

The O.I.E. Ad Hoc Group On Non Tsetse Transmitted Animal Trypanosomoses (NTTAT) With Special Reference To *T. evansi* Infection

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ABSTRACT

Before being designated in 1991 by the OIE administrative Commission as an "ad hoc Group on NTTAT" the Group devoted its activities since 1983 to the following specific aims: (i) economic impact of *T. evansi* infections; (ii) development of diagnostic tests; (iii) studies in variation in pathogenicity of isolates of *T. evansi*; (iv) variation in sensitivity of trypanocidal drugs; (v) exchange of strains between laboratories; (vi) setting up of new means for controlling *T. evansi* infections. After several years (1983-1991) the following achievements were reached: (i) collection of many epidemiological data from Africa, Asia and South America; (ii) free distribution of diagnostic kits for testing in the field and appreciation of results obtained; (iii) greater interest in the study of this infection worldwide mainly in the camel and buffalo breeding; (iv) synthesis of two new trypanocidal drugs followed by the development and marketing of one of them (melarsomine) devoted to the treatment of Surra in camels.

In 1991 the scope of the Group was extended to the other NTTAT, mainly to *T. vivax* and *T. equiperdum* infections due to the persistence of *T. vivax* in tsetse depopulated areas and in some zones of South America and to the difficulty to differentiate *T. evansi* and *T. equiperdum* infections by diagnostic means currently in use.

The 1st International Seminar on NTTAT was held in Annecy France, 14-16 October 1992 with participation of research workers from 22 countries (Africa, Asia, Europe, South America). Conclusions and Recommendations were published in *Rev. Sci. Techn. OIE*, 1993, 12: 273-281.

The ad hoc Group continues to focus its attention to the problem of Surra in camels (in Africa a coordinating project is being developed in West and East Africa) to control the disease and to the immunosuppression of other animal species unapparently or chronically *T. evansi* infected.

ORIGIN

After the great interest which followed the discovery by G. EVANS of *T. evansi*, in 1880, in infected camels and equids in the Dara Ismail Khan district of the Punjab numerous research works were conducted on *T. evansi* infection at the end of the 19th century and on the beginning of the 20th century in several animal species, mainly in equids, camels and buffaloes in India, Burma, Malaysia, South Annam, Java and Sumatra, the Philippines, Turkestan... Then, it appeared that the incidence of the disease decreased probably due to changes in agricultural practices and methods of transport which could have reduced the numbers of more susceptible animals such camels and horses and due to discrete clinical symptoms in other animal species like cattle and buffaloes. But sudden outbreaks at the corner of sixties and seventies in Indonesia (Java) where several thousands animals died; in

the 70's in Central Asia, in Kazakhstan where thousands of bactrian camels (*Camelus bactrianus*) were affected by *T. evansi* and difficult to cure by suramin as the strains were suramin resistant at a high level; outbreaks at the end of the 70's in Vietnam in buffaloes where approximately 20,000 animals died annually in the years 1978-80 out of a population of 650,000 drew again the attention to this peculiar trypanosomosis.

However, the information concerning *T. evansi* infection was always scattered and not regularly disseminated. Attention was already drawn to this point at the 17th meeting of the International Scientific Council for Trypanosomosis Research and Control (ISCTRC) in Arusha, Tanzania, 1981 where some laboratory and field trials on *T. evansi* were recorded from Africa and Asia with the suggestion: "...that exchanges be made between specialists of various countries under the supervision of International Organization". This suggestion was evoked and accepted on the occasion of an informal meeting during the 4th International Conference of Institutes of Tropical Veterinary Medicine in Kissimee, USA, 8th-12th May 1983.

THE O. I. E. WORKING GROUP ON *T. EVANSI* INFECTIONS

To improve the situation recorded above a working group on *T. evansi* has been set up at the OIE Headquarters with the agreement: of the Director General, OIE on 26th May 1983 within the framework of the OIE Norms Commission; of the Director of the Animal Production and Health Division of the FAO, in consultation with the Chief of the Trypanosomosis Unit of WHO. The participants in the funding meeting represented: Ethiopia, Germany, Indonesia, Senegal, Sudan, and the following International Organizations or Institutions' FAO, ILRAD, CIRAD/EMVT, CEBV, OIE. They propose:

