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STUDIES ON *TRYPANOSOMA RANGELI* TEJERA, 1920. IV – A RECONSIDERATION OF ITS SYSTEMATIC POSITION

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The systematic positon of Trypanosoma rangeli *is reconsidered and the creation of a new subgenus.* Tejeraia, *is proposed to remove this trypanosome from the subgenus* Herpetosoma *of the section Stercoraria.*

The characteristics described for the proposed subgenus indicate that it must be located in the section Salivaria rather than in the Stercoraria.

The evidence supporting this proposition is discussed in the text.

Trypanosoma rangeli, the second American trypanosome of man, in contrast to *Trypanosoma cruzi*, the causative agent of Chagas' disease, is not pathogenic to the vertebrate host. However, like *T. cruzi* it has a wide range of hosts and the same triatomine vectors.

Regarding the cycle of development of *T. rangeli* in the vector, Hoare (1968) considered that the life cycle of this parasite has features of both Stercoraria and Salivaria, producing infective metacyclic forms in the posterior and anterior stations of the triatomine vectors. However, Tobie (1964) reported that the trypanosome-forms of *T. rangeli* present in the intestinal contents of *R. prolixus* were not metacyclic in form and were not infective. D'Alessandro (1976) pointed out that while *T. rangeli* shares certain morphological and behavioural characteristics with other members of Stercoraria and Salivaria, it differs from them in other terms. He remarked upon the following affinities:

i) The morphology of the *T. rangeli* blood forms is indistinguishable from that of *T. lewisi*, the type species of subgenus *Herpetosoma*, section Stercoraria (Hoare, 1964).

ii) The ease with which *T. rangeli* can be cultivated in conventional media is likewise characteristic of the Stercoraria.

iii) In *T. rangeli*, as in Stercoraria, epimastigotes are the predominant forms in the gut of the Reduviid vector.

iv) As in Salivaria, the transmission to vertebrate is through the bite of an infected vector which produces infective forms in the salivary glands.

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The differences between *T. rangeli* and other trypanosomes are as follows:

i) *T. rangeli* reaches the salivary glands through a previous invasion of the haemocoele of the infected vector.

ii) In contrast to other members of *Herpetosoma, T. rangeli* has a wide vertebrate and invertebrate host range.

iii) *T. rangeli* is pathogenic to its triatomine vector and non-pathogenic to its vertebrate host.

iv) In contrast to *T. lewisi,* which multiplies and produces high levels of parasitaemia in rats, *T. rangeli* shows a low or "occult" parasitaemia in vertebrate hosts.

Despite these differences *T. rangeli* has been maintained as a member of the subgenus *Herpetosoma* Doflein, 1901 of the Section Stercoraria (Hoare, 1964), where the type species is *T. lewisi* Kent, 1880.

This paper includes some new considerations of the life cycle of *T. rangeli* in both vertebrate and invertebrate hosts and its systematic position is reconsidered.

I - DISTRIBUTION AND HOSTS OF *T. RANGELI*

Apart from *T. rangeli,* strict stenoxeny seems to be the rule in trypanosomes belonging to the subgenus *Herpetosoma,* for example, apparently *T. lewisi,* a cosmopolitan parasite of *Rattus spp.,* cannot infect other vertebrate genera, not even *Mus* (Baker, 1981).

T. rangeli is widespread among human beings throughout the neotropical region, where it has been found in Venezuela (Pifano et al, 1948); Colombia (Paredes & Paredes, 1949; Groot & Uribe, 1951); Guatemala (De Leon, 1965); Panama (Sousa, 1966); El Salvador (Peñalver, 1953); Paraguay (Canese, 1964); Brazil (Lucena & Marques, 1954); Costa Rica (Zeledon, 1954); and Argentina (Borzone, Lapiezacabral & Aizenberg, 1949). *T. rangeli* also occurs in lower mammals and has been reared from dogs in Venezuela (Pifano, 1954), Colombia (Groot & Uribe, 1951), Paraguay (Canese et al, 1963), and Argentina (Borzone, Lapiezacabral & Aizenberg, 1949); from monkeys in French Guiana (Floch & Abonnenc, 1949), Colombia (Dunn, Lambrecht & Duplessis, 1963; Marinkelle, 1966), Peru (Dunn, Lambrecht & Duplessis, 1963) and Brazil (Deane, 1979); from opossums in Venezuela (Pifano, 1954), Brazil (Deane, 1958a and b), Costa Rica (Zeledon & Blanco, 1965), and French Guiana (Floch & Abonnenc, 1948); from raccoon in Panama (Sousa & Johnson, 1973); from sloth in Costa Rica (Zeledon, Ponce & Murillo, 1979); from anteaters in Panama (Walton & Sousa, 1967); and from guinea pigs in Peru (Herrer, 1970).

