Trypanosome parasites and its diverse hosts: A Review

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I. INTRODUCTION

The aim of this review is to summarize what is currently known about the interactions between trypanosomatid parasites, its hosts and thoughts about their impact on environmental health, especially in those regions where hosts are natural reserves of many species. Wild life has been a major source of infectious diseases transmissible to humans [1, 2]. The zoonoses with a wild life reservoir represent an important public health problem all over the continents. A zoonosis is an infectious disease transmittable between animals and humans [3]. It is thought that trypanosomes had a single origin monogenetic as exclusively insect-borne parasites and later become digenetic parasites when vertebrates emerged since the Mesozoic era 230 mya [4]. Trypanosomes belong to the order Kinetoplastida and they infect many organisms.

II. KINETOPLASTIDIC PARASITES

Kinetoplast DNA (kDNA) is the most structurally complex mitochondrial DNA of the order Kinetoplastida, kDNA is best known as a giant network of thousands of catenated circular DNAs. The kDNA circles are of two types, maxicircles and minicircles. Maxicircles usually range from 20 to 40 kb homogeneous in sequence, depending on the species, and are present in 20-30 identical copies/cell. Minicircles, present in several thousand copies per network, are usually nearly identical in sizes (0.5 to 2.5 kb, depending on the species) which are frequently heterogeneous in sequence. Maxicircles encode typical mitochondrial gene products (e.g., rRNAs and subunits of respiratory chain complexes) but, remarkably, some of the protein-coding genes are encrypted. To generate functional mRNAs, transcripts undergo posttranscriptional modification via an intricate RNA editing process that involves insertion and deletion of uridine residues at specific sites in the transcripts [5, 6]. The genetic information for editing is provided by guide RNAs (gRNAs) with about 50-70 nucleotides, that are mostly encoded by minicircles, and few in the maxicircles. Different trypanosomatids have different numbers of gRNAs genes/minicircle(1-4), therefore since a species require many different gRNAs for editing, it also has a diverse set of minicircle sequence classes each with a certain copy number in an individual. However kDNA is fragile, is sometimes altered or even lost in nature, giving rise to induce and natural dyskinetoplastic (Dk) strains of trypanosomatids. This has led to the notion that kDNA is dispensable for certain stages of the life cycle or species of trypanosomatids especially in the salivarian trypanosomes *Trypanosoma equiperdum* and *T. evansi*. The loss of kDNA sequences in Dk strains results in the loss of function of mitochondrial genes encoded in kDNA. Notably, all Dk trypanosomes strains are able to survive with glycolisis as the only source of energy and like bloodstream forms but not as procyclic forms [7]. Considering that minicircles of trypanosomes are so abundant and contain conserved regions separated by hypervariable regions for to join primers in PCR assays are a valuable epidemiological tool. This molecular tool represents and excellent and sensitive target to directly detect different trypanosomatid species [8].

III. ENVIRONMENTAL IMPACT OF TRYPANOSOMATIDS

Plant-infecting trypanosomes are grouped under the single genus *Phytomonas.* They are transmitted by several insects and infect more than 100 plant species. However animal and human -infecting trypanosomes are grouped in four clades. They cause disease in humans and animals among which the following are particularly important: a) *Trypanosoma brucei* cause African sleeping sickness - East African form of disease (Rhodesian sleeping sickness) is acute, West African form (Gambian sleeping sickness) is more chronic. It is restricted to tropical Africa and largely rural areas. Wild and domestic animals are acting as reservoir hosts of disease and it is transmitted by tsetse fly; b) *T. evansi* which causes a disease named Surra has the widest geographical distribution worldwide in which it exhibits highly variable clinical effects, depending on the host and the geographical area. Surra disease affects a large number of wild and domesticated animal species in Africa, Asia, and Central and South America. The principal host species varies geographically, but camels, horses, buffalos and cattle are particularly affected, although other animals, including wildlife, are also susceptible. It is an insects-borne disease. Several species of haematophagous flies, including *Tabanids* and *Stomoxes*, are implicated in transferring infection from host to host, acting as mechanical vectors. In Brazil, vampire bats are also implicated in a unique type of biological transmission.

