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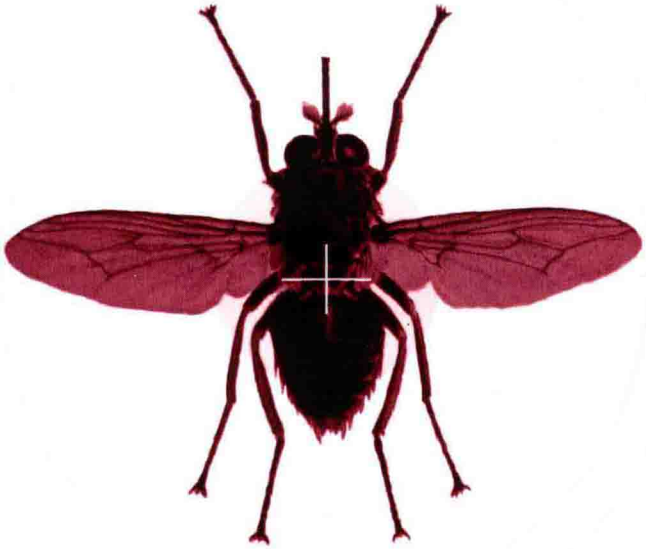
TSETSE AND TRYPANOSOMOSIS INFORMATION



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TSETSE AND TRYPANOSOMOSIS INFORMATION

Numbers 16507-16764

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TSETSE AND TRYPANOSOMOSIS INFORMATION

The Tsetse and Trypanosomosis Information periodical has been established to disseminate current information on all aspects of tsetse and trypanosomosis research and control to institutions and individuals involved in the problems of African trypanosomosis. This service forms an integral part of the Programme Against African Trypanosomosis (PAAT) and is jointly sponsored by the Food and Agriculture Organization (FAO) of the United Nations, the International Atomic Energy Agency (IAEA), the Inter-African Bureau for Animal Resources of the African Union (AU-IBAR), the World Health Organization (WHO), the Research Department for Livestock Production and Veterinary Medicine of the Centre de Coopération Internationale en Recherche Agronomique pour le Développement (CIRAD-EMVT) and the British Government's Department for International Development (DFID).

The half-yearly periodical is prepared for publication, in both English and French editions, by the Food and Agriculture Organization of the United Nations. Each annual volume consists of two parts and an index. Subscription is free for all recipients engaged in trypanosomosis research and control, and requests for enrolment may be sent to: Ms Maria Grazia Solari, AGAH, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy (fax +39 06 5705 5749; e-mail MariaGrazia.Solari@fao.org).

Since the value of this information service depends to a great extent on the receipt of relevant material from research workers, campaign planners and organizers and field workers themselves, readers are requested to submit news items and copies of scientific papers and reports to the Editor: Dr James Dargie, Brunnstubengasse 43, 2102 Bisamberg, Austria (tel. +43 2262 61735; e-mail j.dargie@aon.at).

We regret that we are unable to supply photocopies of the papers quoted in the periodical.

Distribution dates and copy deadlines

	Copy deadline for News items	Distribution (English and French editions)
Part 1	15 April	July/August
Part 2	15 October	January/February

ABBREVIATIONS USED IN TTI

a.i.	active ingredient
ACTH	adrenocorticotrophic hormone
ALAT	alanine aminotransaminase
ASAT	aspartic acid aminotransaminase
b.w.	body weight
BIIT	blood incubation infectivity test
CATT	card agglutination test for trypanosomiasis
CD_{50}	median curative dose
CNS	central nervous system
CSF	cerebrospinal fluid
DNA	deoxyribonucleic acid
ELISA	enzyme linked immunosorbent assay
HAT	human African trypanosomiasis
HCT	haematocrit centrifugation technique
GIS	geographic information system(s)
GPS	global positioning system(s)
i.m.	intramuscular(ly)
i.p.	intraperitoneal(ly)
i.v.	intravenous(ly)
IFAT	indirect fluorescent antibody test
KIVI	kit for *in vitro* isolation of trypanosomes
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
M	molar
mAEC	miniature anion-exchange centrifugation technique
McAb	monoclonal antibody
MW	molecular weight
NARS	National Agricultural Research Services/Systems
p.i.	post-infection
PCR	polymerase chain reaction
PCV	packed cell volume
ppb	parts per billion (10^9)
ppm	parts per million
r.h.	relative humidity
RNA	ribonucleic acid
SIT	sterile insect technique
sp(p).	species (plural)
ssp(p).	subspecies (plural)
UV	ultra-violet
VAT	variable antigen type
VSG	variant surface glycoprotein
WBC	white blood cell

