

Could our medicines boost pathogens? Increased fitness of antimony-resistant *Leishmania donovani*

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Mathematical models predict that the future of epidemics of drug-resistant pathogens depends greatly on the competitive fitness of drug-resistant versus drug-sensitive strains. Several studies on prokaryotes and eukaryotes have demonstrated that drug-resistance generally confers a reduction in fitness expressed as reduced growth, virulence or transmission. In some cases, compensatory mutations may occur which restore, at least partly, the fitness of drug-resistant mutants to that of wild-type forms. The generally accepted dogma of drug-resistance being associated with a fitness cost is questioned by our recent findings on antimony-resistant (SSG-R) *L. donovani*. A mathematical model showed that the prevalence of SSG resistance in Bihar could not be explained without assuming a higher fitness of SSG-R parasites. Experimental evidences demonstrated that SSG-R parasites produced more infectious stages, that they better survived in vitro in macrophages and produced higher parasite burdens in vivo. Field studies also revealed a high prevalence of SSG-R parasites in natural populations of India, despite the low SSG pressure nowadays. Mechanisms of SSG-resistance might contribute to explain this higher fitness, but whole genome and metabolome analyses identified other traits not necessarily linked to SSG-resistance but which might affect the parasite's survival skills. We discuss the possible implications of our findings on the control of visceral leishmaniasis.