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TSETSE AND TRYPANOSOMIASIS INFORMATION

The Tsetse and Trypanosomiasis Information periodical has been established to disseminate current information on all aspects of tsetse and trypanosomiasis research and control to institutions and individuals involved in the problems of African trypanosomiasis. This service forms an integral part of the Programme Against African Trypanosomiasis (PAAT) and is jointly sponsored by the Food and Agriculture Organization of the United Nations (FAO), 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), the British Government's Department for International Development (DFID) and the Institute of Tropical Medicine (ITM), Antwerp.

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 trypanosomiasis 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 John N. Pollock, 25 Palmeira Mansions, Church Road, Hove, East Sussex, BN3 2FA, United Kingdom (tel. +44 1273 326211; e-mail johnnpollock@hotmail.com).

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

The *Index* will be distributed as soon as possible after the completion of each volume.

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)
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
ITM	Institute of Tropical Medicine
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 Trypanosomiasis
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

BOOK PUBLICATION

New Comprehensive Text on the Sterile Insect Technique

Springer (see springeronline.com) announces the publication in November 2005 of a new textbook, *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management.* Editors Dyck, V.A., Hendrichs, J. & Robinson, A.S. 2005, xiv + 787pp. ISBN: 1-4020-4050-4 (€304.95). *TTI* has not yet had a view of this publication, and is here relying largely on the publisher's description of the text, and on IAEA sources.

The publisher points out that the sterile insect technique (SIT) is an environment-friendly method of pest control that integrates well into area-wide integrated pest management (AW-IPM) programmes. A first of its kind, this book takes a generic, comprehensive, and global approach in describing the principles and practice of the SIT. The strengths and weaknesses, as well as the successes and failures, of the SIT are evaluated openly and fairly from a scientific perspective. The SIT is applicable to some major pests of plant, animal and human health importance, and criteria are provided to guide in the selection of pests appropriate for the SIT.

A great variety of subjects is covered, from the history of the SIT to improved prospects for its future application. The book is divided into eight sections: Introduction; Principles of the SIT; Technical Components of the SIT; Supportive Technologies to Improve the SIT; Economic, Environmental and Management Considerations; Application of the SIT; Impact of AW-IPM Programmes that Integrate the SIT; and Future Developments of the SIT. The major chapters discuss the principles, technical components, and application of sterile insects. The four main strategic options in using the SIT – suppression, containment, prevention, and eradication – with examples of each option, are described in detail. Other chapters deal with supportive technologies, economic, environmental, and management considerations, and the socio-economic impact of AW-IPM programmes that integrate the SIT.

This book provides a wealth of information and reference material never before available in one volume. It is claimed that the book will be a standard reference on the subject for many years. The authors, from 19 countries, are highly experienced in the subject, and reflect the international character of SIT activities.

The book's readership is anticipated to be mainly students in general animal and plant health courses, but the in-depth reviews of all aspects of the SIT and its integration into AW-IPM programmes should be of great value to researchers, teachers, animal and plant health practitioners, and policy makers.

WHO/TDR

Seventeenth Programme Report of the UNICEF/UNDP/World Bank/WHO Programme for Research and Training in Tropical Diseases (2004)

The WHO Director-General Dr Jon-Wook Lee remarks in his Message introductory to this report that TDR's long history of combining cutting edge scientific research with the delivery of practical solutions in the fight against tropical diseases is one of WHO's success stories, shared with TDR's other co-sponsors. He urges that all must work towards establishing a research culture in health – a culture that sees both research and control activities as integral components of improved health outcomes and as partner activities in a common health system.

Under the heading of Human African Trypanosomiasis, the Report states that HAT rose steadily in incidence after the 1960s but is now on the wane. WHO estimates that 300 000–500 000 people are affected but it is admitted that there are no accurate figures for this disease that affects mainly remote areas.

Major challenges faced by those attempting to control the disease include inadequate resources, inadequate surveillance, and inadequate knowledge of the disease; lack of effective diagnostics; drugs that are costly and/or cause adverse reactions; human population movements; and agro-ecological changes that alter the tsetse habitat and increase contact between humans and the tsetse fly.

It is accepted that vector control based on insecticides, targets and traps will be important in the control of HAT for the foreseeable future. TDR has recently published a review of traps and targets for tsetse and trypanosomiasis control. Looking to the future of tsetse control, TDR supports a molecular entomology approach, with the objective to generate by 2009 knowledge on the molecular and genomic aspects of the tsetse, so as to be able to create tools to genetically transform them, to identify tsetse genes that might disrupt trypanosome growth, and to find ways of spreading selected genes throughout wild tsetse populations.

Also described are a number of avenues of attack on the trypanosome parasite, using genomic studies. An understanding of the genetic basis of vector competence in natural populations is being sought.