Apart from the large number of mammals reported naturally infected by *T. rangeli,* there is a long list of others which have been infected experimentally and in which *T. rangeli* has succeeded in establishing an infection. These include mice, rats, hamsters, porcupines, foxes, horses and a bat (Groot & Uribe, 1951; Grewal, 1956; Pifano, 1954; D'Alessandro, 1968 and 1976; Paredes & Paredes, 1949; Hernandez, 1979).

Regarding the invertebrate hosts of *T. rangeli,* natural infections have been reported in *Rhodnius prolixus, R. pallescens, R. brethesi, R. ecuadoriensis, R. robustus, R. pictipes, Triatoma dimidiata capitata, T. infestans, T. maculata, Panstrongylus megistus* and *Eratyrus mucronatus* and are found in most of the countries in Central and South America (Tejera, 1920; Uribe, 1929; De Leon, 1965; Pañalver et al, 1965; Zeledon, 1956; Sousa, 1966; D'Alessandro, Barreto & Duarte, 1971; Herrer, 1964; Carcavallo et al, 1975; Marinkelle, 1968; Canese et al, 1963; Cuba et al, 1972).

From the foregoing it is observed that *T. rangeli* has a wide vertebrate and invertebrate host range. This includes 8 species of mammals naturally infected, 7 species of vertebrate hosts used in experimental studies and 11 species of Triatomine bugs reported as being susceptible to *T. rangeli* infections, both under natural and experimental conditions. This host range observed in *T. rangeli* is only comparable to that showed by *T. cruzi*. This fact establishes a remarkable difference between *T. rangeli* and the other species of the subgenus *Herpetosoma*, which are, in general, parasites very restricted to their vertebrate and invertebrate hosts.

II - LIFE CYCLE OF *T. RANGELI*

In the Invertebrate Host

The entire invertebrate cycle of mammalian trypanosomes with cyclic development in the vector is confined to the alimentary canal, with the production of metatrypasomes in the hind gut or posterior station, as in Stercoraria (Hoare, 1964), or it involves migration of the flagellates from the gut to the salivary medium of the anterior station (proboscis and/or salivary glands). Here the development is completed with the formation of metatrypanosomes, as in Salivaria (Hoare, 1972).

According to Hoare (1968), "most observers are convinced that the development of *T. rangeli* in the anterior station, involving transmission by the inoculative method, is the only essential part of its invertebrate cycle. On the other hand, the intestinal phase and the contaminative transmission have been considered of little importance. Nevertheless, there are a number of controversial data concerning this dual cycle that should be put in correct perspective, since the development of *T. rangeli* in its invertebrate host has a direct bearing on its systematic position".

After being ingested from the mammalian host by the triatomine vector, *T. rangeli* always succeeds in establishing an infection in the alimentary tract of the bugs. The ingested blood-forms undergo a sequential transformation and division, terminating with the production of large number of epimastigotes and long trypomastigotes (Añez, 1981a). Metacyclic forms are not produced in digestive tract of triatomine bugs infected with *T. rangeli* (Tobie, 1964; Añez, 1981a) unlike other members of the Stercoraria group, e.g. in *T. lewisi* of the subgenus *Herpetosoma*, in *T. cruzi* of the subgenus *Schizotrypanum* and in *T. theileri* of the subgenus *Megatrypanum*. In addition to this cycle in the bug's gut, *T. rangeli* may penetrate the gut wall to invade the haemocoele of the infected bugs. The invasion of the haemolymph can occur at different times after infection. In some cases it has been observed as early as 24 hours after the infective meal, even before the establishment of the intestinal infection (Añez, 1980).

