**Trypanosoma vivax - out of Africa**

**Tudor W. Jones and Alberto M.R. Dávila**

*Trypanosoma vivax* is a blood parasite of ruminants that was introduced into Latin America in cattle imported from Africa, possibly in the late 19th century. The parasite has now spread to ten of the 13 countries of the South American continent, often resulting in a severe wasting disease and death. Here, we review the current state of knowledge about this parasite and the problems faced by animal health agencies in controlling the disease.

Of the three main species of tsetse-transmitted trypanosomes affecting ruminants in sub-Saharan Africa, only *Trypanosoma vivax* has spread beyond the bounds imposed by its vector in Africa and established itself in South America. It is impossible to place an exact date on its introduction as there are records of cattle being imported into South America from Africa in support of European colonization since 1545 (Ref. 1). Although morphometric studies, DNA fingerprinting and isoenzyme profiling suggest a West African origin for New World *T. vivax*, it differs from African *T. vivax* in the diversity of its surface antigens, and its inability to infect tsetse and grow in vitro.

**History of T. vivax in South America**

First described in oxen suffering from an emaciating disease in French Guiana, *T. vivax* was subsequently identified in the blood of cattle in French Guiana (1919), Venezuela (1920), Guadeloupe (1926), Martinique (1929), Colombia (1931), Surinam (1938), Panama (1941), Guyana (1952) and Brazil (1972); and detected through antibodies to *T. vivax* in cattle from El Salvador (1977), Costa Rica (1977), Ecuador (1977), Peru (1977), Paraguay (1977) (reviewed in Ref. 7) and, most recently, the lowlands of Brazil (1997) and Bolivia (Fig. 1). It is impossible to tell, however, whether these reports represent spread from the initial introduction or the detection of existing infections that had been previously unreported, overlooked and/or confused with other diseases. Nevertheless, the recent reports from the Pantanal area of Brazil are likely to be linked to the accelerated construction of roads in the interior of Brazil in the early 1990s; these probably provided a conduit for the introduction of infected animals from the north into this important cattle-rearing area. There were outbreaks of severe disease in the Pantanal area ascribed to *T. vivax*, characterized by emaciation, abortion and death. Increased cattle trading between the Pantanal area of Brazil and neighbouring Bolivia, again attributed to better road communications and also to decreased cattle prices in Brazil, resulted in the introduction of the parasite into Bolivia, with subsequent severe disease and up to 40% mortality. Current estimates indicate that more than 11 million head of cattle with a value of more than US$ 3 billion are at risk from *T. vivax* infection in the Brazilian Pantanal and Bolivian lowlands, with potential losses in excess of US$ 160 million.

**Transmission of T. vivax**

The unregulated movement of infected animals across national and international borders is probably the principal way that the parasite spreads to new areas. Once introduced into an area, however, the method of subsequent transmission is not clear. Non-cyclical or mechanical transmission by blood-feeding flies, such as tabanids or stable flies (*Stomoxys spp*), is usually cited as the principal method of transmission. It has been shown that New World *T. vivax* can be transmitted by several biting fly species in the Pantanal and Bolivian lowlands, with potential losses in excess of US$ 160 million.

http://parasites.trends.com 1471-4222/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved. PI: S0169-4758(00)01777-4
where tsetse have been eliminated. Ticks have also been cited as potential vectors of T. vivax, but this is unsubstantiated. Perinatal transmission of T. vivax has also been demonstrated, but it is likely that iatrogenic transmission via needles and instruments makes an important, but largely unrecognized contribution to local propagation during vaccination and mass treatment regimens. Therefore, in the light of uncertainties about the way that New World T. vivax is transmitted, consideration continues to be given to the possible existence of cyclical transmission by one or more vector species, whose distribution is limited by environmental factors that might explain the distribution of T. vivax in South America.

Diagnosis of T. vivax infection
The earliest reports of T. vivax in the New World were based on the detection of the parasite in blood films, but the typically sporadic parasitaemia associated with trypanosome infection limits the usefulness and sensitivity of such simple diagnostic methods. To improve diagnosis, a range of indirect, serologically based methods has been developed, although most of these also have their own limitations. Most of these indirect methods are based on the detection of parasite-specific antibodies, but recently, methods have been developed to detect parasite components such as proteins or DNA. Most of the technologies used for studies on South American T. vivax have been adapted from those developed for African trypanosomes. The serological diagnosis of T. vivax in South America is complicated by the need to differentiate between infections with the two other trypanosomes infecting cattle - T. evansi and T. theileri - which have components in common with T. vivax, and can give rise to false positive results.