FAO/IAEA JOINT DIVISION

FAO/IAEA Agriculture and Biotechnology Laboratory, Seibersdorf, Austria.

Pupal sexing

As part of the drive to automate the routines involved in tsetse rearing, tests have been under way to find if tsetse pupae can be sorted by sex, using near infra-red spectrometry. Progress has been made using *Glossina pallidipes* as the test insect. Good results have been obtained using pupae 4–5 days before emergence: the sexing accuracy obtained was about 96 percent. Other species are being worked on in the same manner, but the results have yet to be analysed. The use of the spectrometer is anticipated to become standard in the maintenance on the colony at Seibersdorf and in operations aimed at the provision of

male pupae for irradiation and field release. Sexing of flies using the normal chilling procedures will no longer be required.

Salivary gland hyperplasia

It has been known for some time that a virus induces salivary gland hyperplasia in the tsetse. It appears also to cause reproductive abnormalities, and such pathological effects may be especially severe in *G. pallidipes*. In the field, low levels are normally found (0.5–5 percent) but laboratory colonies can be more seriously affected leading to decreases in the reproductive capacity.

In order to understand better the biology of the virus, steps are being taken to obtain its nucleotide sequence. Various methods of inducing virus infections are being tried out. Eventually it is hoped to extract sufficient purified virus for the molecular biology routines to be applied for the completion of the sequencing studies. Setting up cell cultures of salivary gland and other material proved difficult, but further attempts to do so are continuing.

Colony status

Due to shortages in resources, future supplies of tsetse pupae to Technical Cooperation projects will not be free, but will instead be charged to the respective project. It is planned to stabilise the Bratislava colonies at approximately 50 000 breeding females for each of *G. pallidipes* and *G. fuscipes fuscipes*, and approximately 20 000 breeding females for *G. morsitans centralis*. A *G. pallidipes* colony of about the same size will be housed in the new Tsetse Production Unit 3 at Siebersdorf. A number of relatively minor problems associated with the TPU3 have been identified and corrective measures taken. Collaborating scientists requiring pupae of *G. m. morsitans* should contact Peter Takac in Bratislava (uzaetaka@savba.sk).

SECTION B - ABSTRACTS

1. GENERAL (INCLUDING LAND USE)

13284 **Ash, C. & Jasny, B.R., 2005.** The trypanosomatid genomes. *Science*, **309** (5733): 399–400.

This editorial introduction serves to give background to a Special Section in the journal *Science*, dealing with the genomes of three trypanosomatid parasites, *Trypanosoma brucei*, *T. cruzi* and *Leishmania major*. Particular attention is drawn to unusual organization of the papers on trypanosomatid genomes: the paper of Berriman *et al.* [see 13398] focuses on metabolic and biochemical pathways of the three trypanosomatids; the one by Ivens *et al.* [see 13422] places its spotlight on molecular biology; whereas the account by El-Sayed *et al.* [see 13410] emphasises repetitive elements, DNA replication and repair, and signalling pathways. This useful comparative approach was made possible by careful early planning of the research effort carried out by the major research centres and by laboratories within developing countries. It was to be hoped that the advances reported in the genome papers would be translated into more effective treatments for the diseases caused by these parasites.

13285 **Bloom, G. & Sherman, P.W., 2005.** Dairying barriers affect the distribution of lactose malabsorption. *Evolution and Human Behavior*, **26** (4): 301–312.

Sherman: Department of Neurobiology and Behaviour, Cornell University, Ithaca, NY 14853, USA.

Most mammals stop drinking milk at weaning, which is also the time when they cease producing lactase, the digestive enzyme that hydrolyzes lactose. Cessation of lactase production and milk drinking also characterize most human populations, especially those of African and Asian descent. However, a genetic mutation that maintains the functionality of lactase production into adulthood occurs commonly among populations from northern Europe, where dairying is practiced routinely. Indeed, the ability to absorb lactose is nutritionally beneficial for adults only if milk consistently is available. What determines the distribution of dairying? We hypothesized that specific environmental circumstances affect where milk-producing ungulates can be raised safely and economically, thus influencing the geographical occurrence of dairying and lactase persistence. To evaluate this hypothesis, we compiled data on adult lactose absorption and malabsorption (LM) frequencies in 270 indigenous African and Eurasian populations. Partial correlation analyses revealed that, as predicted, adult LM is associated with extreme climates (at high and low latitudes) and, more significantly, with the historical (pre-1900) geographical occurrence of nine deadly, communicable diseases of cattle. These results suggest that areas where adult LM predominates are those where it is impossible or dangerous to maintain dairy herds.

13286 **Brun, R., 2005.** Human Asian trypanosomiasis, a new threat to human health? [Editorial] *American Journal of Tropical Medicine and Hygiene*, **73** (3): 484.