Organizations

ANDE	Agence Nationale de Développement de l'Elevage
AU	African Union
AU/STRC	African Union/Scientific, Technical and Research Commission
BICOT	Biological Control of Tsetse by the Sterile Insect Technique
CEBV	Communauté Economique du Bétail et de la Viande
CEMV	Centre Universitaire de Formation en Entomologie Médicale et Vétérinaire
CGIAR	Consultative Group on International Agricultural Research
CIRAD	Centre de Coopération Internationale en Recherche Agronomique pour le Développement
CIRAD-EMVT	Département d'Elevage et de Médecine Vétérinaire des Pays Tropicaux du CIRAD
CIRDES	Centre International de Recherche-Développement sur l'Elevage en Zone Subhumide
CNERV	Centre National d'Elevage et de Recherches Vétérinaires
CNRS	Centre National de Recherche Scientifique
CREAT	Centre de Recherche et d'Elevage, Avétonou, Togo
CRSSA	Centre de Recherches du Service de Santé des Armées Emile Pardé
CTVM	Centre for Tropical Veterinary Medicine
DFID	Department for International Development (UK)
DNDi	Drugs for Neglected Diseases Initiative
DSE	German Foundation for International Development
EC/EU	European Community/European Union
EDF	European Development Fund
FAO	Food and Agriculture Organization of the United Nations

FITCA	Farming in Tsetse Control Areas of Eastern Africa
GTZ	Deutsche Gesellschaft für Technische Zusammenarbeit
IAEA	International Atomic Energy Agency
IBAR	Interafrican Bureau for Animal Resources
ICIPE	International Centre of Insect Physiology and Ecology
ICPTV	Integrated Control of Pathogenic Trypanosomes and their Vectors
IFAD	International Fund for Agricultural Development
ILRI	International Livestock Research Institute
INRA	Institut National de Recherche Agronomique
IPR	Institut Pierre Richet
IRD	Institut de Recherche et de Développement (formerly ORSTOM)
ISCTRC	International Scientific Council for Trypanosomiasis Research and Control
ISRA	Institut Sénégalais de Recherches Agricoles
ITC	International Trypanotolerance Centre
KARI	Kenya Agricultural Research Institute
KETRI	Kenya Trypanosomiasis Research Institute
LCV	Laboratoire Central Vétérinaire
LNERV	Laboratoire National de l'Elevage et de Recherches Vétérinaires
LSHTM	London School of Hygiene and Tropical Medicine
MRC	Medical Research Council
MRU	Mano River Union
NITR	Nigerian Institute for Trypanosomiasis Research
NRI	Natural Resources Institute
OCCGE	Organisation de Coopération et de Coordination pour la Lutte contre les Grande Endémies
OCEAC	Organisation de Coordination pour la Lutte contre les Endémies en Afrique Centrale
OGAPROV	Office Gabonais pour l'Amélioration de la Production de la Viande
OIE	Office International des Epizooties
OMVG	Organisation pour la Mise en Valeur du Fleuve Gambie
PAAT	Programme against African Trypanosomosis
PATTEC	Pan-African Tsetse and Trypanosomiasis Eradication Campaign
PRCT	Projet de Recherches Cliniques sur la Trypanosomiase
RDI	Rural Development International
RUCA	Rijksuniversitair Centrum Antwerpen
SADC	Southern African Development Community
SIDA	Swedish International Development Authority
SODEPRA	Société pour le Développement des Productions Animales
TDR	UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases
TDRC	Tropical Diseases Research Centre
TPRI	Tropical Pesticides Research Institute
TTRI	Tsetse and Trypanosomiasis Research Institute
UNDP	United Nations Development Programme
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
UTRO	Uganda Trypanosomiasis Research Organisation
WHO	World Health Organization

CONTENTS

SECTION A – NEWS

AFRICAN UNION (AU) - PAN AFRICAN TSETSE AND TRYPANOSOMIASIS ERADICATION CAMPAIGN (PATTEC)