Once in the haemolymph the flagellates succeed in multiplying both extracellularly and within the haemocytes, producing huge numbers of epimastigotes and trypomastigotes. In advanced infections, constant divisions and transformations produce large numbers of metacyclic forms in the haemolymph. These are the product of both the extra-and intracellular development of *T. rangeli* in the body cavity of its triatomine vector (Cuba, 1975; Añez, 1981a).

Shortly after the invasion of the haemolymph, the salivary glands are actively penetrated by flagellates. Salivary gland invasion by *T. rangeli* occurs when a well established haemocoelomic infection is produced in the bugs. Thus it is possible to observe parasites in the glands 3-5 days after the invasion of the haemolymph. Infected salivary glands have been reported as early as 6-7 days after invasion of the heamolymph (Añez, 1980; Ellis, Evans & Stanford, 1980). Once in the glands the products of the constant multiplication and transformation of *T. rangeli* are the enormous numbers of metacyclic trypanosomes, which constitute the infective forms to the vertebrate host.

The foregoing points suggest that a primary characteristic of *T. rangeli* is its establishment and multiplication in the haemolymph and salivary glands, rather than in the gut of its vector. This indicates that *T. rangeli* is a species adapted to develop in the anterior station of its triatomine-vector.

In the Vertebrate Host

Añez (1981b) reported that the majority of the infective forms of *T. rangeli*, including metacyclic, rounded and dividing forms, are deposited by infected bugs in the host tissue while probing for a blood vessel. He also observed that the metacyclic forms of *T. rangeli* move rapidly from the site of deposition to the blood stream and are responsible for the early increase of the parasitaemia. Rounded and dividing forms, deposited in the tissues by the bug, complete their transformation into metacyclics or even into blood form-like trypanosomes, which then penetrate the blood stream. Once in the blood of the vertebrate *T. rangeli* undergoes a continous process of growth until 72 hours later. The parasites then remain unchanged in the blood until their complete disappearance from the circulation.

T. rangeli does not divide in the vertebrate host (Herbig-Sandreuter, 1957; Añez, 1981b). Although transformation is observed in the site of deposition, no evidence of division has been observed either at this site or in sectioned organs including kidney, spleen, liver, brain, heart, bone marrow and lymphatic nodule (Herbig-Sandreuter, 1957; Añez, 1981a).

Contrary to what is found in other species of the subgenus *Herpetosoma*, Añez (1981a) observed no signs of division of *T. rangeli* in infected mice examined from 5 minutes to 10 days after the infective bite.

The life cycle of *T. rangeli* in the vertebrate host shows remarkable differences with that of *T. lewisi*, the type species of the subgenus *Herpetosoma*. Indeed, while *T. rangeli* does not divide in the vertebrate host, where it produces an "occult" or low grade parasitaemia, *T. lewisi* divides in the blood stream as well as in the vasa recta of the kidney of rat (Ormerod & Killick-Kendrick, 1956), producing a high level of parasitaemia easily observed in fresh blood samples from infected animals.

III - PATHOGENICITY OF *T. RANGELI* TO TRIATOMINE BUGS

The pathogenicity of *T. rangeli* for triatomine bugs was first reported by Grewal (1957), who observed that nymphs of *R. prolixus* with a heavy infection in the haemolymph showed a higher mortality than those with lighter infections. These observations were later confirmed by Tobie (1965), Gomez (1967), Watkins (1971) and Añez (1981a), who demonstrated that the invasion of the parasite into most tissues of infected bugs produces severe damage which constitutes a prime cause of mortality.

During the process of development, Añez (1981a), reported 39% mortality in *R. prolixus* infected with *T. rangeli*, while the uninfected controls showed only a 5% mortality during the same period and under the same conditions. This indicates that the infection by *T. rangeli* was responsible for the reduction in survival to 61%. Añez's results agreed well with those observed by Tobie (1965), who reported that in infected bugs survival decreases to 62% compared to 84% for the uninfected control.

The pathogenecity of *T. rangeli* to its invertebrate host establishes a remarkable difference between this parasite and others of the subgenus *Herpetosoma*, supporting the idea that taxonomic position of *T. rangeli* must be reconsidered.

