

## Chapter 4

# Human Trypanosomiasis in India: Is it an Emerging New Zoonosis?

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### HUMAN TRYPANOSOMIASIS

Trypanosomes are flagellated protozoan parasites infecting man (human trypanosomiasis) and a wide range of animals (animal trypanosomiasis) (Figures 1 and 6).

Human trypanosomiasis is confined to Sub-Saharan Africa and Latin America and exists in two forms:

1. Human African trypanosomiasis (HAT) (sleeping sickness) is endemic in Sub-Saharan Africa. It is a dreadful fatal disease and was responsible for devastating epidemics in 1920s, with resurgence in 1990s. It is caused by *Trypanosoma brucei* (*T.b.*) *gambiense* (chronic form) or *Trypanosoma brucei rhodesiense* (acute form) and
2. American trypanosomiasis (Chagas disease) caused by *T. cruzi* is endemic in Latin America.

Both diseases are transmitted by vectors: Human African Trypanosomiasis by infected saliva of Tsetse fly, and chagas by infected feces of bugs (Figure 2). Clinically, HAT has two stages: Stage 1 or hemolymphatic stage characterized by fever, cervical lymphadenopathy, especially in the posterior triangle

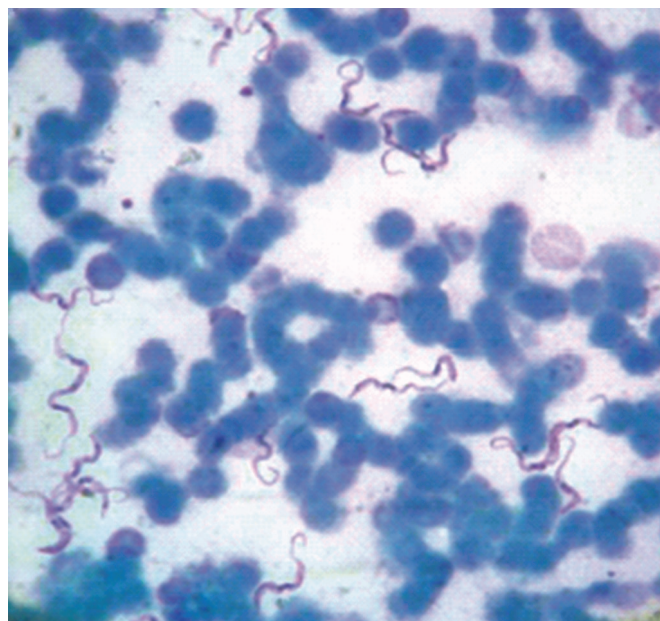


Figure 1: PS (Geimsa stain)—plenty of long, slender, flagellated, dividing forms of trypanosomes



Figure 2: Tsetse fly—the vector for HAT is not found in India

(Winterbottom's sign), splenomegaly, rash, pruritus, muscular pain, anemia, thrombocytopenia and carditis, which can sometimes be fatal. This is followed by stage two, the neurological phase or the meningoencephalitic stage with CNS invasion, in which there is marked sleep disturbance characterized by day-time somnolence and night-time insomnia.