Brun: Swiss Tropical Institute, CH-4002 Basel, Switzerland.

13287 **Croft, S.L., Vivas, L. & Brooker, S., 2003.** Recent advances in research and control of malaria, leishmaniasis, trypanosomiasis and schistosomiasis. *Eastern Mediterranean Health Journal*, **9** (4): 518–533.

Croft: Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.

In the Eastern Mediterranean Region of the World Health Organization (WHO), malaria, schistosomiasis, leishmaniasis and trypanosomiasis are the parasitic diseases of major importance. Our review focuses on recent advances in the control and treatment of these diseases with particular reference to diagnosis, chemotherapy, vaccines, vector and environmental control. The Roll Back Malaria Programme, for example, emphasizes the use of insecticide treated bednets in Africa and targets a 30-fold increase in treated bednet use by 2007. Increasing risk factors for leishmaniasis include urbanization, extended agricultural projects and civil unrest, and the increase in patients with *Leishmania infantum* and HIV co-infection in the Region may signal a new threat. In the past 20 years, human African trypanosomiasis has resurged in sub-Saharan Africa; within the Region it has become more common in the southern Sudan where anthroponotic and zoonotic sub-species infections overlap. Schistosomiasis in the Region is caused by either *Schistosoma haematobium* or *S. mansoni* and large-scale control efforts include providing regular treatment to at-risk groups and supporting drug delivery through schools.

13288 **Giblin, J.L., 2005.** Lords of the fly: Sleeping sickness control in British East Africa 1900-1960, by K.A. Hoppe. *African Affairs*, **104** (414): 153–155.

Giblin: University of Iowa, Iowa City, IA 52242, USA.

This is a book review of "Lords of the fly: Sleeping sickness control in British East Africa 1900–1960" by Kirk Arden Hoppe, publ. Westport CT: Praeger, 2003. xii + 203pp. ISBN 0-325-07123-3.

13289 **Joshi, P.P., Shegokar, V.R., Powar, R.M., Herder, S., Katti, R., Salkar, H.R., Dani, V.S., Bhargava, A., Jannin, J. & Truc, P., 2005.** Human trypanosomiasis caused by *Trypanosoma evansi* in India: The first case report. *American Journal of Tropical Medicine and Hygiene*, **73** (3): 491–495.

Truc: Institut de Recherche pour le Développement, Unité de Recherche 117 Trypanosomoses Africaines, TA 207/G Campus International de Baillarguet, 34 398 Montpellier Cedex 5, France. [truc@mpl.ird.fr]

13290 **Kioy, D. & Mattock, N., 2005.** Control of sleeping sickness – time to integrate approaches. *Lancet*, **366** (9487): 695–696.

Kioy: WHO Special Programme for Research and Training in Tropical Diseases, World Bank, UNDP,UNICEF, CH-1211 Geneva, Switzerland.

13291 **Nunn, C.L., Altizer, S.M., Sechrest, W. & Cunningham, A.A., 2005.** Latitudinal gradients of parasite species richness in primates. *Diversity and Distributions*, **11** (3): 249–256.

Cunningham: Department of Integrative Biology, University of California, Berkeley, CA 94720-3140, USA.

Infectious disease risk is thought to increase in the tropics, but little is known about latitudinal gradients of parasite diversity. We used a comparative data set encompassing 330 parasite species reported from 119 primate hosts to examine latitudinal gradients in the diversity of micro and macroparasites per primate host species. Analyses conducted with and without controlling for host phylogeny showed that parasite species richness increased closer to the equator for protozoan parasites, but not for viruses or helminths. Relative to other major parasite groups, protozoa reported from wild primates were transmitted disproportionately by arthropod vectors. Within the protozoa, our results revealed that vector-borne parasites showed a highly significant latitudinal gradient in species richness. This higher diversity of vector-borne protozoa near the tropics could be influenced by a greater abundance or diversity of biting arthropods in the tropics, or by climatic effects on vector behaviour and parasite development. Many vector-borne diseases, such as leishmaniasis, trypanosomiasis, and malaria pose risks to both humans and wildlife, and nearly one-third of the protozoan parasites from free-living primates in our data set have been reported to infect humans. Because the geographical distribution and prevalence of many vector-borne parasites are expected to increase due to global warming, these results are important for predicting future parasite-mediated threats to biodiversity and human health.

13292 **Plourde, P.J., 2005.** Statement on personal protective measures to prevent arthropod bites. *Canada Communicable Disease Report*, **31** (ACS-4): 1–18.

Protective measures that can be taken by individuals to avoid bites from arthropod vectors are reviewed. Brief remarks are made concerning the bite of the tsetse.

13293 **Riethmiller, S., 2005.** From Atoxyl to Salvarsan: Searching for the magic bullet. *Chemotherapy*, **51** (5): 234–242.

