Medicine in Antwerp, Belgium proposes that along with transmitting the *Onchocerca volvulus* parasite, blackflies are also passing along a second pathogen that is responsible for NS. “We hypothesize that blackflies infected with *Onchocerca volvulus* microfilariae may also transmit another pathogen,” notes lead investigator Robert Colebunders, MD, PhD, who is head of the HIV/STD Unit, Department of Clinical Sciences at the Institute of Tropical Medicine, and Professor of Infectious Diseases at the University of Antwerp. “This may be a novel neurotropic virus or an endosymbiont of the microfilariae, which causes not only NS, but also epilepsy without nodding.”

The hypothesis draws on other research that shows that parasites and viruses can have a symbiotic relationship, allowing insects to pass on diseases they would not normally be able to transmit. "Many laboratory studies have shown that arboviral transmission is enhanced in mosquitoes and other blood feeding flies that concurrently ingest microfilariae, and the same could be true for blackflies," explains Dr. Colebunders. "The biting midge, *Culicoides nubeculosus*, became infectious after ingesting blue tongue virus and *Onchocerca cervicalis* microfilariae, but not after ingesting the virus alone."

There are still many key questions surrounding the spread of NS, but this new theory attempts to deliver possible answers. For example, as to why NS epidemics seem to come and go, the study asserts that indigenous populations may become immune to the NS pathogen over time, but that when forced migration moves a non-immune population into an area with a large number of blackflies, NS cases erupt. "Population displacement resulting from civil conflict has preceded NS outbreaks in both northern Uganda and South Sudan," Dr. Colebunders states.

The study also illustrates how aerial spraying of insecticides and ground application of larvicides to rivers—two key actions to control the blackfly population—have affected the rates of NS in locations like Northern Uganda. When steps were taken to reduce the blackfly population around known breeding grounds in 2012, it was followed by a decrease in cases of NS and no new cases were reported in 2013. Northern Uganda also began a comprehensive ivermectin (the anti-parasitic drug used to prevent river blindness) distribution program in 2012, which may also account in part for the drop in NS cases.

Dr. Colebunders suggests several courses of action based on the new theory, including collecting more precise incidence data on NS, epilepsy, and onchocerciasis in relation to blackfly distribution; continuing and increasing the systematic use of larvicides to control the blackfly population; and improving ivermectin coverage and increasing the frequency of its administration, as it appears it may limit the blackfly's ability to transmit the novel NS pathogen.

"The burden of disease may be considerable, as the 'NS pathogen' may also cause epilepsy without nodding," concludes Dr. Colebunders. "The planning of a clinical trial to evaluate these strategies, either alone or in combination, should be considered."

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NOTES FOR EDITORS

"Nodding syndrome—A new hypothesis and new direction for research," by Robert Colebunders, MD, PhD; Adam Hendy, MSc; Miriam Nanyunja, MD; Joseph Francois Wamala, MD; Marieke Van Oijen, MD, PhD. DOI: http://dx.doi.org/10.1016/j.ijid.2014.08.001, *International Journal of Infectious Disease*, Volume 27, (October 2014), published by Elsevier.

Full text of the study is openly available at www.ijidonline.com/article/S1201-9712(14)01579-3/abstract. Journalists wishing to interview Dr. Robert Colebunders may contact him directly at bcoleb@itg.be.

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