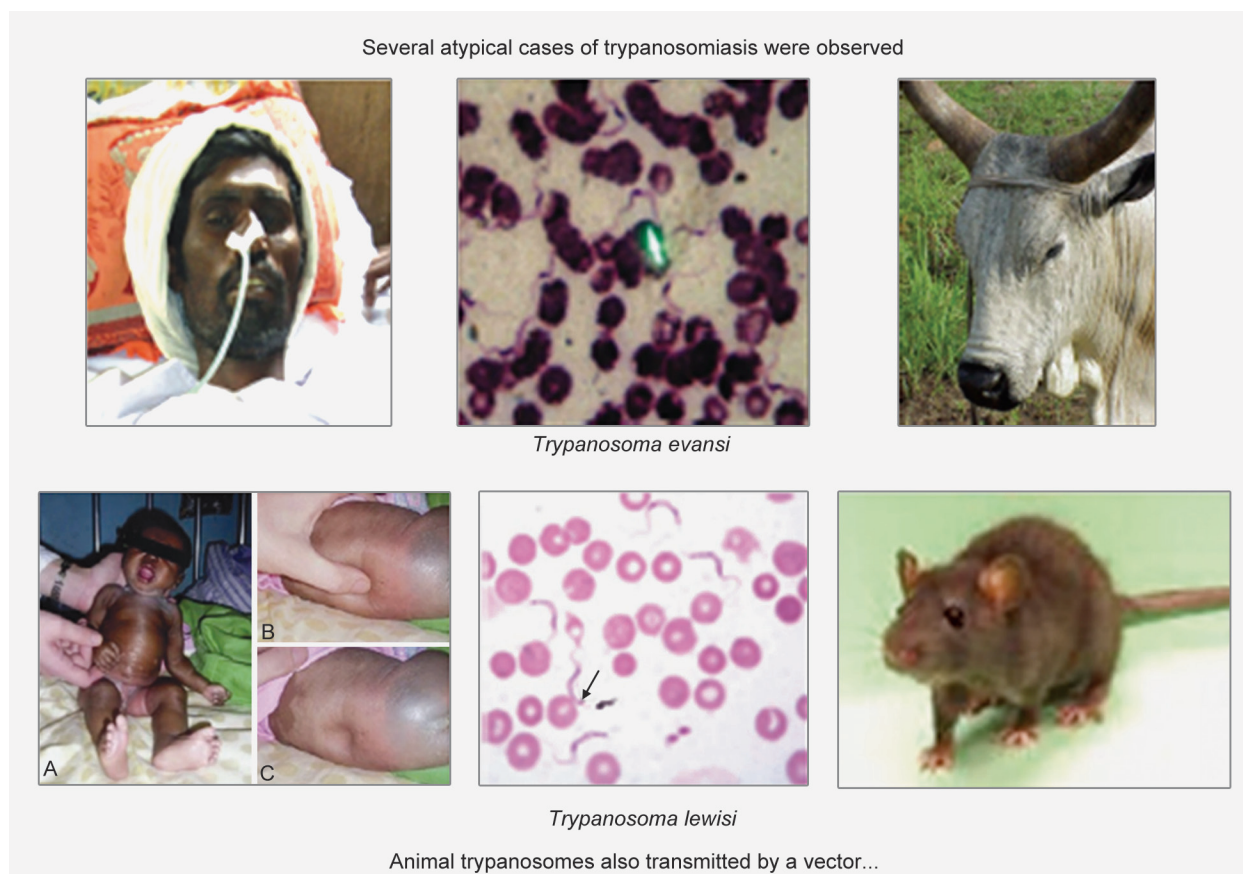
However, human trypanosomiasis of neither the kind which is evidenced in Africa and America, nor their vectors is found in India.

### ANIMAL TRYPANOSOMIASIS

In contrast to human trypanosomiasis, animal trypanosomiasis has a worldwide distribution and is common in India. India has the unique distinction of being the country where the first two mammalian trypanosomes, i.e. *T. lewisi* and *T. evansi* were discovered. *T. lewisi* is a natural parasite of rats while *T. evansi* is a pathogenic species of number of domesticated animals like cattle horses and causes a disease called “surra” in animals. High prevalence of these two animal trypanosomes in India is now a matter of concern.

### ATYPICAL HUMAN TRYPANOSOMIASIS DUE TO ANIMAL TRYPANOSOMES: A NEW FORM OF HUMAN TRYPANOSOMIASIS

Though human infection by animal species is “not possible” because of a trypanolytic factor in human serum, there are several reports of atypical human infection caused by animal trypanosomes, such as *T. evansi*, *T. lewisi* and *T. congolense*, especially from India.



**Figure 3:** Several atypical cases of human trypanosomiasis have been reported recently in India caused by *T. evansi* and *T. lewisi*

A new form of human trypanosomiasis has emerged with our description of the first human case in the world caused by *T. evansi*.<sup>1</sup> *T. evansi*—identified for the first time in horses and camels in 1881 in the Punjab region (India) by Griffith Evans, an English veterinary surgeon—causes disease in animals called “surra” which is commonly found not only in livestock in India, but has a worldwide distribution (**Figure 3**). Authors reported the first confirmed case of human trypanosomiasis caused by *T. evansi* in a farmer from Seoni village, near Nagpur in 2005.<sup>1</sup> The patient had fluctuating trypanosome parasitemia associated with febrile episodes for 5 months. Morphologic examination of the parasites indicated the presence of large numbers of trypanosomes belonging to the species *T. evansi*, which is normally a causative agent of animal trypanosomiasis known as surra. Basic clinical and biologic examinations were performed, using several assays, including parasitologic, serologic and molecular biologic tests, all of which confirmed the infecting species as *T. evansi*. Analysis of cerebrospinal fluid (CSF) indicated no invasion of the central nervous system (CNS) by trypanosomes. The possibility of acquired immunodeficiency (HIV/AIDS) was eliminated by a number of tests. A double test also allowed a hypothesis of familial lipoprotein deficiency (Tangier disease) to be eliminated. The patient was successfully treated and cured with Suramin, a drug used exclusively for treatment of early-stage human African trypanosomiasis with no CNS involvement. Patient follow-up indicated that the drug and specific regimen used were well tolerated. Clinical, serological and parasitological investigations at 6 months and 1 year indicated complete cure of the patient.<sup>2</sup> Suramin should be considered in the treatment of other cases of human *T. evansi* infection, if they occur. This is the first case reported of human infection due to *T. evansi*, which was probably caused by