Riethmiller: Chemistry Department, Virginia Military Institute, Lexington, Virginia, USA.

March 15th of 2004 marked the 150th anniversary of the birth of Paul Ehrlich. He was the founder of modern chemotherapy and in fact coined the word and invented the

science of chemical therapy. He and his chemist Alfred Bertheim were the first people to do three things: (1) identify a substance, either man-made or from natural products, which showed promise in killing certain invading organisms; (2) determine the correct structure of the active compound in this substance, and (3) modify the chemical structure of this compound to make it more potent to invading organisms and less harmful to the host.

13294 **de la Rocque, S., Michel, V., Plazanet, D. & Pin, R., 2004.** Remote sensing and epidemiology: examples of applications for two vector-borne diseases. *Comparative Immunology, Microbiology & Infectious Diseases*, **27** (5): 331–341.

de la Rocque: CIRAD, BP 5035, 34032 Montpellier cedex 1, France. [stephane.de_la_rocque@cirad.fr]

Remote sensing techniques have contributed greatly to increase our capacity to observe our environment and its dynamics. For about 15 years, the use of satellite images for epidemiological purposes has been promoted mainly to update disease distribution maps. When diseases are strongly related to environmental data such as climate, vegetation or land-use, remote sensing data can be directly correlated with the presence or absence of pathogens and/or vectors. In other cases, remote sensing data provide information for drawing thematic layers, the use of which requires an accurate knowledge of epidemiological processes, which may differ according to the different ecotypes and ecosystems. According to its final goal, the users can choose from the panel of available radiometers with specific characteristics including spatial resolution and frequency of data. In this paper, two examples of major vector-borne diseases, namely Animal Trypanosomosis and Bluetongue, illustrate these applications.

13295 **Skipper, M., 2005.** Three deadly trypanosomatids decoded. *Nature Reviews Genetics*, **6** (9): 665.

The publication of the genome sequences of three trypanosomatids parasites, *Trypanosoma brucei*, *T. cruzi* and *Leishmania major*, is hailed in this editorial as an opportunity for drug development against the diseases caused by these parasites. The papers are the result of international collaborative effort, and they place emphasis on cross comparisons between the three parasites. These related organisms share a core of some 6 200 genes. Light is thrown on the manner in which trypanosome gene expression is regulated, and curiosities of DNA replication and repair are revealed. The oddities of trypanosome biology as indicated in these studies point to areas in which the parasites might be attacked by new effective treatments.

2. TSETSE BIOLOGY

(a) REARING OF TSETSE FLIES

13296 **Dowell, F.E., Parker, A.G., Benedict, M.Q., Robinson, A.S., Broce, A.B. & Wirtz, R.A., 2005.** Sex separation of tsetse fly pupae using near-infrared spectroscopy. *Bulletin of Entomological Research*, **95** (3): 249–257.

Dowell: USDA-ARS Grain Marketing and Production Research Center, 1515 College Avenue, Manhattan, KS 66502, USA.

Implementation of the sterile insect technique for tsetse (*Glossina* spp.) requires that only sterile male insects be released; thus, at some stage of the fly production process the females have to be removed. A further constraint in the use of the sterile insect technique for tsetse is that the females are needed for colony production and hence a non-destructive method of sex separation is required. In most tsetse sterile insect technique programmes thus far, females have been eliminated from the released material by hand-separation of chilled adults. Using near-infrared (NIR) spectroscopy, significant differences have been found between the spectra for the pupae of male and female *G. pallidipes*. Significantly, the differences appear to be maximized 4–5 days before emergence of the adults. Tsetse fly pupae up to five days before emergence can be sexed with accuracies that generally range from 80–100 percent. This system, when refined, will enable effective separation of male and female pupae to be carried out, emerged females being returned to the colony and males being irradiated and released. If separation can be achieved five days before emergence, this would also enable irradiated male pupae to be shipped to other destinations as required. Other Diptera were evaluated using this system but had lower classification accuracies of 50–74 percent. This may be due to the difference in reproductive physiology between these different fly groups.

(b) TAXONOMY, ANATOMY, PHYSIOLOGY, BIOCHEMISTRY

13297 **Darby, A.C., Lagnel, J., Matthew, C.Z., Bourtzis, K., Maudlin, I. & Welburn, S.C., 2005.** Extrachromosomal DNA of the symbiont *Sodalis glossinidius*. *Journal of Bacteriology*, **187** (14): 5003–5007.