Readers of TTI should note that thanks to the efforts of Dr Hassane Mahamat (Coordinator) and staff of the PATTEC Coordination Office, the amount and timeliness of information on the African Union webpages about activities and developments within PATTEC itself and in individual Member States have been substantially enhanced (see http://pattec.au.int/about). Information now includes:

- An Overview and Organizational Structure of PATTEC;
- Participating Member States;
- Animal and Human Trypanosomiasis;
- Publications (including, for example, about revision of the PATTEC Strategic Framework and Action Plan, PATTEC and Veterinary Governance – A Case of One Health, PATTEC in Gabon and the Campaign in Kinshasa);
- Links to useful contacts e.g. Country Focal Points, International Organizations, Development Partners and Institutions; and
- News and Events.

Included under this last heading is information concerning the many and varied activities undertaken by the Coordination Office and many others in support of the PATTEC Initiative since publication of the previous volume of TTI. These include *inter alia:*

- A meeting to review the feasibility of using the sterile insect technique (SIT) on the islands of Kalangala District, Uganda;
- Launch and first Board Meeting of the Kenya Tsetse and Trypanosomiasis Eradication Council (KENTTEC);
- Visit of HE Mr Abdelaziz Khelef, Director General of the Arab Bank for Economic Development of Africa (BADEA) to the STEP Kality tsetse fly mass rearing facility in Ethiopia. In his presentation of the facility, the DG of STEP and the Director of the Insectory explained that the facility in Kality is the largest in Africa for rearing tsetse flies. It has more than 1.3 million *Glossina fuscipes* and about 150 000 *G. pallidipes* that are being used for SIT release in Southern Ethiopia. Plans are underway with the support of the International Atomic Energy agency (IAEA) to sell SIT flies to needy countries;
- A GIS Training Workshop at the Southern Ethiopia Tsetse Eradication Project's Headquarters in Kality;
- The agreement reached by African Ministers and BADEA to support AUC efforts to implement the PATTEC Initiative at a meeting in Khartoum, Sudan; and
- The direct technical support of Dr Giuliano Cecchi from FAO to the AU-PATTEC Coordination Office, Addis Ababa, Ethiopia.

32ND GENERAL CONFERENCE OF THE INTERNATIONAL SCIENTIFIC COUNCIL FOR TRYPANOSOMIASIS RESEARCH AND CONTROL (ISCTRC)

The International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) is a statutory Council of the African Union Commission with the Secretariat at African Union Interafrican Bureau for Animal resources (AU-IBAR) in Nairobi, Kenya. It was established in the early 1960s as a vehicle to promote international cooperation in the fight against trypanosomiasis which is one of Africa's greatest constraints to socio-economic development, severely affecting human and livestock health, limiting land use, causing poverty and perpetuating underdevelopment on the continent. The Membership of the Council includes Member States, Africa Union Pan African Tsetse and Trypanosomiasis Eradication Campaign (AU-PATTEC), International organizations, including Food and Agriculture Organization (FAO), World Health Organization (WHO), International Atomic Energy Agency (IAEA) and Programme against African Trypanosomiasis (PAAT).

To achieve its objectives, the Council facilitates information sharing and exchange on matters regarding tsetse and trypanosomiasis research and control by holding regular General scientific conferences since 1949. The next General Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) will be held on **8 to 12 September 2013 in Khartoum, Sudan**. The theme of the Conference is "**T&T Research and Control for Sustainable Agriculture and Rural Development: Promoting Partnership and Learning Agenda in the context of African Renaissance".** Its overall objective is be to promote information sharing on tsetse, human and animal trypanosomiasis problem, review control strategies and recommend appropriate approaches in research and control for the next two years. It will be a five-day event with over 300 participants from the 36 T&T affected African countries and international organizations expected to attend with over 100 presentations.