IV - DISCUSSION

The large differences existing between *T. rangeli* and the trypanosomes of the subgenus *Herpetosoma* (i. e. *T. lewisi*) include the behaviour in the invertebrate hosts, the wide host range of *T. rangeli* and the strict stenoxeny of the *Herpetosoma* trypanosomes, as well as the differences observed in the life cycle both in the invertebrate and vertebrate hosts. These differences force the conclusion that *T. rangeli* has been maintained for a long time in a mistaken taxonomic position. The only characteristcs that link *T. rangeli* with the type-species of subgenus *Herpetosoma* are the morphology of the blood forms and their easy growth in culture media. These features do not seem to be more important than the biological ones observed during the study of the behaviour of *T. rangeli* in its vertebrate and invertebrate hosts.

Experimental studies carried out by Añez (1981a), using two fresh isolates of *T. rangeli*, two species of triatomine bugs, opossum and laboratory mice revealed morphological and biological differences between *T. rangeli* and the trypanosomes of the subgenus *Herpetosoma.* Some of the differences observed by this author are considered here to throw some light on the controversial systematic position of *T. rangeli.*

1. Metacyclic forms are not produced by *T. rangeli* in the digestive tract of triatomine bugs at any time, and transmission by the contaminative method must be considered atypical. This fact makes *T. rangeli* different from the Stercoraria trypanosomes, in which the major characteristic is the completion of the life cycle in the posterior station of the invertebrate host. The same conclusion was arrived at by Tobie (1964) who considered that the forms of *T. rangeli* in the faecal material of infected bugs were not metacyclic and therefore not infective, and the transmission to a vertebrate can only be via the anterior station, from the bite of an infected vector.

2. The intestine of triatomine bugs acts as a reservoir of parasites, constantly producing flagellates for the invasion of the haemolymph and subsequently the salivary glands, followed by the completion of the life cycle of *T. rangeli* and the production of the infective metacyclic forms. This fact constitutes a particular characteristic in the life cycle of *T. rangeli* in its vector in nature. Apart from the suspected development of *T. cruzi* in the haemolymph of infected bugs reported in South America (Chagas, 1909; Lacombe, 1980) and the experimental infections obtained by Mshelbwala (1972) and Otieno (1973; 1976) in the haemolymph of tsetse flies infected with *T. (T.) brucei,* no other trypanosome appears to complete its life cycle as *T. rangeli* does.

3. The rapid invasion by *T. rangeli* of the haemolymph in triatomine bugs from 24 hours after the infective meal (Añez, 1980), followed by the successful multiplication of the parasite in this medium, suggests that *T. rangeli* is a species fully adapted to develop in the anterior station of the triatomine vector.

4. The invasion by *T. rangeli* of the salivary glands of infected bugs is an active process of penetration by the flagellates from the haemolymph, which cross the outer membrane of the gland anterior end first, as demonstrated with the scanning electron microscope (Añez, 1981a). This fact has also been demonstrated by Ellis, Evans & Stanford, (1980) using transmission electron microscopy, indicating that *T. rangeli* has a manner of reaching the salivary glands of the vector different from that shown by salivarian trypanosomes.

5. The capacity of local strains of *T. rangeli* to invade the salivary glands of their vectors (16-28%), is independent of the conditions of the infections. Thus, the results obtained under experimental conditions using a Vezezuelan strain of *T. rangeli* to infect *R. prolixus* and *R. robustus* (Añez, 1981a) were about the same as those reported by Rossell, Mogollon & Pacheco (1977) working in the same area where this strain was isolated.

6. *T. rangeli* is pathogenic to its invertebrate host. When triatomine bugs are infected experimentally, the survival of the bugs decreases significantly if compared with uninfected controls. This fact has been reported repeatedly and discussed by many authors (Grewal, 1956; Tobie, 1961; Gomez, 1967; D'Alessandro, 1976). This unusual characteristic of *T. rangeli* has not been observed in other groups of trypanosomes.

7. Triatomine bugs heavily infected with *T. rangeli* probe significantly more frequently and for longer periods than uninfected bugs (Añez, 1981c). The frequent probing by infected bugs increases the chance of transmission of *T. rangeli* to mammalian hosts, and infection can be produced by probing bugs without taking any blood. This modification of the feeding behaviour in *T. rangeli* infected bugs may provide the parasite with biological and evolutionary advantages. It should be noted that this particular effect of the parasite on the vector has been reported for the kinetoplastid parasites of mammals whose transmision is produced by the inoculative method. This includes *Leishmania* parasites (Killick-Kendrick et al, 1977), salivarian trypanosomes (Molyneux, Lavin & Elce, 1979) and *T. rangeli* (Añez, 1981c).