Darby: Centre of Infectious Diseases, College of Medicine and Veterinary Medicine, University of Edinburgh, Easter Bush, Edinburgh EH25 9RG, UK. [alistair.darby@ed.ac.uk]

The extrachromosomal DNA of *Sodalis glossinidius* from two tsetse fly species was sequenced and contained four circular elements: three plasmids, pSG1 (82 kb), pSG2 (27 kb), and pSG4 (11 kb), and a bacteriophage-like pSG3 (19 kb) element. The information suggests *S. glossinidius* is evolving towards an obligate association with tsetse flies.

13298 **Geiger, A., Ravel, S., Frutos, R. & Cuny, G., 2005.** *Sodalis glossinidius* (Enterobacteriaceae) and vectorial competence of *Glossina palpalis gambiensis* and *Glossina morsitans morsitans* for *Trypanosoma congolense* savannah type. *Current Microbiology*, **51** (1): 35–40.

Geiger: IRD, UR035, Laboratoire de Recherche et de Coordination sur les Trypanosomoses, IRD-CIRAD, TA 207/G, Campus International de Baillarguet, 34398 Montpellier cedex 5, France. [Anne.Geiger@mpl.ird.fr]

Sodalis glossinidius is an endosymbiont of *Glossina palpalis gambiensis* and *Glossina morsitans morsitans*, the vectors of *Trypanosoma congolense*. The presence of the symbiont was investigated by PCR in *Trypanosoma congolense* savannah type-infected and noninfected midguts of both fly species, and into the proboscides of flies displaying either mature or immature infection, to investigate possible correlation with the vectorial competence of tsetse flies. *Sodalis glossinidius* was detected in all midguts, infected or not, from both *Glossina* species. It was also detected in proboscides from *Glossina palpalis gambiensis* flies displaying mature or immature infection, but never in probosces from *Glossina morsitans morsitans*. These results suggest that, a) there might be no direct correlation between the presence of *Sodalis glossinidius* and the vectorial competence of *Glossina*, and b) the symbiont is probably not involved in *Trypanosoma congolense*-savannah type maturation. It could however participate in the establishment process of the parasite.

13299 **Kinyua, J.K., Nguu, E.K., Mulaa, F. & Ndung'u, J.M., 2005.** Immunization of rabbits with *Glossina pallidipes* tsetse fly midgut proteins: effects on the fly and trypanosome transmission. *Vaccine*, **23** (29): 3824–3828.

Kinyua: Kenya Agricultural Research Institute-Trypanosomiasis Research Center (KARI-TRC), P.O. Box 362, Kikuyu, Kenya.

Proteins isolated from the midgut of *Glossina pallidipes* were used to immunize rabbits and their efficacy as vaccine candidate(s) against the fly, and their potential to block transmission of *Trypanosoma brucei rhodesiense*, assessed. Two fractions, detergent (DET) and aqueous (AQ) fractions were separated using a non-ionic detergent (Triton X-114) and a series of bioassay experiments carried out using serum obtained from rabbits immunized with either of the two fractions. The mortality rates of tsetse flies fed on serum from rabbits immunized with DET and AQ was 56 and 35 percent, respectively, as compared to 20 percent mortality in controls. The DET antigen(s) caused considerably higher mortality than that on controls. These findings suggest that midgut proteins contain antigens that are lethal to tsetse flies, and are potential candidates for the development of anti-tsetse vaccine. When flies fed on serum derived from DET immunized rabbits were fed on *T. b. rhodesiense* infected blood, only 20 percent of them picked the infection. Very few flies (20 percent) fed on serum derived from DET immunized rabbits had infection of *T. b. rhodesiense*. In the control flies 45 percent of them had infection in the midgut with a higher and actively motile parasite load. Assessment of fecundity indicated significantly higher larviposition for the control flies

when compared to the AQ group of flies. Significant differences in abortions and pupal weights were also observed. These results suggest that midgut proteins contain antigens with potential for use in development of vaccine to block transmission of trypanosomes through tsetse.

13300 **Haddow, J.D., Haines, L.R., Gooding, R.H., Olafson, R.W. & Pearson, T.W., 2005.** Identification of midgut proteins that are differentially expressed in trypanosome-susceptible and normal tsetse flies (*Glossina morsitans morsitans*). *Insect Biochemistry and Molecular Biology*, **35** (5): 425–433.

Pearson: University of Victoria-Genome British Columbia Proteomics Centre, #3101-4464 Markham Street, Victoria, BC V8Z 7X8, Canada.

Molecules in the midgut of tsetse flies are thought to play important roles in the life cycle of African trypanosomes by influencing initial parasite establishment and subsequent differentiation events that ultimately lead to maturation of mammal-infective trypanosomes. The molecular composition of the tsetse midgut is, therefore, of critical importance to disease transmission by these medically important vectors. In this study we compared protein expression profiles of midguts of the *salmon* mutant and wild type *Glossina morsitans morsitans* that display marked differences in their susceptibility to infection by African trypanosomes. Isotope coded affinity tag (ICAT) technology was used to identify 207 proteins including 17 that were up regulated and nine that were down regulated in the *salmon* mutants. Several of the up regulated molecules were previously described as tsetse midgut or salivary gland proteins. Of particular interest was the up regulation in the *salmon* flies of tsetse midgut EP protein, a recently described molecule with lectin-like activity that was also found to be induced in tsetse by bacterial challenge. The up regulation of the EP protein in midguts of *salmon* mutants was confirmed by two-dimensional gel electrophoresis and tandem mass spectrometry.