- (i) To study the pathological and economic impact of *T. evansi* infections worldwide as they are poorly evaluated;
- (ii) To develop and standardize diagnostics that are sensitive, reliable and easily applied in the field to provide more accurate information to Veterinary Services and to make easier the reporting service;
- (iii) To determine the extent of variations in pathogenicity of isolates of *T. evansi* from different geographical locations and different host species;
- (iv) To determine the variations in sensitivity of trypanocidal drugs in susceptible host species of different countries, particularly with reference to the testing of new compounds;
- (v) To standardize the storage of isolates of *T. evansi* in the laboratory and to encourage the exchange of material between laboratories;
- (vi) To study the pathogenesis of disease caused by *T. evansi*.
- (vii) To meet at every opportunity e.g. during international meetings dealing with related matters of interest waiting for the organisation of a special meeting or seminar.

In accordance with these objectives members of the Group met:

- 16 times at the OIE General Sessions in Paris, France between 1983 and 1998;
- Three times at ISOTRC meetings of OAU/IBAR held in Harare, Zimbabwe in 1985; Lome, Togo in 1987; Monbasa, Kenya in 1989;
- Once at the 5th International Conference of Institutes of Tropical Veterinary Medicine in Kuala Lumpur, Malaysia in 1986.

MAIN FACTS RESULTING FROM THE ACTIVITIES OF THE OIE WORKING GROUP ON *T. EVANSI* INFECTIONS

A number of laboratories and investigation centres developed research work in agreement with the aims enumerated above e.g.:

- Genetic, biomolecular and immunological studies of several strains of various origins in Europe, in Asia, in Africa and in South America.
- Collection of many epidemiological data which allow to expand the distribution of *T. evansi* in Asia, Africa, South America.
- Setting up of several banks of *T. evansi* isolates in Africa, Asia, Europe.
- Free distribution to research workers of infected countries of diagnostic kits for detecting *T. evansi* thanks to the participation and the kindness of the Institute of Tropical Medicine in Antwerp, the Institute of Molecular Biology of the Free University, Brussel, Belgium; CTVM, Edinburgh, UK; ILRAD (now ILRI) and Brentec Lab., Nairobi, Kenya. –Techniques employed: direct microscopy by using a detergent; slide agglutination test; enzyme linked immunosorbent assay (ELISA) for antibodies or antigens; card agglutination test for trypanosomosis (CATT) with a cold probe.
- Greater interest in the study of *T. evansi* infections by many countries either in relationship to camel breeding (e.g. Mautan, Tunisia) or in relationship to other animal species e.g. buffaloes, cattle, goats, pigs, horses (India, P.R. China, Indonesia, Vietnam, Thailand, Brazil, Argentina, Venezuela).
- Research, synthesis, development and marketing of the first new effective trypanocidal drug since more than thirty years: melarsomine, registered as CYMELARSAN, active against *T. evansi* and other members of the sub-genus *Trypanozoon* recommended for use in camels and still in development in other animal species. – Synthesis and laboratory trials of another active molecule at the Free University Brussel but not marketed due to the high cost of the development and registration.
- Exchange of information with the International Commission of the Zoological Nomenclature, with the World Association for Advancement of Veterinary Parasitology and the World Federation of Parasitologists.

APPOINTMENT OF THE OIE AD HOC GROUP ON NTTAT

Considering the work carried out by the *T. evansi* working Group and its various achievements the OIE Administrative Commission decided, at its meeting of February 1991, to extend the scope of this working Group to all non tsetse transmitted animal trypanosomoses (NTTAT) worldwide. Designated as an ad hoc expert Group, the NTTAT ad hoc Group is now attached to the “OIE Foot-and-Mouth Disease and other Epizootics Commission”. – The aim of the Group is to study the problems related to the non-cyclically transmitted trypanosomoses in animals.

The terms of reference of this Group which will meet once a year in May during the OIE General Session are:

- to study, discuss and inform OIE Member Countries of the following points:
 - the pathological and economic impact of NTTAT in Africa, Asia and America;
 - the possible interference of NTTAT with other diseases and immune responses to vaccinations for other diseases [e.g. FMD and Haemorrhagic septicaemia (HS)];
 - the reliability of diagnostic tests, the cost involved and the ease with which trypanosomes may be differentiated from each other (e.g. *T. evansi* / *T. brucei*; *T.*

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evansi / *T. equiperdum*; *T. evansi* / *T. vivax*....)

