

Leishmania parasites with greater infectivity associated with treatment failure

October 8 2013

Relapses after treatment for *Leishmania* infection may be due to a greater infectivity of the parasite rather than drug resistance, as has been previously thought, according to a study published in *mBio*, the online open-access journal of the American Society for Microbiology.

Visceral leishmaniasis, also called kala-azar, is a parasitic disease that strikes 400,000 people every year and kills around 1 in 10 of its victims. The disease has proven difficult to treat, in part because a large percentage of [patients](#) who take the drug of choice, miltefosine, relapse after treatment, coming down with the same disease all over again. Doctors and scientists have long suspected that [drug resistance](#) was behind the failure of miltefosine, but that's not so, according to the researchers. The study reveals that parasites in patients who relapse after leishmaniasis treatment have a greater infectivity than parasites from patients who were treated successfully. They are essentially a worse, more dangerous form of the parasite.

"Parasites from relapsed patients show an increased capacity to infect host cells," says co-author Manu Vanaerschot of the Institute of Tropical Medicine in Antwerp, Belgium. The authors write that it remains to be seen whether miltefosine treatment causes the increased infectivity of the parasite, or if parasites with greater infectivity are capable of escaping treatment.

Miltefosine is at the heart of a vast program aimed at ending [visceral leishmaniasis](#) on the Indian subcontinent (India, Bangladesh and Nepal),

but 6.8% of Indian patients redevelop symptoms of the disease within 6 months after treatment and 20% of Nepalese patients relapse within 12 months after miltefosine treatment. Parasites collected from patients before and after treatment have been fingerprinted and are very close genetic matches, indicating that these patients are not simply re-infected with new parasites once their treatment ends, they are still carrying the same strain that sickened them before treatment. Other work revealed another surprising fact: parasites from relapsed patients were sensitive to miltefosine, so the failure of treatment was not due to drug resistance, a common suspect in cases where infectious disease treatment fails.

With re-infection and drug resistance now crossed off the list of possible reasons for the high relapse rate, the researchers set out to see what factors might really be at work. They examined the morphology of parasites taken from visceral leishmaniasis patients who were treated successfully and patients who relapsed. They found a significant association between the number of parasites in the metacyclic stage of their life cycle and patient treatment outcome. In other words, patients who relapsed were infected with parasites that have a greater infectivity, meaning they were more capable of infecting human cells.

The precise link between infectivity and [treatment failure](#) is not known, write the authors, but they propose that parasites with greater infectivity might cause a greater parasite load in the patient, making the case more difficult to treat, or perhaps they are able to evade the drug by hiding in parts of the body it doesn't easily penetrate, like the skin.

Vanaerschot says he and his colleagues saw a similar correlation between infectivity and [treatment](#) failure in patients who had been treated with the types of drugs that used to be favored in the region, pentavalent antimonials. "At the time we thought that it was a very special case. But now that we've also seen this in parasites treated with other drugs, this indicates that it might be a more common problem than we originally

thought."

Co-author Jean-Claude Dujardin, of the Institute of Tropical Medicine and the University of Antwerp, in Belgium, says regardless of the underlying cause-and-effect relationship, the findings are a wake-up call about the possible effects a therapy might have on pathogens it's supposed to kill.

"When we develop a drug to fight against a pathogen, we need to think about possible collateral damage. Of course we have to use these drugs, but we need surveillance to see if more aggressive [parasites](#) start to spread," says Dujardin.

Provided by American Society for Microbiology

Citation: Leishmania parasites with greater infectivity associated with treatment failure (2013, October 8) retrieved 25 April 2024 from <https://medicalxpress.com/news/2013-10-leishmania-parasites-greater-infectivity-treatment.html>

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