13301 **Haines, L.R., Jackson, A.M., Lehane, M.J., Thomas, J.M., Yamaguchi, A.Y., Haddow, J.D. & Pearson, T.W., 2005.** Increased expression of unusual EP repeat-containing proteins in the midgut of the tsetse fly (*Glossina*) after bacterial challenge. *Insect Biochemistry and Molecular Biology*, **35** (5): 413–423.

Pearson: Department of Biochemistry and Microbiology, University of Victoria, Petch Building, PO Box 3055, Victoria, British Columbia V8W 3P6, Canada.

Proteins containing a glutamic acid-proline (EP) repeat epitope were immunologically detected in midguts from eight species of *Glossina* (tsetse flies). The molecular masses of the tsetse EP proteins differed among species groups. The amino acid sequence of one of these proteins, from *Glossina palpalis palpalis*, was determined and compared to the sequence of a homologue, the tsetse midgut EP protein of *Glossina morsitans morsitans*. The extended EP repeat domains comprised between 36 percent (*G. m. morsitans*) and 46 percent (*G. p. palpalis*) of the amino acid residues, but otherwise

the two polypeptide chains shared most of their sequences and predicted functional domains. The levels of expression of tsetse EP protein in adult teneral midguts were markedly higher than in midguts from larvae. The EP protein was detected by immunoblotting in the fat body, proventriculus and midgut, the known major immune tissues of tsetse, and is probably secreted as it was also detected in haemolymph. The EP protein was not produced by the bacterial symbionts of tsetse midguts as determined by genome analysis of *Wigglesworthia glossinidia* and immunoblot analysis of *Sodalis glossinidius*. Bacterial challenge of *G. m. morsitans*, by injection of live *E. coli*, induced augmented expression of the tsetse EP protein. The presence of EP proteins in a wide variety of tsetse, their constitutive expression in adult fat body and midguts and their upregulation after immunogen challenge suggest they play an important role as a component of the immune system in tsetse.

13302 **Hamilton, J.V. & Lehane, M.J., 2005.** Tsetse midgut immunity - DiGE-ESTing for clues into African sleeping sickness. *Outlooks on Pest Management*, **16** (1): 19–22.

Lehane: Institute of Biological Sciences, University of Wales, Aberystwyth, SY23 3DA, UK.

13303 **Lehane, M.J., Aksoy, S., Gibson, W., Kerhornou, A., Berriman, M., Hamilton, J., Soares, M.B., Bonaldo, M.F., Lehane, S. & Hall, N., 2003.** Adult midgut expressed sequence tags from the tsetse fly *Glossina morsitans morsitans* and expression analysis of putative immune response genes. *Genome Biology*, **4** (10): R63.

Lehane: School of Biological Sciences, University of Wales, Bangor, LL57 2UW, UK.

Tsetse flies transmit African trypanosomiasis leading to half a million cases annually. Trypanosomiasis in animals (nagana) remains a massive brake on African agricultural development. While trypanosome biology is widely studied, knowledge of tsetse flies is very limited, particularly at the molecular level. This is a serious impediment to investigations of tsetse-trypanosome interactions. We have undertaken an expressed sequence tag (EST) project on the adult tsetse midgut, the major organ system for establishment and early development of trypanosomes. It has been found that a total of 21 427 ESTs were produced from the midgut of adult *Glossina morsitans morsitans* and grouped into 8 876 clusters or singletons potentially representing unique genes. Putative functions were ascribed to 4 035 of these by homology. Of these, a remarkable 3 884 had their most significant matches in the *Drosophila* protein database. We selected 68 genes with putative immune-related functions, macroarrayed them and determined their expression profiles following bacterial or trypanosome challenge. In both infections many genes are downregulated, suggesting a malaise response in the midgut. Trypanosome and bacterial challenge result in upregulation of different genes, suggesting that different recognition pathways are involved in the two responses. The most notable block of genes upregulated in response to trypanosome challenge is a series of Toll and

Imd genes and a series of genes involved in oxidative stress responses. The project increases the number of known *Glossina* genes by two orders of magnitude. Identification of putative immunity genes and their preliminary characterization provides a resource for the experimental dissection of tsetse-trypanosome interactions.

