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Dr. Anurag Kushwaha is currently working as a Postdoctoral Research Fellow at the Department of Biochemistry, Institute of Science, Banaras Hindu University, Varanasi, India. His primary focus lies in comprehending the transmission dynamics of Visceral leishmaniasis, and immunotherapies to infectious diseases using in vitro and in vivo models as well as elucidating the many mechanisms contributing to sand fly resistance against different insecticides. His PhD work focused on understanding the transmission mechanisms of vector-borne pathogens in their reservoir animals, informing the reservoir targeted prevention. Dr. Kushwaha possesses extensive knowledge and expertise in the fields of microbiology and parasitology pertaining to infectious diseases, together with substantial practical experience in fieldwork epidemiology and medical entomology.

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## Project

### Sustaining India's efforts to eliminate Visceral Leishmaniasis by mitigating insecticide resistance in sand flies

Visceral Leishmaniasis (VL), known as Kala-azar on the Indian subcontinent, is a parasitic disease caused by *Leishmania donavani. L. donovani* is transmitted by infected female sand flies *Phlebotomus argentipes* (Diptera: Psychodidae). VL elimination goals are very close to being reached in India. To maintain these case levels post-elimination, it is critical to reduce vector populations and prevent potential transmission. *P. argentipes* is the only proven vector of VL in the Southeast Asia region. VL control in this region has relied on use of synthetic insecticides for IRS. *P. argentipes* are tiny and fragile insects that prefer to rest in dark corners of human dwellings, cattle sheds, and mixed dwellings of both humans and cattle. The sheltered resting behavior makes them a suitable target for control by IRS with insecticides. IRS undertaken by the Indian national malaria program using DDT for malaria control had an immense beneficial effect of controlling sandflies and significantly reducing VL cases. This unplanned control of VL led to the adoption of IRS by the Indian VL elimination program as the focus for *P. argentipes* control. VL resurged in the 1990s, and in 2003, India launched a kala-azar elimination program using DDT with the aim of eliminating VL from the country by 2015. Given the paramount importance of IRS to VL control effort, insecticide resistance poses a very real threat to achieving and sustaining the elimination goals. With declining DDT effectiveness for sand fly control, a synthetic pyrethroid, alpha-cypermethrin (5% WP), was introduced as an alternative in the second phase of IRS. As India enters the post-elimination phase of VL, it will be critical to ensure that resistance does not significantly develop against alpha-cypermethrin. Alpha-cypermethrin uses a similar mode of action as DDT to kill sandflies, increasing the risk of resistance development in sand flies under the pressure of regular exposure to insecticides. Focusing on villages where VL was previously endemic or where there is a current outbreak as measured by rK39 ELISA or RDT sero-positivity allows the team to focally target areas where insecticide resistance is most likely to lead to new cases. Once sites are selected based on sero-survey, the next aim is to evaluate IRS effectiveness in homes before/after the first post-serosurvey spraying, and for five specific time points weeks and months following. The CDC bottle bioassay, which we have used extensively will be used to assess endemic or outbreak village-caught sand fly insecticide susceptibilities. Based on our findings, as this tool is optimized for sand flies from

wild populations, it could be readily adopted by public health professionals to evaluate resistance and determine recommended adjustments, when needed, to sand fly control plans.