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Blood Platelets Can Kill Malaria Parasites

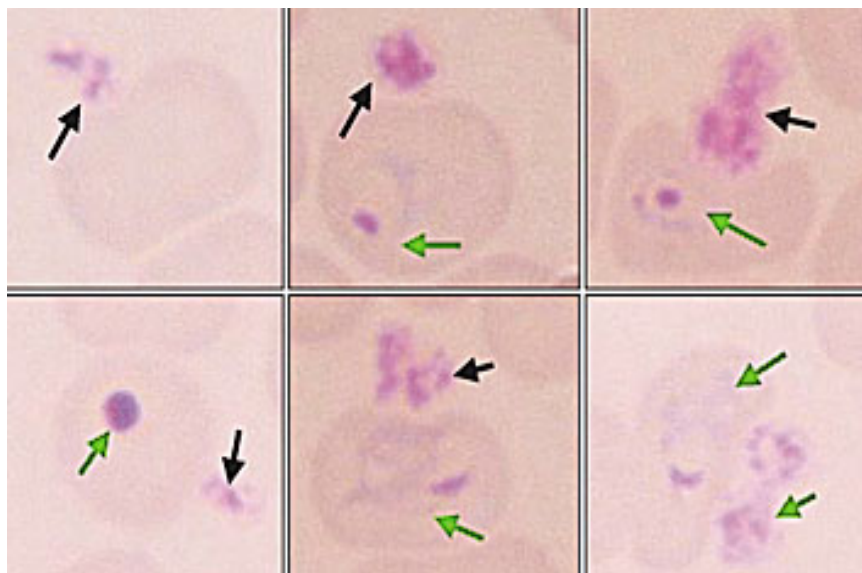


Image Title: Blood platelets help mice fight malaria. This photo shows platelets, marked by black arrows, binding to infected red blood cells in an attempt to reach the malaria parasites, marked by green arrows. See video below. - Simon Foote

New studies in mice suggest that blood platelets can destroy deadly malaria parasites. But a single dose of aspirin may interfere with platelets enough to thwart their killing power.

The findings could have important implications for malaria treatment in the developing world, where aspirin is often used to alleviate the high fever that accompanies the disease. “If our results pan out and actually have some relevance in humans, it might not be wise to use aspirin to treat malaria,” said Simon Foote, a Howard Hughes Medical Institute international research scholar at the Menzies Research Institute, University of Tasmania.

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- **Simon Foote**

This study, published in the February 6, 2009 issue of the journal *Science*, is the first to demonstrate that platelets can kill parasites in the Petri dish and in mice. In fact, previous studies suggested that platelets might make the disease worse by causing cerebral malaria, a potentially lethal complication. But Foote's research presents a different picture--showing that platelets actively fight malaria infection.

Platelets are well known for their role in blood clotting and blood vessel repair. Previous studies have shown that platelets are active in the body's innate immune system, which responds rapidly to invading pathogens. Innate immunity is complemented by the adaptive immune system, which kicks in later and has the amazing ability to recall the specific molecular features of any pathogen it has encountered in the past.

The innate immune response is particularly important in fighting malaria, which causes symptoms once the parasite has invaded the victim's red blood cells. There are several types of malaria – each caused by a different type of parasite--so infection with one type does not train the adaptive immune system how to fight against another form of malaria.

"From a biological perspective, I think this finding is likely to be very important in understanding the host's response to infection by malarial parasites," Foote said. "We think that platelets are one of the major factors that prevent people from dying early on in a malarial infection."

When Foote and his colleagues began their experiments, platelets were not their interest. He and postdoctoral fellow Brendan McMorrان were examining whether genetic mutations make malaria-resistant mice susceptible to the disease. During those studies, they discovered that platelet-deficient mice were much more likely to die of malaria than mice with normal platelets.

They used a specific type of mouse that was missing the *Mpl* gene. As a consequence of that mutation, the mouse produced just one-tenth the normal amount of platelets. When these platelet-deficient mice were infected with

Plasmodium chabaudi, a rodent version of the malaria parasite, half of the females and all of the males died of malaria. Only five percent of females and 20 percent of males with normal platelet counts died. “The entire project stemmed from that original observation,” Foote said.

That accidental finding led Foote and his colleagues to ask whether platelets had a direct role in malarial infection. To ensure that their original observation was not due to other genetic changes caused by knocking out the *Mpl* gene, the researchers eliminated platelets by giving the mice aspirin, which inactivates platelets. They found that the aspirin-treated mice were also much more likely to die of malaria. Although there is more work to do, the researchers believe that the aspirin is preventing some sort of anti-malarial effect produced by the platelets.

Using the mouse models, the researchers couldn’t directly see how the platelets interacted with the parasites. So they conducted similar experiments in a Petri dish in which they added human platelets to red blood cells infected with *Plasmodium falciparum*, the most deadly human malaria parasite. Those studies showed that the platelets were indeed killing the parasites. And when aspirin was added, the platelets no longer held back the parasites.

“Out of this entire work, the most practical outcome is that one should seriously reinvestigate whether aspirin is really a good antipyretic [fever-reducing] drug to use in the context of a malarial infection,” Foote said.

Foote cautions that the current experiments were done in mice, but he said they may have some relevance for understanding how humans respond to malaria infection. For example, low platelet counts are often seen in malaria patients in the early stages of infection. “We believe that’s because platelets bind to infected red blood cells and are taken out of circulation because of that,” Foote said. “What we think is happening during those first few days of malarial infection is that platelets are actually a buffer against rapid growth of malarial parasites. We definitely see this in mouse experiments.”

Foote says this means platelets are part of the innate response to malarial infection. But how platelets are actually able to kill the parasites is still unclear and will be the subject of future research. “There will still be quite a lot to do in the field to show that this would really have some effect in humans in the real world,” he acknowledged.