transmission of blood from an infected animal. *T. evansi* is not known to be pathogenic to humans, but is the cause of a common animal disease called surra. Surra is highly prevalent in cattle and livestock in the village of origin of the patient. The parasites may have entered through the wound in right index finger, possibly while conducting delivery of infected cattle or through mechanical transmission by *Tabanid striatus* flies, similar to transmission of parasites in animals. Subsequently, this human infection was linked to lack of Apo L1 (trypanolytic factor) in the patient.<sup>3</sup> This is the first formally identified human case in the world of trypanosomiasis caused by *T. evansi*. A few cases of human carriers of animal trypanosomes were reported during the last century in India, Malaysia and in Sri Lanka, although none were scientifically confirmed and the cases always had transient infections (suggesting infection with *T. lewisi*, a common rat parasite) (**Figure 4**).

After our discovery of the first recorded case of human infection with *T. evansi*, author performed serologic screening of 1,806 persons from the village of origin of the patient, using the card agglutination test for trypanosomiasis and *T. evansi* (**Figure 5**).<sup>4</sup> A total of 410 (22.7%) people were positive by whole blood, but only 81 were confirmed positive by serum. However, no trypanosomes were detected in the blood of 60 people who were positive at a high serum dilution. The results probably indicate frequent exposure of the human population to *T. evansi* in the study area, which suggests frequent vector transmission of parasites to humans. Although *T. evansi* is not infective for humans, a follow-up of seropositive persons is required to observe the evolution of human infection with this parasite. Subsequent to the description of this new disease, Reto Brun christened this new zoonosis as “Human Asian Trypanosomiasis” which could pose a threat to human health.<sup>5</sup>



Nineteen atypical human cases of trypanosomiasis caused by animal trypanosomes are reported: 8 to *T. lewisi*, 5 to *T. evansi* and 4 of them are due to *T. brucei*, one to *T. vivax*, one to *T. congolense* and *T. brucei* species. All cases due to *T. lewisi* were observed in Asia. Out of 19 cases, 6 are infants and 8 are from India. Two more cases have very recently been detected in Puducherry (unpublished). Particularly in the State of Maharashtra the concern is more serious because one case of *T. evansi* and two cases of *T. lewisi* have been reported in a span of 3 years. The environmental conditions in India are conducive to the spread of the parasite from animals to human beings.

*Trypanosoma lewisi* is an obligatory parasite of rodents with a worldwide distribution. It is transmitted by fleas and is usually self-limiting in its rodent host because of its limited capacity for antigenic variation atypical human trypanosomiasis due to *T. lewisi* was first reported in a 4 months old infant in Malaysia<sup>6</sup> in 1933 and subsequently in 2 adults from Raipur, India<sup>7</sup> in 1974. These cases recovered spontaneously without specific treatment within days. Further reports of *T. lewisi* infection in infants have been reported in infants from Gambia (2006) causing more severe disease with CNS involvement, Thailand (2007)<sup>8</sup>, Mumbai, India (2007),<sup>9</sup> an adult from Pune (2007),<sup>10</sup> (who died despite treatment with Suramin) and recently in a 37 days old infant from Delhi.<sup>11</sup> These cases indicate that some *T. lewisi* or *T. lewisi*-like strains might be naturally resistant to lysis by normal human serum.