REPORT OF A WHO MEETING ON ELIMINATION OF AFRICAN TRYPANOSOMIASIS (*Trypanosoma brucei gambiense*), 3–5 DECEMBER 2012, GENEVA

Mention was made of this meeting in the previous volume of TTI. Now, the full report of the meeting has been published by WHO and is available at http://apps.who.int/iris/bitstream/10665/79689/1/WHO_HTM_NTD_IDM_2013.4_eng.pdf. After a brief introduction, this comprehensive report (80 pages with many coloured maps, tables and figures) has excellent sections describing, among others, the background to disease elimination, the epidemiological situation and the road to elimination including: the concept of elimination; indicators and milestones; strategies for intervention to reach zero cases in different categories of foci; monitoring, evaluation and validation of elimination; tools available/required (including for screening and diagnosis, treatment, vector control and epidemiology); and issues and challenges. There then follows a set of conclusions which are reproduced here for the benefit of TTI readers:

Conclusions

The participants in the WHO meeting on elimination of human African trypanosomiasis (*Trypanosoma brucei gambiense*) concluded that:

1. Commitment to eliminating the disease as a public-health problem, as agreed at a meeting of countries in which the disease is endemic in Geneva in 2007, should be maintained in response to resolution WHA56.7 of the World Health Assembly of 2003, resolution AFR/RC55/R3 of the 55th WHO Regional Committee for Africa of 2005, and the target of WHO's Roadmap on neglected tropical diseases, which includes elimination of human African trypanosomiasis as a public-health problem by 2020. Nevertheless, elimination of Gambiense trypanosomiasis as a public-health problem by 2020 represents an intermediate objective, which should be followed by the elimination of the disease as defined by the Strategic and Technical Advisory Group for neglected tropical diseases. Thus, the newly adjusted objective for HAT elimination is the absence of transmission resulting in zero cases reported in all foci. Participants estimated the deadline for this new outcome by 2030. Partners should consider this new concept and objective.

2. The geographical unit for elimination is the focus, as defined by a WHO Expert Committee in 1986, whereas the village is the unit for intervention.

3. The parameters for global indicators of elimination are:

a. Number of new cases reported annually
b. Number of foci eliminated.

A threshold of less than 1 new case per 10 000 population in at least 90 percent of HAT foci reporting annually less than 2 000 new cases at continental level was established as the objective of elimination of HAT as a public-health problem by 2020.

The milestones for the two indicators for eliminating HAT as a public-health problem have been considered and accepted as follows:

Indicator/milestone	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of new cases reported annually	6000	5500	5000	4500	4000	3500	3000	2500	< 2000
Number of foci validated as eliminated (reporting less than 1 new case per 10 000 inhabitants)				10%	30%	40%	60%t	80%	>90%

4. The elimination agenda involved:

i. Endorsing in December 2012 the concept of elimination and the milestones agreed by disease endemic countries during a WHO meeting on elimination of Gambiense trypanosomiasis.
ii. Convening a WHO Expert Committee on HAT control and surveillance in 2013.
iii. Creating in 2013 a consultative group of experts to advise WHO annually on the process of eliminating Gambiense trypanosomiasis.

iv. As of 2013, convening annual meetings with current partners to advocate new potential partners.
v. As of 2014, convening biennial meetings with endemic countries to report countries' progress.
vi. As of 2014, preparing biennial updates on the disease's distribution, the populations at risk and the coverage of people at risk as secondary indicators.

5. Strategies for control and surveillance to achieve the elimination objective combine three elements:

i. active case-finding through mobile teams;
ii. passive case-finding involving available health facilities; and
iii. vector control.

The selection and "dosage" of each element must be flexible and dynamic, adapted to the epidemiological situation, and defined according to the intensity of transmission and the characteristics of existing local health services in each focus.
Active case-finding using mobile teams is more important when the intensity of transmission is high, while passive case-finding integrated in health-care facilities should be present in all epidemiological situations, but is more prominent in the low transmission settings. Vector control should be applied according to medical needs.

6. Since elimination is not eradication and the risk of re-establishing transmission exists, continued and adapted actions will be required to sustain zero cases within a focus during and after elimination.

7. Gaps in knowledge have been identified. Operational research is needed to fill these gaps, including among others:

a. improved knowledge of current gaps in geographical distribution;
b. better knowledge of the epidemiological role of animal reservoirs, aparasitemic seropositive individuals and "healthy carriers" in transmitting the disease;
c. current control tools are not the most appropriate for elimination. Continuous research is needed to improve control tools in order to facilitate the engagement of health services in HAT elimination. This research has to include mainly (i) development of improved diagnostic tools and (ii) development of new drugs.

8. Following the meeting's agreement of HAT elimination principles, WHO will elaborate a strategic plan for pilot countries in planning and implementing national elimination strategies.

