

The curious case of antimony resistant *Leishmania donovani* – the first naturally emerged drug resistant pathogen with a higher fitness.

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The future of epidemics of drug-resistant pathogens depends greatly on the competitive fitness of drug-resistant versus drug-sensitive strains. Studies on various pathogens have demonstrated that drug-resistance generally confers a reduction in fitness expressed as reduced growth, virulence or transmission. However, this generally accepted dogma of drug-resistance being associated with a fitness cost is questioned by recent findings on antimony-resistant (SSG-R) *L. donovani*. Several experimental studies have found that SSG-R parasites have the advantage over their SSG-sensitive (SSG-S) counterparts at the level of their *in vitro* infectivity and *in vivo* survival capacity. Also at the genomic and metabolomic level, SSG-R *L. donovani* show traits of a higher adaptability and greater survival capacity. Field studies reveal that SSG-R parasites are still highly prevalent in natural populations of India despite the low SSG pressure in the past 5 years. In addition, mathematical modeling supports the notion that SSG-R *L. donovani* have a higher fitness compared to its wild-type counterparts. This higher fitness of SSG-R *L. donovani* can at least partly be explained by SSG affecting general defense mechanisms of the parasite and at the same time interacting with the immune system of the host to kill the parasite: resistance to this drug might thus also imply a higher tolerance to the effectors of the immune system of the host. This talk will review and discuss the available data on the fitness of natural SSG-R *L. donovani*, its possible origin and its implications for the control of visceral leishmaniasis.