These characteristics make Surra not only a multispecies but also a polymorphic disease [9]; c) *Trypanosoma cruzi* cause Chagas' disease, with an initial acute phase of several weeks, subsides into chronic phase, this may continue for decades and can generate in humans mega syndromes, or heart damage and sudden death. *Opossums* and other wild animals of South America are particularly important in zoonotic infections. The vectors are *Triatomine* bugs of several genera; d) *Leishmanias* are very diverse all over the world. The relationships between trypanosomes showed trypanosomes to be monophyletic with the genus split into eight well supported clades [10]. These include: 1. the Aquatic clade, comprising trypanosomes of mainly aquatic and amphibious vertebrates; 2. the *T. cruzi* clade, which includes two infective mammalian trypanosomes (*T. cruzi* and *Trypanosoma rangeli*, bat trypanosomes from both the Old and New Worlds and a trypanosome from an Australian kangaroo); 3. the *T. brucei* clade, many of which are pathogens of domestic livestock; 4. the *Trypanosoma lewisi* clade, which contains trypanosomes from a wide range of rodents, a lagomorph and an insectivore; 5. the *Trypanosoma theileri* clade, which contains trypanosomes from marsupial and placental mammals; 6. the *Trypanosoma avium* clade ; 7. the '*Trypanosoma corvi* clade'; and 8. the 'lizard clade', which contains trypanosomes of squamate reptiles . According to recent molecular phylogenetic studies, bird trypanosomes form three distinct clades named after the principal species: *T. avium*, *T. corvi* and *T. bennetti*. The vectors of avian trypanosomes are blackflies, hippoboscid flies and mosquitoes. Phylogenetic trees clustered the snake trypanosomes together in a clade closest to lizard trypanosomes, forming a strongly supported monophyletic assemblage (i.e. lizard– snake clade) [11, 12]. Trypanosomes have adapted to all classes of vertebrates, and to a variety of invertebrate blood-sucking, leech, bed bugs some of which act as vectors [13, 14, 15]. Closer examinations of the trypanosome hosts in each clade suggest absence of strict co-speciation with the vertebrate host. One example is the parasite *T. cruzi*, which is transmitted by blood-sucking insect vectors (*Reduviidae* the subfamily *Triatominae*) to a variety of vertebrates including small mammals and humans. *Cavernicola pilosa* meantime transmits to bats *Trypanosoma cruzi marenkellei*, *Trypanosoma dionisii* and *Trypanosoma vespertilionis*, the two first present in the New and the last in the Old World.

IV. TRYPANOSOMATIDS IN EMERGING ENVIRONMENTAL HEALTH SITUATIONS

Increasing interaction between wildlife and humans or domestic animals may lead to disease emergence and require innovative methods and strategies for disease surveillance and management in wildlife. This apparent increased involvement of wildlife in livestock and human disease is likely due to several changing factors, most of them anthropogenic. When animals are translocated into a new environment, not just a single species is being introduced but rather an entire micro-ecosystem consisting of the target species and all its accompanying microbes and parasites. Any significant change occurring in the environment and management of the population, or even other populations in the same ecosystem, may imbalance the equilibrium of the host, agent, and environment, allowing a newly introduced agent or subclinical infection to manifest as an emerging disease [16]. Although there are no parasitic diseases classified as serious transmissible diseases, there are some that would affect trade in agricultural. In addition, parasitic diseases by nature are chronic and difficult to detect in host populations, often able to use several host species, and easily transported in infected hosts that show no overt symptoms of infection. One case is *T. evansi* in pigs, which are common in Papua New Guinea. Rats and bats were the only placental mammals on the island until pigs were brought in by humans, 5000 years ago [17]. Another example is in Australia. The long isolation has resulted in the evolution of a unique, extremely rich and varied native fauna and one that is potentially susceptible to introduced parasites [18, 19]. Concern has been expressed that should *T. evansi*, be introduced into Australia it could devastate native mammalian fauna [20]. Many small and medium sized mammal species, for example, those were once widespread across the continent are now restricted to isolated areas in the south west or on off-shore islands. In the last 10 years there has been a further decline of many of these native mammals, with evidence that parasitic diseases may be implicated [21]. Longitudinal molecular ecological studies have demonstrated an overall pattern of widespread distribution, with *Trypanosoma* genotypes/species occurring in many different host species, often at high prevalence, on the mainland of Australia as well as on off-shore islands [17, 20, 21, 22]. Another emerging situation occurs with Chagas disease in non endemic countries free of vectors with low prevalence, now report a growing number of cases [23, 24]. This is the consequence of increased human immigration worldwide in the last decade and congenital transmission. There is a great challenge for clinicians in non endemic countries able to recognize the disease symptoms and further perform diagnosis and treatment. Great difficulty has represented the recognition of species of trypanosomes but now, thanks to the development of numerous molecular techniques has facilitated this goal.