WORK SUPPORTED BY THE JOINT FAO/IAEA AND IAEA TECHNICAL COOPERATION PROGRAMMES

Activities conducted include: R&D conducted through Coordinated Research Projects (CRPs) as well as at the Insect Pest Control (IPC) Laboratory, Seibersdorf, Austria; support to operational field activities on planning, feasibility assessment and implementing area-wide integrated national and regional tsetse and trypanosomosis control efforts; and assistance to policy and strategy development to Member States in close collaboration with AU, FAO and

WHO making use of the PAAT forum. The IPC sub-Programme publishes a Newsletter each six months, the most recent one being available at http://www-naweb.iaea.org/nafa/ipc/public/IPC-NL-81.pdf, while the IPC laboratory publishes an annual Activity Report. Below is a brief summary of some of the main activities carried out over the past six months concerning T&T. Further information is available by consulting the Newsletter and the website of the Joint FAO/IAEA Division itself (http://www-naweb.iaea.org/nafa/ipc/public/newsletters-ipc.html).

Final Research Coordination Meeting of CRP on Applying Population Genetics and GIS for Managing Livestock Insect Pests. 15-19 April 2013, London, UK

This meeting, hosted by the Natural History Museum (NHM) was attended by 16 scientists from Australia, Brazil, Burkina Faso, Ethiopia, France, Indonesia, Iraq, Israel, Italy, Kenya, UK, USA, and Yemen. Twelve progress report papers on population genetics and geometric morphometrics of new and old world screwworm flies and of tsetse fly species in East and West Africa, as well as new findings to generate geographic information systems (GIS) aided maps illustrating the research findings were presented and reviewed.

A special session focused on a new tutorial DVD on the use of GIS in insect pest control operations. The meeting agreed on a procedure and time frame for publishing the scientific work done and findings generated under the CRP. The RCM participants highly appreciated the opportunity provided by the NHM management to undertake special tours though the NHM's unique and impressive entomology, parasitic worms and molecular collections.

First Research Coordination Meeting of CRP on Enhancing Vector Refractoriness to Trypanosome Infection. 3-7 June 2013, Vienna, Austria

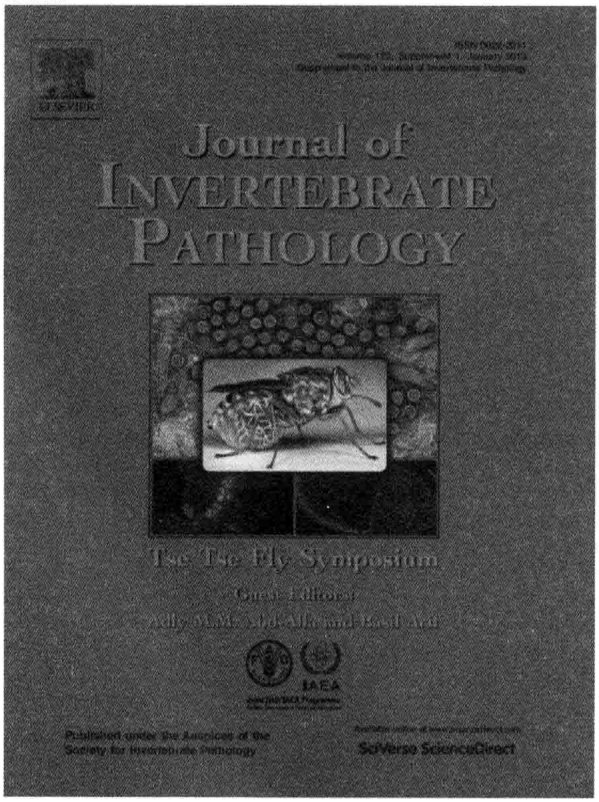
The first RCM of this new CRP was attended by 21 participants from Africa (6), Asia (1), Australia (1) Europe (11), and the USA (2), as well as one consultant and four observers. The first two days of the meeting were devoted to presentations on the ongoing and future research of the participants.

