Patients treated for visceral leishmaniasis can still transmit the disease, study shows

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The results of an innovative "infectivity" study conducted by the *Drugs for Neglected Diseases initiative* (DND*i*) and the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) confirm that people successfully treated for visceral leishmaniasis in South Asia can still infect others if they develop a skin condition known as post-kala-azar dermal leishmaniasis (PKDL). The results were published in *Clinical*

Infectious Diseases this week.

Patients can develop PKDL—skin lesions in the form of rashes and nodules—usually six months to one year after successfully completing treatment for visceral leishmaniasis, a deadly parasitic disease transmitted by sandflies also known as kala-azar, or black fever. PKDL lesions contain the same parasite that causes kala-azar. The objective of the study was to assess whether parasites in the skin of PKDL patients could be transmitted to the sandflies that transmit kala-azar.

"This is the largest study of its type to date. Until now, information on the role of PKDL was scarce and scattered across decades of different research initiatives," said Dr. Jorge Alvar, senior leishmaniasis advisor at DND*i* and co-principal investigator of the study. "The results unequivocally show that PKDL is of pivotal importance for maintaining transmission of the disease in-between epidemics."

As part of the trial, PKDL patients allowed themselves to be bitten by laboratory-reared sandflies (which were free from infection) by plunging their hands into a cage for 15 minutes containing male and female sandflies. The sandflies were then analysed for the parasites that cause kala-azar.

The results showed that nearly 60% of the 47 PKDL patients in the study passed on the parasites to sandflies. This means the insects could then go on to infect someone else.

"Because PKDL is not fatal it has largely been ignored by public health efforts, and many scientific questions around its role have remained unaddressed," said Dr. Dinesh Mondal, senior scientist at the icddr,b and principal investigator of the study. "While these new findings don't answer all our questions, they do show that early treatment of PKDL patients will be a critical element of any leishmaniasis public health and

elimination strategy."

People with PKDL sometimes remain untreated for a long time. Transmission of the disease could therefore be occurring even when kala-azar is controlled and small numbers are being reported.

"Great strides have been made in the control of kala-azar in South Asia, but this study shows that now we must engage in active PKDL case detection and provide prompt treatment as an integral part of kala-azar control and elimination," said Dr. Suman Rijal, Director of the DND*i* Regional Office in India. "PKDL must be addressed in order to sustain elimination or we risk jeopardizing our earlier successes."

Forty-seven PKDL and 15 kala-azar patients were tested by xenodiagnosis. The results showed that depending on the type of PKDL lesion, 35% (9/26) of the macular to 86% (18/21) of the nodular PKDL patients in the study passed on the parasites to sandflies (p 0,0009), while 67% of the 10/15 kala-azar control patients did. This means the insects biting the skin of a PKDL patient could then go on to infect someone else.

DND*i* is now preparing a similar study in Sudan. DND*i* is also running clinical trials to test two treatment regimens for patients with PKDL, in South Asia and East Africa, in a bid to make treatments simpler, safer, and more effective.

More information: Dinesh Mondal et al. Quantifying the Infectiousness of Post-Kala-Azar Dermal Leishmaniasis Toward Sand Flies, *Clinical Infectious Diseases* (2018). DOI: 10.1093/cid/ciy891

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