V. LEISHMANIASIS

Human leishmaniasis is a spectral disease caused by several *Leishmania* species and subspecies. These clinical manifestations of the disease in part are devoid on the particular infecting *Leishmania* species. These *Leishmanias* have different animal reservoirs and insect vectors (sand fly). The parasites have two main forms in their life cycle: promastigotes in the insect gut, and amastigotes that infect the lymphoid macrophage system of the mammalian host. There are the old world species (*Leishmania tropica* and *Leishmania major*), and the South American or new world species (*Leishmania mexicana, Leishmania brasiliensis* complex) which presumably diverged before the break up of the Gondwanaland some 80 mya [25, 26]. The relevance of identification of *Leishmania* spp will depend on the biology of the parasite and the epidemiology of the disease. Clinical applications are relevant in leishmaniasis since established links between some *Leishmania* spp and disease severity or treatment outcome exist [27]. *Leishmania donovani,* widespread in tropics and subtropics, causes visceral disease in old and new worlds; *Leishmania tropica* causes cutaneous leishmaniasis (oriental sore) in old world; *Leishmania mexicana* and *Leishmania braziliensis* cause muco-cutaneous leishmaniasis in new world. Dogs and rodents are particularly important in zoonotic infections and it is transmitted by sandflies of the genus *Phlebotomus* and *Lutzomyia.* In visceral Leishmaniasis, *L infantum and L. donovani* are characterized by different epidemiological profiles, being transmitted zoonotically and anthropologically, respectively. Therefore treatments of the disease depend on rapid, accurate identification of the *Leishmania* spp in biological samples. The *Leishmanias* can be dividing into four morphologically similar main groups, including the visceral and cutaneous types that infect man, geographical provenance, definitive hosts and the sand fly vector. Human leishmaniasis cause a wide range of clinical symptoms lesion of old world cutaneous leishmaniasis caused by *L. tropica* in Asia and North Africa, often heal spontaneously or *L. major* and *L. aethiopica*, whereas new world mucocutaneous leishmaniasis are caused by *L. brasiliensis brasiliensis* and *L. mexicana* in South America, which tend to metastasize causing terrible disfigurement and even death. Visceral leishmaniasis or Kala Azar due to *L. donovani* in Africa and Asia has a high mortality rate, same *L. infantum* in the Mediterranean region and *L. chagasi* in South America.

VI. THE PHYTOMONAS PROBLEM

Phytomonas are ubiquitous and a diverse group of plant parasites that exhibiting both pathogenic and endophytic lifestyles. Species of the genus Phytomonas are found in a wide range of geographical areas, including Northern and Central Africa, China, India, several European countries, and the American continent [28, 29, 30]. They are transmitted to the plants in the saliva of phytophagous hemipterous bugs [31]. They are distributed primarily in tropical and subtropical zones, by multiplying in latex tubes, fruits and seeds or colonizing the phloem sap inside the sieve tubes. *Phytomonas* infection can occur without apparent pathogenicity, but conversely it can cause lethal disease in plants of substantial economic value, including the coffee tree, coconut and oil palms. This results in important economic losses in Latin America and the Caribbean. [32]. Two species are definitively known to cause plant disease. *Phytomonas staheli* causes wilt of palm and *Phytomonas leptovasorum*, causes coffee phloem necrosis, both are problematic in areas of South America. *P. staheli* and *P. leptovasorum* exclusively inhabit the phloem during the plant stage of their life cycle. Individual Phytomonas species may be spread between plant hosts by a broad range of different insects. However the natural host was shown to be the nocturnal coreid spurgebug *Dicranocephalus agilis* [33]. From the earliest descriptions of Phytomonas, it was noted these parasites exhibited extreme morphological polymorphism. The majority of Phytomonas species isolated exhibit promastigote morphology [34, 35]. A unifying feature of phylogenetic analyses of Phytomonas is that there appears to be large diversity within the group. For example, the kDNA sequence data shows that the divergence between the phloem limited Phytomonas HART1 and the fruit parasite *Phytomona serpens* is greater than that spanning all sampled Leishmania species and similar to the divergence between *T. cruzi* and *T. brucei* . The Phytomonas nuclear genomes analyzing to date are much smaller than those of their Leishmania or Trypanosoma relatives; for example, the genome of EM1 is 17.8 mega bases (Mb) in comparison to 32.9 Mb of *Leishmania major,* 62.3 Mb of *Trypanosoma brucei* and 32.5 Mb of *Trypanosoma cruzi* [36, 37, 38, 32]. Analysis of the genes encoding metabolic proteins in the Phytomonas genome sequences revealed a cohort of enzymes consistent with life in a plant environment. Both HART1 and EM1 genomes encode glucoamylase, alpha-glucosidase, and alpha, alpha-trehalose phosphorylase genes, allowing them to utilise plant carbohydrates. Interestingly, only the phloem restricted pathogen, Phytomonas HART1, encodes invertase genes for degradation of sucrose. Another remarkable feature of Phytomonas parasites is the loss of genes encoding the cytochrome c oxidase subunits I–III (COI, COII, COIII), and cytochrome b (cytB) of the bc1 complex same as the diskenoplastic *T. evansi* describe before [39, 40, 32].

VII. CONCLUDING REMARKS

It has been suggested that parasite evolution is influenced by biology and opportunity [41]. It is now widely accepted that novel infectious disease can be a leading cause of serious population decline [42]. In the case of mammals, however, there are still no well-corroborated instances of such diseases having caused or significantly contributed to the complete collapse of species. However during 2008 it was reported the first molecular evidence for a pathogen emerging in a native mammal species immediately prior to its final collapse [43]. As mentioned that it is not convenient unconditionally accept as definitive to the respects that affect ecology of parasite, vector competence and parasite interactions within an intermediate host or permanent rather keep in mind that global issues including climate change, populations migration, environmental changes and others factors serve to exacerbate parasite zoonoses and this problem continue to have a significant impact on public health throughout the world [44].

ACKNOWLEDGEMENTS

This work was supported by FONDECYT-Chile 1160080 to A. Solari.

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