

'Window into the brain' reveals deadly secrets of malaria

January 15 2009

Looking at the retina in the eyes of patients with cerebral malaria has provided scientists with a vital insight into why malaria infection in the brain is so deadly. In a study funded by the Wellcome Trust and Fight for Sight and published today in the *Journal of Infectious Diseases*, researchers in Malawi have shown for the first time in patients that the build-up of infected blood cells in the narrow blood vessels of the brain leads to a potentially lethal lack of oxygen to the brain.

Malaria is one of the world's biggest killers, killing over a million people every year, mainly children and pregnant women in Africa, and adults in South-east Asia. Malaria parasites enter the bloodstream from bites by infected mosquitoes and live in red blood cells, making them stick to the inside of narrow blood vessels and causing blockages. Most deaths occur as a result of cerebral malaria, where red blood cells infected by malaria parasites build up into the brain, leading to coma and convulsions and, if not treated swiftly, death.

Scientists have known for some time that cerebral malaria is accompanied by changes in the retina, known as malarial retinopathy which can be seen by examining the eye. Because the retina can be considered as an extension of the central nervous system, it has been used previously as a "window into the brain", allowing for swifter diagnosis of cerebral malaria. However, until now it was not clearly understood why the disease should be so deadly.

In new research, Dr Nick Beare of the Royal Liverpool University

Hospital, together with colleagues at the Queen Elizabeth Central Hospital in Blantyre, Malawi, examined the retinas of 34 children admitted to the hospital with cerebral malaria. They used a technique known as fluorescein angiography, which involves injecting a special dye into the arm intravenously and photographing its passage through the blood vessels of the retina. It is used to identify fluid leakage or blockages in the small blood vessels at the back of the eye.

More than four in five of the children examined by Dr Beare and colleagues were found to have impaired blood flow in the blood vessels of their eyes. Three-quarters had whitening to areas of the retina where blood did not appear to reach, implying that the parasites were disrupting the supply of oxygen and nutrients.

"We have previously used the retina to accurately diagnose severe malaria, but now this window into the brain has opened up our knowledge of what makes cerebral malaria so deadly," says Dr Beare.

"This is the first study to clearly show impaired blood flow in the eyes of patients with cerebral malaria. It has provided strong evidence to support what, until now, had been merely hypothesised: that cerebral malaria causes inadequate blood flow to the brain, depriving it of oxygen and causing potentially life-threatening damage."

If caught in time, the effects of cerebral malaria can be reversed with no lasting damage to the patient's cognitive functions or vision. Dr Beare believes these new findings point to new therapeutic measures for treating cerebral malaria more effectively, particularly in comatose children.

"Many children are dying across Africa with cerebral malaria because we don't understand how to help them whilst the anti-malarial drugs have an affect," he says. "Drugs that improve circulation and limit the damage caused by the lack of oxygen could help prevent many deaths."

The research has been welcomed by Michele Acton, Chief Executive of Fight for Sight, who comments: "The findings of Dr Beare's work on malaria are incredibly important. Fight for Sight is delighted to have helped to fund such progress towards better therapies to prevent children dying from cerebral malaria."

Source: Wellcome Trust

Citation: 'Window into the brain' reveals deadly secrets of malaria (2009, January 15) retrieved 5 May 2024 from <https://medicalxpress.com/news/2009-01-window-brain-reveals-deadly-secrets.html>

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