8. Unlike trypanosomes of the subgenus *Herpetosoma, T. rangeli* does not divide in its vertebrate host and only a growth in size of the parasites which reach the blood stream is observerd (Añez, 1981b).

These conclusions added to the well known facts that: i) *T. rangeli* does not share the strict stenoxeny observed in the subgenus *Herpatosoma* species, having a wide natural vertebrate, host-range, including Marsupialia, Edentata, Rodentia, Carnivora and Primates, ii) *T. rangeli* is harmless to its vertebrate hosts and harmful to its vectors, establishing contraditions between the general characteristics considered for the subgenus and those observed in this species.

The evidence given above suggests the necessity of separating *T. rangeli* from the subgenus *Herpetosoma*, where it has been maintained solely by its morphological similarities with trypanosomes of this taxonomic group. The creation of a new subgenus with its own characteristics, in which *T. rangeli* would be the type species and *T. rangeli*-like trypanosomes the other componentes of this group, is thus required. This belief is supported by the opinion of Tobie (1961, 1964), who suggested that either *R. prolixus* is not the natural vector of *T. rangeli*, or that trypanosomes attributed to this species actually belong to several species. Also, D'Alessandro (1976) stated that, because of its known behavioural variations, *T. rangeli* can be considered as a biological complex of species with a wide distribution both in vertebrate and invertebrate hosts and that this group of trypanosomes could constitute an evolutionary link between Stercoraria and Salivaria.

V - SYSTEMATIC POSITION OF *T. RANGELI*

Hoare (1967) stated that the transition of *T. rangeli* from the primitive stercorarian pattern of development to the more specialized salivarian pattern is taking place under our eyes. He also considered that the classification of *T. rangeli* is complicated by the fact that its development in the vector and the method of its transmission have features of both Stercoraria and Salivaria. However, in the light of the criteria considered in the present paper, the author considers that *T. rangeli* must be removed from the section Stercoraria to the Salivaria because this parasite does not fulfill the characteristics of behaviour in the vertebrate and invertebrate hosts established for the trypanosomes belonging to the Stercoraria group.

At the present time, the author also believes that *T. rangeli* has sufficient unique characters to be considered as belonging to an independent taxonomic group (i.e. subgenus). Therefore, it is proposed to create a new subgenus which would include *T. rangeli* and similar parasites of mammals and Reduviid-bugs, so far called *T. rangeli*-like trypanosomes.

The classifying features of the proposed new subgenus are as follows: "Trypanosomes of medium size and small kinetoplast with no reproduction in the mammalian host, where the trypanosomes produce low or "occult" infections. Reproduction and development in the vector (Reduviid-triatomine) take place in the midgut, haemolymph and salivary glands with production of metatrypanosomes in the last two regions. Homogeneous assemblage of morphologically indistinguishable species". It is proposed that this new subgenus be named *Tejeraia* in honour of the great Venezuelan parasitologist Dr. Enrique Tejera, who discovered *Trypanosoma rangeli* and made important contributions to the neotropical parasitology. The full name thus being:

Type species: *Trypanosoma (Tejeraia) rangeli* Tejera, 1920.

In the light of the criteria considered above the taxonomic status and nomenclature of *T. rangeli* can be defined as follows:

Order: Kinetoplastida Honiberg & Balamuth, 1963.
Family: Trypanosomatidae Doflein, 1901
Genus: *Trypanosoma* Gruby, 1843.
Subgenus: *Tejeraia* New Subgenus.
Species: *Trypanosoma (Tejeraia) rangeli* Tejera, 1920.

RESUMO

Reconsidera-se a posição sistemática do *Trypanosoma rangeli* e se propõe a criação de um novo subgênero, *Tejeraia*, com a remoção deste tripanosoma do subgênero *Herpetosoma* da Seção Stercorária a sua transferência para a Seção Salivária

As evidências que apóiam esta proposição são discutidas no texto.

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