Participants were divided into groups covering two main topics: (i) The symbionts of tsetse including *Sodalis*, *Wolbachia* and *Wigglesworthia*, with the general objective to better understand the relation between the symbionts and tsetse to make them refractory to trypanosome infection by symbiont-based technologies. The specific objectives are to determine the prevalence of *Wolbachia* in field and laboratory populations; the occurrence of cytoplasmic incompatibility; and the localization of the symbionts in tsetse tissues and the impact of different nutritional treatment and irradiation on tsetse microbiota; (ii) the parasites and pathogens of tsetse including the trypanosomes, the salivary gland hypertrophy virus and a pathogenic fungus. The objectives are to determine the virus latency in the asymptomatic state and the reason for an infection switching status from asymptomatic to symptomatic state, the impact of fungal infection on the vector trypanosome transmission and the interaction between virus infection and the prevalence of tsetse microbiota.

The future work plan for each participant was discussed and agreed to and collaborations were established. The topics for training some participants on microbiota detection from natural tsetse species and analysis by *in silico* methods and fluorescence microscopy in a workshop to be held in conjunction with the second RCM were discussed and the timing and location were tentatively set for Addis Ababa, Ethiopia from 1-5 December 2014.

Proceedings of the CRP on Improving SIT for Tsetse Flies through Research on their Symbionts and Pathogens

Sleeping sickness or human African trypanosomosis affects people in approximately 36 countries in sub-Saharan Africa and is caused by *Trypanosoma brucei gambiense* (T.b.g.) or *Trypanosoma brucei rhodesiense* (*T. b. r.*). The former is responsible for about 95 percent of the chronic cases in Central and West Africa, whereas *T. b. r.* causes the acute form of the disease in eastern Africa. The parasites are transmitted by one or more blood-feeding tsetse fly species belonging to the genus *Glossina*. Other *Glossina* transmitted trypanosomes also infect cattle and cause a disease called nagana, a Zulu word meaning "to be depressed". Nagana results in millions of dollars of economic losses to countries that can ill afford such losses.



The management of nagana based on the recurrent treatment of livestock with trypanocidal drugs is costly and not sustainable in view of increasing resistance of the parasites. In attempts to develop more sustainable approaches to the management of the disease in mainland Africa, several Governments adopted the sterile insect technique (SIT). This technique, when integrated with other control tactics, has been previously successful in

eradicating tsetse flies from the Island of Unguja (Zanzibar), United Republic of Tanzania. It relies on limiting the reproductive capacity of the flies by releasing large numbers of reproductively sterilized, colony reared males.

In order to initiate an SIT strategy against *Glossina pallidipes* in Ethiopia, tsetse fly colonies were established in Seibersdorf, Austria and in Addis Ababa, Ethiopia. However, two colonies in Seibersdorf collapsed due to infection by the *Glossina pallidipes* salivary gland hypertrophy virus (GpSGHV). The virus also caused low production and poor stability of the colonies in Ethiopia. The question of how to limit the spread of the virus in the colonies so as to produce sufficient flies for an SIT strategy became paramount.

Approximately seven years ago a CRP entitled "Improving SIT for Tsetse Flies through Research on Their Symbionts and Pathogens" was initiated under the auspices of the Joint FAO/IAEA Division. This FAO/IAEA coordinated research project included 23 scientists from 18 countries representing a broad range of expertise to investigate the problem and to develop solutions. These scientists had expertise in insect viruses and especially in a closely related virus that causes similar symptoms in the common house fly, *Musca domestica* (MdSGHV), as well as in tsetse symbionts, parasites and fungal pathogens.

The individual studies in the CRP involved detailed investigations into the biology of the insect in relation to the causative trypanosomes, parasites, and symbionts, as well as epidemiological investigations of the disease in various parts of Africa and practical procedures to manage the virus that have been transferred to tsetse mass-rearing facilities. The scientists convened at about 18-month intervals to report their findings and to coordinate their research, the last of which was held in Vienna in March 2012, when the CRP was completed.

This special issue of the Journal of Invertebrate Pathology contains the final peer-reviewed research results of the CRP, including an introductory review paper, two invited reviews to provide the background to the project and additionally 17 research articles. Further research, carried out by CRP participants and collaborators during the CRP and published previously, is listed in Table 1 of the introductory paper.

It is our hope that this issue of the Journal of Invertebrate Pathology will provide an extensive treatise on the tsetse fly and its symbionts and pathogens that will inform the insect pathology community about this extremely important problem that continues to affect both humans and cattle in sub-Saharan Africa.