- the similarities and differences between strains, isolates and stabilates of various origins, so that possible differences in their genetics, immunological and biochemical characteristics may be determined.
- The problem of chemoresistance to trypanocidal drugs;
- The current research into new drugs and drug evaluation;
- New means for the control of NTTAT.

The work of the Group will be conducted in close cooperation with other bodies which are working in related fields:

- the ISCTRC of the OAU/IBAR,
- the FAO trypanosomosis unit and the joint FAO/IAEA division;
- the WHO Tropical Disease Division (Steering committee on chemotherapy, immunology and pathology of African trypanosomosis and Leishmaniosis).

After each annual meeting of the ad hoc Group in Paris, a draft report is compiled by the Secretary as well as the minutes then sent to each participant for corrections, alterations and/or amendments before publication in the official set of documents of the following OIE General Session in the three official languages of the OIE: English, French and Spanish.

ACTIVITIES CARRIED OUT BY THE AD HOC GROUP

Keeping the spirit of its promoters the Group always tried to meet interested and qualified individuals working from the basic research to the applications of control measures in the field. In this way many contacts were or are being developed for the exchange of ideas and experience. It resulted many publications either directly in specialised journals or on the occasion of several international meetings.

A few months after its inception the Group prepared and held the *First International Seminar on NTTAT* in Annecy, France, 14th-16th October 1992 with the representatives of 22 countries of Africa, Asia and South America and the presentation of 80 papers or posters. Conclusions and Recommendations of this First Seminar were presented at the end of the sessions and published in the *Rev. sci. techn. Off. Int. Epiz.*, 1993, 12, 273-281. Taking account of the matters which were presented and discussed in the Seminar numerous studies were initiated in several countries:

In Africa, surveys of vectors of *T. vivax* in tsetse depopulated areas where the infection persisted (Cameroon); comparison of several diagnostic methods in *T. evansi* infections of camels (Mali, Mauritania); evaluation of ELISAs assays in the Sudan; comparison of the sensitivity and specificity of AgELISA in *T. vivax* infections of cattle in Africa and South America (French Guiana); tentative trials to isolate new strains of *T. equiperdum* from equids (Namibia, South Africa);

In Asia, comparison of several diagnostic methods in buffaloes and cattle, surveys of *Tabanidae* SPP. In Vietnam, studies on the role of immunosuppression due to *T. evansi* in vaccination campaigns against HS (Vietnam);

In South America, development of research work in the Argentine, Brazil, Colombia, Venezuela, the Plateau of Guyanas (French Guiana, Surinam Guyana) mainly in epidemiological surveys and control of *T. vivax* infections in cattle with the use of trypanocidal drugs (Venezuela).

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On the other hand outbreaks of *T. vivax* infection in cattle and *T. evansi* infection in equids which occurred at the end 1994/beginning 1995 in Pantanal, MS, Brazil and which developed in 1996/97 drew the attention to this zone on the border of 3 countries: Brazil, Paraguay, Bolivia. –Approaches were made with the ad hoc Group by the laboratory of Corumba, Pantanal on the beginning of 1995 who sent a representative to the 19th annual meeting of the ad hoc Group (May 1995). An expert from the KETRI (Kenya Trypanosomosis Research Institute), Kikuyu, Kenya was sent to Brazil to evaluate the situation and to elaborate a report in 1996 about measures to be taken.

Moreover, colleagues of the research investigation centre of Corumba which is depending on the Brazilian agricultural research administration (EMBRAPA/CPAP) organised a “ First World Symposium Meeting on Salivarian Trypanosomes by Internet” in December 1996 which had a great success and opened a site on Internet: TRYPLINK-L. A second Symposium (SWMSTI) followed in March 1998 in which the Secretary of the ad hoc Group gave the introductory lecture. Facts and data collected in these meetings give a current description of the situation in South America in each field of the study of NTTAT. In February/March, 1998 an FAO mission visited Pantanal (Brazil) and the neighbour zones of Paraguay and Bolivia. It concluded, among many of other remarks regarding the need for information on the distribution, seasonality and prevalence of the disease, ...” it is likely that control will rely on a combination of cattle movement control and the strategic use of trypanocidal drugs”.

