African sleeping sickness today

Human African trypanosomiasis (HAT), or African sleeping sickness, is one of 20 neglected tropical diseases listed by the World Health Organization (WHO). HAT can become a severe meningoencephilic disease developing after severe haemo-lymphatic infection. HAT takes two clinical forms, gambiense (caused by *Trypanosoma brucei gambiense* g-HAT) in West and Central Africa and the clinically more severe rhodesiense (*T. b. rhodesiense* r-HAT) in Southeastern Africa. g-HAT reservoir are humans. R-HAT is a zoonosis occurring in domestic cattle and wild ungulates. A zoophilic form, nagana, is an economically significant disease of domestic animals (*T. b. brucei*). The genetics of genus *Trypanosoma* is in flux and awaits representative sampling of natural populations. Confined to 36 countries in sub-Saharan Africa, the agents of HAT are transmitted by tsetse flies, a monogeneric (*Glossina*) family (Glossinidae) of some 34 species and sub-species including 3 major allopatric species complexes. There is convincing and important evidence that gHAT can be inherited congenitally and asymptomatically. Regarding HAT in the interval between January 2000 and 16 September 2019, 82% of 7497 Pubmed citations concerned *T. brucei* and 18% *Glossina*, testifying to the difficulty and expense of field work, tsetse colonization, and ease of obtaining longstanding *T. brucei* laboratory cultures.

Tsetse reproduction involves live births of mature larvae and long intervals between successive larvipositions. Age at first larvaposition is ~15 days and subsequent larvipositions occur at 10-d intervals. Generation time is ~50d. Adults are long-lived and population densities tend to be small compared to mosquitoes, house flies, etc. Prevailing opinion is that prevention of HAT requires vector suppression. The WHO anticipates elimination of HAT by the year 2030 but presently ~70 million people are at risk. Fieldwork established the premise that local elimination of tsetse vectors is rapidly compromised by immigration but genetic work demonstrated small rates of gene flow and high levels of genetic drift among subpopulations of savannah-inhabiting tsetse (principally Morsitans species group tsetse). Rather more gene flow has been detected among riverine-inhabiting tsetse (largely the Palpalis group). The picture of genetically differentiated tsetse locally could be explained hypothetically by small population numbers, local adaptations to prevailing climates, sexual and host preferences and bacterial symbionts. Contrasting geographical distributions of mitochondrial, microsatellite and allozyme diversities demonstrated that balancing selection acts on allozyme diversities Hypotheses related to mammalian host, vector, and trypanosome co-adaptations have not been rigorously tested but only recently has it become possible to evaluate the genetic population structures of sylvan trypanosomes and their vertebrate hosts.

Trypanosome reproduction is rarely sexual, but if so, takes place in the vector. Instead, reproduction is predominantly clonal with important genetic consequences. The genomes of tsetse and *Trypanosoma* are now available opening the way to studies of population structures and vector-parasite-host adaptations.

Ecological research has demonstrated that rapid, highly effective, inexpensive vector control can

be obtained by deploying small insecticide-laced targets in infested areas and/or by treating cattle legs to insecticidal applications. The Restricted Application Protocol of Torr et. al (2007) is highly effective and particularly useful for small farms. Alternative genetically-based methods, including the sterile insect technique (SIT), have been suggested but seem contraindicated because they would require expensive technical investments and long-term support arising from vector long, temperature-dependent life cycles.

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