SECTION B – ABSTRACTS

1. GENERAL (INCLUDING LAND USE)

16507. **Alsford, S., Kelly, J. M., Baker, N. & Horn, D., 2013.** Genetic dissection of drug resistance in trypanosomes. *Parasitology*: 1-14. **E Publication ahead of print, April 3.**

London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. [sam.alsford@lshtm.ac.uk].

The trypanosomes cause two neglected tropical diseases, Chagas disease in the Americas and African trypanosomiasis in sub-Saharan Africa. Over recent years a raft of

molecular tools have been developed enabling the genetic dissection of many aspects of trypanosome biology, including the mechanisms underlying resistance to some of the current clinical and veterinary drugs. This has led to the identification and characterization of key resistance determinants, including transporters for the anti-*Trypanosoma brucei* drugs, melarsoprol, pentamidine and eflornithine, and the activator of nifurtimox-benznidazole, the anti-*Trypanosoma cruzi* drugs. More recently, advances in sequencing technology, combined with the development of RNA interference libraries in the clinically relevant bloodstream form of *T. brucei* have led to an exponential increase in the number of proteins known to interact either directly or indirectly with the anti-trypanosomal drugs. In this review, we discuss these findings and the technological developments that are set to further revolutionise our understanding of drug-trypanosome interactions. The new knowledge gained should inform the development of novel interventions against the devastating diseases caused by these parasites.

16508. **Baker, N., de Koning, H. P., Maser, P. & Horn, D., 2013.** Drug resistance in African trypanosomiasis: the melarsoprol and pentamidine story. *Trends in Parasitology*, **29** (3): 110-118.

London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. [david.horn@lshtm.ac.uk].

Melarsoprol and pentamidine represent the two main classes of drugs, the arsenicals and diamidines, historically used to treat the diseases caused by African trypanosomes: sleeping sickness in humans and nagana in livestock. Cross-resistance to these drugs was first observed over 60 years ago and remains the only example of cross-resistance among sleeping sickness therapies. A *Trypanosoma brucei brucei* adenosine transporter is well known for its role in the uptake of both drugs. More recently, aquaglyceroporin 2 (AQP2) loss of function was linked to melarsoprol-pentamidine cross-resistance. AQP2, a channel that appears to facilitate drug accumulation, may also be linked to clinical cases of resistance. Here, we review these findings and consider some new questions as well as future prospects for tackling the devastating diseases caused by these parasites.

16509. **Deborggraeve, S. & Buscher, P., 2012.** Recent progress in molecular diagnosis of sleeping sickness. *Expert Review of Molecular Diagnostics*, **12** (7): 719-730.

Department of Biomedical Sciences, Institute of Tropical Medicine Antwerp, Nationalestraat 155, 2000 Antwerpen, Belgium. [pbuscher@itg.be].

This article will review the most recent progress in the molecular diagnosis of sleeping sickness and its potential role in patient management and disease control. While PCR remains restricted to research and reference laboratories, promising alternative molecular platforms have emerged over the last few years. Several loop-mediated isothermal amplification assays have been developed for detection and identification of the parasite with reported high analytical sensitivity and specificity. Simplified loop-mediated isothermal amplification formats have been designed and are undergoing evaluation studies in the field. Accurate diagnosis based on specific detection of the parasite's ribosomal RNA has been made possible by the isothermal nucleic acid sequence-based amplification and by direct hybridization with fluorescent detection probes. In addition to the technological progress, the authors also

discuss the diagnostic performance of molecular tests in the most recent clinical evaluation studies and briefly present some viewpoints for the near future.

16510. **Holmes, P., 2013.** Tsetse-transmitted trypanosomes-their biology, disease impact and control. *Journal of Invertebrate Pathology*, **112 Suppl**: S11-14.

University of Glasgow Veterinary School, 464 Bearsden Road, Glasgow G61 1QH, UK. [Peter.Holmes@glasgow.ac.uk].

Tsetse-transmitted trypanosome infections of man and animals occur across large areas of sub-Saharan Africa and are a major cause of ill-health and death. Although many details of the biology of tsetse-transmitted trypanosomes and the diseases they cause have been clearly established their control has proved extremely difficult. In part this is because trypanosomes show amazing antigenic variation of their surface coat and this has prevented the development of an effective vaccine. Also the few drugs which are available for treatment are unsatisfactory and often have severe side-effects. Significant progress has been made through tsetse control but such programmes are expensive and frequently re-infestation occurs. There is an urgent need for more effective disease diagnostic methods, new safer drugs and more sustained international support for integrated control programmes.

