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Malaria parasites resist drugs by changing lifecycle

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Malaria parasites that are sensitive to anti-malarial drugs could evolve to cause more serious illness in people who don't get treated with drugs, researchers have discovered.

Scientists found that stressing drug-sensitive *Plasmodium falciparum* parasites by exposing them to low levels of anti-malarial drugs makes them change their behaviour.

Rather than putting their energy into developing specialised forms, which can be transmitted to other people by mosquitoes, the parasites replicate within the hosts they're already living in.

'It's this replication stage of the parasite's lifecycle that causes the classic fever and chills symptoms of malaria,' explains Dr Sarah Reece from the University of Edinburgh, who led the research.

The researchers think this change in behaviour is the parasite's attempt to improve its overall chances of survival. It takes more energy to develop the

specialised transmission form of the parasite needed to spread the disease, so sticking to a simple replication – 'safety in numbers' – approach to survival is likely to serve the parasite well.

Before this research, there was some evidence that malaria parasites stressed by anti-malarial drugs put all their resources into developing transmissible forms to get out of the existing host via mosquitoes.

'But evolutionary theory doesn't always support this 'jumping ship' strategy,' says Reece.



All creatures, from insects and birds to mammals, have to make decisions about how to spend their limited energy resources.

Both survival and reproduction are important if you want to spread your genes. This means malaria parasites that put all their eggs in one basket won't necessarily do very well in the long term.

Instead, they have to allocate their limited resources according to their own health and environmental conditions. Malaria parasites have to produce the right balance of replicating and transmissible forms to make sure that they not only survive within their current hosts, but also spread to new ones.

The new study, published this week in *Proceedings of the Royal Society B*, shows for the first time that exposing drugsensitive strains of the human malaria parasite to low doses of anti-malarial drugs upsets that balance.

'We think that parasites sensitive to drugs invest in their survival and future transmission by diverting resources from reproduction to replication when exposed to drugs.'

'It may be that the parasites aren't responding directly to drugs, but are adjusting their reproduction in response to changes in their numbers. There's some evidence to suggest the parasite counts to ensure there's an optimum number of parasites within a host,' adds Reece.

The researchers, including scientists from Sudan and Oman, collected parasites from people with malaria in Eastern Sudan. Here treatment of the disease with anti-malarial drugs is common.

These findings will have implications for understanding and predicting the spread of anti-malarial drug resistance. The researchers hope their results will help inform disease control strategies.

Sarah E Reece, Eltayeb Ali, Petra Schneider and Hamza A Babiker, May 19, 2010, Stress, drugs and the evolution of reproductive restraint in malaria parasites, *Proceedings of the Royal Society B: Biological Sciences*, doi: 10.1098/rspb.2010.0564

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A mosquito feeding on a human host and

becoming engorged with blood.