13304 **Matthew, C.Z., Darby, A.C., Young, S.A., Hume, L.H. & Welburn, S.C., 2005.** The rapid isolation and growth dynamics of the tsetse symbiont *Sodalis glossinidius*. *FEMS Microbiology Letters*, **248** (1): 69–74.

Welburn: Centre for Tropical Veterinary Medicine, Royal (Dick) School of Veterinary Studies, The University of Edinburgh, Easter Bush, Roslin, Midlothian, EH25 9RG, UK. [sue.welburn@ed.ac.uk]

Sodalis glossinidius is known exclusively in endosymbiosis with tsetse flies (*Glossina*) and is one of the few insect bacterial symbionts that have been successfully cultured *in vitro*. This study details improved isolation and solid culture protocols that allow for a standardised and rapid preparation/maintenance of clonal material from individual flies. The isolation and culture of *S. glossinidius* was confirmed by partial sequencing of the 16S rDNA gene and specific PCR. In addition, the growth dynamics and changes in cell viability during liquid culture are described. The potential for culture of other endosymbiont taxa is discussed.

13305 **Munks, R.J.L., Sant'Anna, M.R.V., Grail, W., Gibson, W., Igglesden, T., Yoshiyama, M., Lehane, S.M. & Lehane, M.J., 2005.** Antioxidant gene expression in the blood-feeding fly *Glossina morsitans morsitans*. *Insect Molecular Biology*, **14** (5): 483–491.

Lehane: Liverpool School of Tropical Medicine, Liverpool, UK

We report the characterization of eleven antioxidant genes from the tsetse fly *Glossina m. morsitans*. Through similarity searches which detected homology we suggest that these genes consist of two superoxide dismutases (one with a putative signal peptide), three thioredoxin peroxidases (one with a putative signal peptide), three peroxiredoxins, one further signal peptide-containing peroxidase with its closest similarity to a glutathione peroxidase, one catalase and one thioredoxin reductase. We describe the changes occurring in the expression levels of these genes during fly development, in different adult tissues, in the adult midgut through the digestive cycle and following trypanosome infection. Overall, nine of the eleven genes studied showed responses to changes in physiological circumstance, with the peroxiredoxin group showing the smallest variations throughout.

13306 **Patterson, J.S. & Schofield, C., 2005.** Preliminary study of wing morphometry in relation to tsetse population genetics. *South African Journal of Science*, **101** (3–4): 132–134.

Schofield: Department of Infectious and Tropical Disease, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK.

Comparative morphometric analysis of shape variation in the wings of different tsetse species reveals close accordance with the phylogenetics of these species indicated by DNA sequence analysis. In practice, the morphometric analysis is economical and simple to carry out, suggesting that this could become a useful surrogate or complementary tool for large-scale studies of tsetse population genetics, designed to identify discrete population targets amenable to local elimination.

13307 **Rio, R.V.M., Lefevre, C., Abdelaziz Heddi & Aksoy, S., 2003.** Comparative genomics of insect-symbiotic bacteria: influence of host environment on microbial genome composition. *Applied and Environmental Microbiology*, **69** (11): 6825–6832.

Aksoy: Department of Epidemiology and Public Health, Yale University School of Medicine, 60 College St., 606 LEPH, New Haven, CT 06510, USA. [serap.aksoy@yale.edu]

Commensal symbionts, thought to be intermediate between obligate mutualists and facultative parasites, offer insight into forces driving the evolutionary transition into mutualism. Using macroarrays developed for a close relative, *Escherichia coli*, we utilized a heterologous array hybridization approach to infer the genomic compositions of a clade of bacteria that have recently established symbiotic associations: *Sodalis glossinidius* with the tsetse fly (Diptera, *Glossina* spp.) and *Sitophilus oryzae* primary endosymbiont (SOPE) with the rice weevil (Coleoptera, *Sitophilus oryzae*). Functional biologies within their hosts currently reflect different forms of symbiotic associations. Their hosts, members of taxonomically distant insect taxa, occupy distinct ecological niches and have evolved to survive on restricted diets of blood for tsetse and cereal for the rice weevil. Comparison of genome contents between the two microbes indicates statistically significant differences in the retention of genes involved in carbon compound catabolism, energy metabolism, fatty acid metabolism, and transport. The greatest reductions have occurred in carbon catabolism, membrane proteins, and cell structure-related genes for *Sodalis* and in genes involved in cellular processes (i.e. adaptations towards cellular conditions) for SOPE. Modifications in metabolic pathways, in the form of functional losses complementing particularities in host physiology and ecology, may have occurred upon initial entry from a free-living to a symbiotic state. It is possible that these adaptations, streamlining genomes, act to make a free-living state no longer feasible for the harnessed microbe.