16511. **Horn, D., 2013.** High-throughput decoding of drug targets and drug resistance mechanisms in African trypanosomes. *Parasitology.* **E Publication ahead of print, April 8: 1-6.**

London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. [david.horn@lshtm.ac.uk].

The availability of genome sequence data has facilitated the development of high-throughput genetic screening approaches in microbial pathogens. In the African trypanosome, *Trypanosoma brucei*, genome-scale RNA interference screens have proven particularly effective in this regard. These genetic screens allow for identification of the genes that contribute to a particular pathway or mechanisms of interest. The approach has been used to assess loss-of-fitness, revealing the genes and proteins required for parasite viability and growth. The outputs from these screens predict essential and dispensable genes and facilitate drug target prioritization efforts. The approach has also been used to assess resistance to anti-trypanosomal drugs, revealing the genes and proteins that facilitate drug uptake and action. These outputs also highlight likely mechanisms underlying clinically relevant drug resistance. These findings are reviewed in the context of what we know about current drugs. Potential contributions that these high-throughput approaches could make to the development and implementation of new drugs are also described.

16512. **Kennedy, P. G., 2013.** Clinical features, diagnosis, and treatment of human African trypanosomiasis (sleeping sickness). *Lancet Neurology*, **12** (2): 186-194.

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Human African trypanosomiasis, or sleeping sickness, is caused by infection with parasites of the genus *Trypanosoma*, transmitted by the tsetse fly. The disease has two forms, *Trypanosoma brucei* (*T. b.*) *rhodesiense* and *T. b. gambiense*; and is almost always fatal if untreated. Despite a recent reduction in the number of reported cases, patients with African trypanosomiasis continue to present major challenges to clinicians. Because treatment for CNS-stage disease can be very toxic, diagnostic staging to distinguish early-stage from late-stage disease when the CNS is invaded is crucial but remains problematic. Melarsoprol is the only available treatment for late-stage *T. b. rhodesiense* infection, but can be lethal to 5 percent of patients owing to post-treatment reactive encephalopathy. Eflornithine combined with nifurtimox is the first-line treatment for late-stage *T. b. gambiense*. New drugs are in the pipeline for treatment of CNS Human African trypanosomiasis, giving rise to cautious optimism.

16513. **Kling, J. C. & Korner, H., 2013.** Different regulatory mechanisms in protozoan parasitic infections. *International Journal of Parasitology*, **43** (6): 417-425.

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The immune response to the protozoan pathogens, *Leishmania* spp., *Trypanosoma* spp. and *Plasmodium* spp., has been studied extensively with particular focus on regulation of the immune response by immunological mechanisms. More specifically, in diseases caused by parasites, immunosuppression frequently prevents immunopathology that can injure the host. However, this allows a small number of parasites to evade the immune response and remain in the host after a clinical cure. The consequences can be chronic infections, which establish a zoonotic or anthroponotic reservoir. This review highlights some of the identified regulatory mechanisms of the immune system that govern immune responses to parasitic diseases, in particular leishmaniasis, trypanosomiasis and malaria, and discusses implications for the development of efficient vaccines against these diseases.

16514. **Lejon, V., Bentivoglio, M. & Franco, J. R., 2013.** Human African trypanosomiasis. *Handbook of Clinical Neurology*, **114**: 169-181.

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Human African trypanosomiasis or sleeping sickness is a neglected tropical disease that affects populations in sub-Saharan Africa. The disease is caused by infection with the *gambiense* and *rhodesiense* subspecies of the extracellular parasite *Trypanosoma brucei*, and is transmitted to humans by bites of infected tsetse flies. The disease evolves in two stages, the haemolymphatic and meningoencephalitic stages, the latter being defined by central nervous system infection after trypanosomal traversal of the blood-brain barrier. African trypanosomiasis, which leads to severe neuroinflammation, is fatal without treatment, but the available drugs are toxic and complicated to administer. The choice of medication is determined by the infecting parasite subspecies and disease stage. Clinical features include a constellation of non-specific symptoms and signs with evolving neurological and psychiatric