The indirect fluorescent antibody staining technique was the first serological method applied to the study of cattle trypanosomiasis in South America and results confirmed the extensive distribution of T. vivax in South America. More recently, antibody-trapping, enzyme-linked immunosorbent assays (ELISAs) using soluble extracts of an African strain of T. vivax as antigen have been used in studies on the distribution and epidemiology of T. vivax infection in the Caribbean and French Guiana. Attempts to overcome the limitations imposed by antibody detection assays in Africa, in particular the persistence of antibody after treatment, led to the development of monoclonal antibody-based, antigen-capture ELISA (antigen-ELISA). Three antigen-capture assays provided by the International Livestock Research Institute (ILRI), Kenya were evaluated in cattle in French Guiana, but these gave disappointing results, with unacceptably low sensitivity when compared with parasitological methods and antibody-ELISA. Current opinion is that further efforts to improve trypanosome diagnosis should concentrate on standardizing antibody detection assays – possibly designing assays for particular needs such as surveys and monitoring.

Similarities in DNA sequences between South American and African T. vivax stimulated the application of DNA detection assays, such as PCR assays, to try to overcome some of the problems associated with parasitological and serological techniques. A PCR assay using primer pairs designed for African T. vivax was evaluated in French Guiana and found to have a detection limit of one trypanosome per millilitre of blood, but the threshold sensitivity was dependent on sample preparation. Currently, most DNA-based assays are technically very demanding and unsuitable for routine use in many basic veterinary diagnostic laboratories in South America. However, because of difficulties in expanding New World T. vivax populations in vitro and in vivo, DNA technologies such as PCR are likely to be the most appropriate methods for examining the genetic diversity of field isolates of T. vivax.

Control of T. vivax
Currently, little attempt is made to control the spread of the parasite in South America by restricting animal movements from infected areas. The absence of a clearly defined vector makes it practically impossible to incorporate targeted vector reduction methods for control of South American T. vivax in the way that they have been used in Africa for tsetse-transmitted trypanosomes. Consequently, the control of New World T. vivax relies heavily on drug therapy, principally based on diminazene aceturate, with isometamidium used in some areas. In many South

http://parasites.trends.com
American countries, however, antitrypanosome drugs are freely available, with farmers treating animals if they suspect infection with trypanosomases based on criteria such as poor weight gain or reduced milk yield. Such an indiscriminate use of drugs is thought to be a major factor in encouraging the appearance of drug-resistant populations, and resistance to diminazene aceturate has been reported in Colombia28 and French Guiana29. Furthermore, unrestricted animal movements are likely to add to the problem by spreading resistant populations. As with other trypanosomases, T. vivax undergoes antigenic variation during the course of infection30,31, which acts as a major constraint on vaccine development. However, evidence suggests that antigenic diversity between strains of T. vivax in South America is more limited than in Africa9, and this could lead to the establishment of endemic stability over time, characterized by high infection rates but low disease rates. Identifying the factors that lead to the maintenance of such stability might help in developing new control regimens that are less dependent on the use of drugs.

Prospects for T. vivax in South America
Trypanosoma vivax in the New World is an example of a pathogen that has spread beyond its original distribution range though human intervention – both in spanning the thousands of miles between Africa and South America and in propagating itself on arrival. To date, intensive research on New World T. vivax has been limited to a few endemic areas, and there is a need to expand these studies to the entire distribution range in South America to see whether common strategies can be developed or lessons learned from different endemic situations. Future research needs to identify polymorphic markers for New World T. vivax that can be linked to subpopulations with epidemiologically important features such as pathogenicity and drug resistance. The vast distances between many research centres have often limited contacts between research groups in South America, but recently established networks such as TRYNET32 and TRYPLINK33 will have important roles to play in promoting cooperation between researchers, extension staff and livestock owners across South America.

Acknowledgements
TWJ was supported by the Animal Health Programme, Defra for International Development, London, UK. AMRO is currently supported by Instituto Oswaldo Cruz, Brasil and previously by Empresa Brasileira de Pesquisa Agropecuária (EMBRAPA), Brasil.

References

http://parasites.trends.com