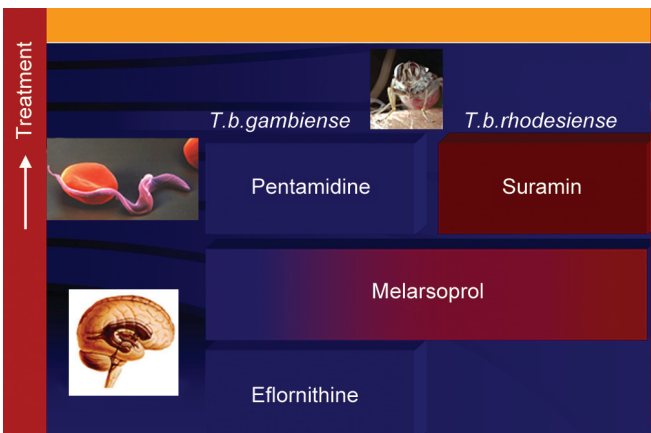


Figure 4: Treatment of human African trypanosomiasis

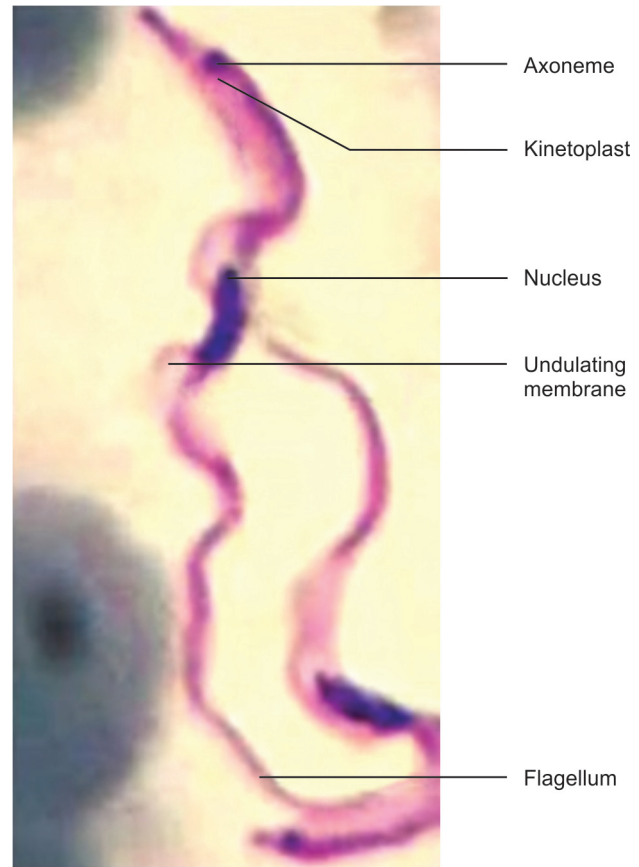


Figure 6: Trypomastigote form (dividing)

### Is this Atypical Human Trypanosomiasis an Emerging Zoonosis?

These several reported cases raise the question whether this "atypical human trypanosomiasis" signals an emerging new zoonosis or they just represent an unlucky biological accident. Another question remains—do many more trypanosomes have the latent potential to become human pathogens or are these examples just chance events?

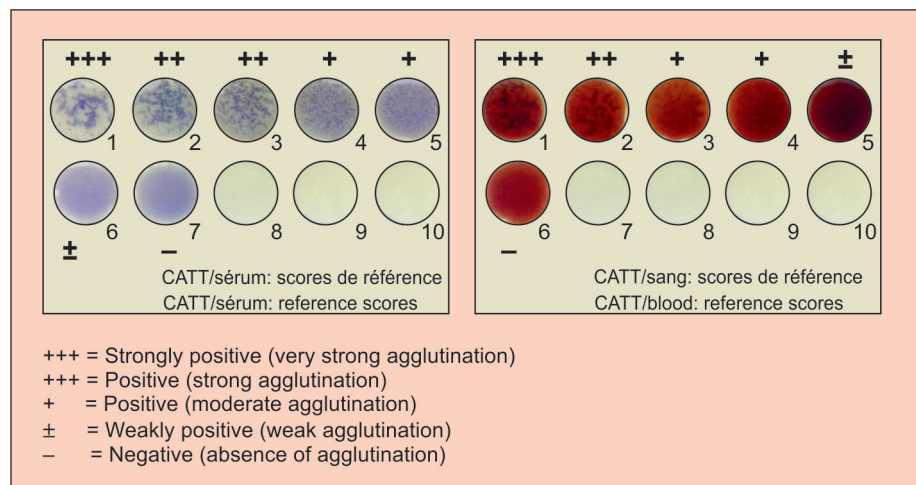


Figure 5: Card agglutination test for trypanosomiasis-interpretation

These numerous reported cases of human trypanosomiasis from India probably represent only the tip of the iceberg, with many more undetected and unreported cases present in the community, which should be detected by increasing awareness and through surveillance.

### CHALLENGES

However, there are numerous challenges in the diagnosis and monitoring of atypical human trypanosomiasis, since the laboratories for molecular studies needed for a species-specific diagnosis, are limited in India. As a first step, it is essential to perform sero-surveillance studies to determine the magnitude of the problem and to establish a case management protocol of detected cases. Training of malaria technicians, who examine millions of blood smears to also look for trypanosomes, is an important strategy to detect more cases. A network for studying atypical trypanosomiasis involving Food and Agricultural Organization (FAO), World Animal Health Organization (WAHO/OIE Organization Internationale des Epizooties) and World Health Organization (WHO) also needs to be established.

### CONCLUSION

It is imperative that the possibility of human infection by animal trypanosomes, which has the potential to emerge as a new zoonosis, needs to be taken seriously and given more attention. Further investigations in the field and laboratory are warranted. Livestock should also be handled with care to minimize accidental infection.

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