In liaison with the ad hoc Group, a network on Haemoparasites was set up in Georgetown, Guyana with the objective to study the related diseases and particularly Trypanosomoses in the Guyanas (Guyana, Suriname, French Guiana) with the edition of a quarterly “ Trypnews” giving information about Trypanosomoses in this sub-region thanks to the close cooperation, under the name “ TRYPNET”, of IICA/CIRAD/EMVT/Institute Pasteur Cayenne and in relationship with Venezuela. TRYPNET organised a symposium in November 1996 in Georgetown. A science thesis was presented in September 1997 on : “ Trypanosomoses in livestock in Latin America with special reference to the Guyanas Plateau” (502 references, 402 pages) constituting a reference work for this part of South America.

In Asia the Group keeps its fruitful contacts: with *Indonesia* either directly with the Bogor veterinary laboratory or thanks to the research workers of CTVM, Edinburgh, UK; with *Vietnam* either directly with the veterinary institute, Hanoi or through the research workers of the Vrije Universiteit, Brussel, Belgium; with *Thailand* thanks to the courtesy of the GTZ, Berlin Germany and with *India* directly with research centres or veterinary institutions. The secretary of this Group was invited to give the inaugural lecture to the IX National Congress of Veterinary Parasitology which took place in Ludhiana, India, 6th-8th October 1997. Moreover, regular information are received from the Punjab Agricultural Univaersity; the College of Veterinary and Animal Science, Bikaner; Patani Surgical Hospital, Palanpur; Animal Disease Research Laboratory, National Dairy Development Board, Anand.

The Conferences of the OIE Regional Commissions took the activity of the NTTAT ad hoc Group into consideration in their Recommendations as it was the case for:

- the 3rd Conference of the OIE Regional Commission for the Middle East, Khartoum, Sudan, 18-21 September 1995 “...some diseases such as camel trypanosomosis, it is necessary to work beyond the limits of regional borders to address the problem on a global scale”;

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- the 20th Conference of the OIE Regional Commission for Asia, the Far East and Oceania, New Delhi, India, 25-28 November 1997 which wished to use “rapid and accurate animal disease diagnostic tests”;
- the Seminar on the Control of quality of veterinary drugs, Niamey Niger, 8-12 December 1997 which underlined the need for “the control of quality of veterinary drugs”.

Concerning the means of *NTTAT control* some work was dedicated to the identification of vectors and their control, a basic research work (genetics of trypanosomes, glucose transporters, macrophage role and presence of nitric oxid, TNF, interferon gamma, interleukines) synthesis of new molecules (e.g. tribrizin), improvement of ‘ancient trypanocidal drugs’ with new formulations.

A few positive results were obtained in the practical control of NTTAT in the field. However, modified traps for *Tabanidae* and *Stomoyinae* spp. were described and the treatment by spot-on with remanent insecticides was recognised as helpful at the 24th Meeting of the ISCTRC, Maputo, Mozambique, 29 September-3 October 1997.

New formulations with SRD (Slow release devices) of existing trypanocidal drugs (isometamidium, homidium/ethidium salts) are claimed efficacious and more persistent, as well as diminazene aceturate in combination with another molecule. For human trypanosomosis a topical preparation of melarsoprol was recommended to avoid serious side effects of the melarsoprol injections. Melarsomine (Mel B) was studied in the Spice Island of Zanzibar against human sleeping sickness.

PERSPECTIVES

Created for a better understanding of Non Tsetse Animal Trypanosomoses (NTTAT) this OIE ad hoc Group triggered a lot of studies worldwide since its setting up in 1983. However, many points which were raised on its origin remained unanswered. Among them: the case of the *T. evansi* isolates on camel (*Camelus bactrianus*) in Kazakhstan causing the Su-auru (Surra). Some isolates which are Suramin sensitive are isometamidium resistant but some other strains which are Suramin-resistant are strongly isometamidium sensitive. Such strains (or isolates) could be obtained just a few years ago thanks to spirit of international cooperation of several colleagues of different countries. Their peculiar behavior has to be elucidated

Other problems continue to be under investigation: e.g. evaluation of immunosuppression in unapparent or chronically infected animals before vaccination campaigns; recommended diagnostic methods (sensitive and reliable) according to regional conditions and animal species; differentiation of *T. evansi* / *T. equiperdum* with the preliminary isolation of *T. equiperdum* isolates from the field; deepening of the knowledge in the vectors of NTTAT and ‘relay’ insects in tsetse depopulated territories of Africa where *T. vivax* infection persists at a some extent; surveillance and control of animal trypanosomoses in Latin America.