MedicalXpress

For treating malaria, less drugs may be best drugs

November 26 2007

The current dosage of drugs used in treating malaria may be helping the parasites become resistant to the drugs faster, without improving the long-term outcome in patients. According to evolutionary biologists, studies using mice suggest that the optimal use of the drugs might slow the spread of drug resistance while making the patient just as healthy.

Most malaria infections in the world comprise a mix of parasites, so that as resistant parasites spread in a population, they usually share their human hosts with other parasites that are susceptible to drugs. Over the course of infection, these bugs are locked in competition for the same space – and the same blood cells – within the body.

Normally in the absence of drugs, the susceptible pathogens keep the resistant ones from proliferating. But when infections are treated with drugs, the dynamic changes.

"Drugs kill off the susceptible parasites letting their competitors, the resistant ones, fill the vacant space and expand their numbers," said Andrew Read, professor of biology at Penn State, and an associate at the Center for Infectious Disease Dynamics.

Mutations within the parasites create new resistant strains all the time but scientists argue that the ways drugs are currently used could be accelerating the spread of such strains after they have arisen.

Read and his colleagues Andrew R. Wargo, now a post-doctoral

researcher at the University of Washington, Seattle, Jacobus C. de Roode, now an assistant professor at Emory University, and Silvie Huijben and James Shephard, doctoral student and undergraduate student respectively at the University of Edinburgh, infected mice with malaria to see how the parasites respond to drug treatment.

They found that once the drugs eliminated the susceptible microbes, the number of resistant bugs increased twice as much, compared to when the susceptible microbes were present, or when the infections comprised only resistant bugs.

"The more drugs you use, the worse you make the situation in terms of the evolution of drug resistance," said Read, whose findings appear online in the *Proceedings of the National Academy of Sciences*. "This massively increases the rate of spread of resistance, so the drugs become less and less useful," he added.

Researchers also found the spurt in parasite numbers to be directly proportional to the duration of drug treatment. The resistant bugs reproduced normally after a day of treatment. But after two days of antimalarial treatment, their numbers increased significantly, compared to infections in which they were the sole type of parasite.

"Resistant parasites not only survive but do much better because the drugs have successfully removed their competitors," Read explained. "We suspect this is what is causing the short lifespan of many antimalarial drugs," he added.

For instance, the Penn State researcher pointed out, the usefulness of antimalarial drugs such as chloroquine lasted for decades, while other drugs such as pyrimethamine have been effective for less than a decade.

If the infections in mice mirror malarial infections in humans, the

findings may offer a promising solution in slowing the spread of such drug resistance.

According to Read, public health policy places an undue attention on killing every last parasite in a person and that creates a massive selection for resistance because the drugs remove just those parasites that are susceptible to treatment.

"We should examine patterns of drug use that lead to stronger or less stronger selection for drug resistance," said Read. "What you actually want is to use less drugs, after the point where you are still making people healthy."

In other words the idea is to kill just enough pathogens to make a person healthy, but still save an ample number of them to compete with the resistant strain.

"The standard claim that one should take a very large dose designed to annihilate every single parasite in the body… might not always be the best thing to do," he added.

Source: Penn State