13308 **Terblanche, J.S., Klok, C.J. & Chown, S.L., 2005.** Temperature-dependence of metabolic rate in *Glossina morsitans morsitans* (Diptera, Glossinidae) does not vary with gender, age, feeding, pregnancy or acclimation. *Journal of Insect Physiology*, **51** (8): 861–870.

Terblanche: Spatial, Physiological and Conservation Ecology Group, Department of Botany and Zoology, University of Stellenbosch, Private Bag X1, Matieland, 7602 Stellenbosch, South Africa.

While variation in metabolic rate at a single temperature can occur for a variety of reasons and the effect of temperature is well established in insects, within-generation variation of metabolic rate-temperature relationships has been relatively poorly explored. In this study, we investigate the effects of gender, age, feeding and pregnancy, as well as three acclimation temperatures (19, 24, 29 degrees C), on standard metabolic rate and its temperature-dependence within post-developmental (i.e. non-teneral) adult *G. morsitans morsitans*. Although most of the independent variables influenced metabolic rate at a single test temperature, and cold-acclimation at 19 degrees C (in contrast to acclimation at 24 or 29 degrees C) resulted in significant up-regulation of metabolic rate at all test temperatures; however, mass-independent metabolic rate-temperature relationships were surprisingly invariant over all experimental groups. Slopes of $\log_{10}$ metabolic rate (ml CO_2 h^{-1}) against temperature (degrees C) ranged from a minimum of 0.03035 (+/- S.E. = 0.003) in young fasted females to a maximum of 0.03834 (+/- 0.004) in mature fasted males. These findings have implications for predicting the metabolic responses of tsetse flies to short-term temperature variation and may also have applications for modelling tsetse population dynamics as a function of temperature.

13309 **Zientz, E., Dandekar, T. & Gross, R., 2004.** Metabolic interdependence of obligate intracellular bacteria and their insect hosts. *Microbiology and Molecular Biology Reviews*, **68** (4): 745–770.

Gross: Lehrstuhl für Mikrobiologie, Biozentrum der Universität Würzburg, Theodor-Boveri-Institut, Am Hubland, D-97074 Würzburg, Germany. [roy.gross@mail.uni-wuerzburg.de]

Mutualistic associations of obligate intracellular bacteria and insects have attracted much interest in the past few years due to the evolutionary consequences for their genome structure. However, much less attention has been paid to the metabolic ramifications for these endosymbiotic microorganisms, which have to compete with but also to adapt to another metabolism – that of the host cell. This review attempts to provide insights into the complex physiological interactions and the evolution of metabolic pathways of several mutualistic bacteria of aphids, ants, and tsetse flies and their insect hosts.

(c) DISTRIBUTION, ECOLOGY, BEHAVIOUR, POPULATION STUDIES

13310 **Ahmed, A.B., 2004.** A peridomestic population of the tsetse fly *Glossina palpalis palpalis* Robineau-Desvoidy, 1830 (Diptera: Glossinidae) at Kontagora Town, Niger State, Nigeria. *Entomología y Vectores*, **11** (4): 599–610.

Ahmed: Entomology & Parasitology Division, Nigerian Institute for Trypanosomiasis Research (NITR), P.M.B. 2077, Kaduna, Nigeria. [adoahmed2001@yahoo.com]

Data on the ecology of *G. p. palpalis* were collected in 1995 and 1999. Twenty-four and 39 flies were caught in Kontagora town, Nigeria in the respective years. The results are summarised.

13311 **Ahmed, A.B, Okiwelu, S.N & Samdi, S.M., 2005.** Species Diversity, Abundance and Seasonal Occurrence of Some Biting Flies in Southern Kaduna, Nigeria. *African Journal of Biomedical Research*, **8**: 113–118.

Ahmed: Divisions of Entomology, Nigerian Institute for Trypanosomiasis Research, PMB 2077, Kaduna State, Nigeria. [adoahmed2001@yahoo.com]

A survey of biting dipterans was conducted in Kaura LGA of Kaduna State between November 2000 and October 2001. Fifteen species of biting flies were caught in two families, Tabanidae and Muscidae, distributed in the following 4 genera: *Tabanus* 10, *Haematopota* 2, *Chrysops* 1 and *Stomoxys* 2. The genus *Stomoxys*, represented by *Stomoxys calcitrans* and *S. nigra*, had the highest abundance (62.5 percent), followed by *Tabanus* (34.6 percent), *Haematopota* (1.8 percent) and *Chrysops* (1.1 percent). Generally, more flies were collected during the wet (1 431: 85.1 percent) than the dry season (250: 14.9 percent) with some species occurring all year round. The widespread presence of haematophagous dipterans in the study area suggest that they could be playing a greater role in disease transmissions than previously thought. Optimum temperatures that stimulate rapid reproduction appear to fall between mean temperatures of 22.8–24.1°C. The species showed a general increase in relative abundance during the wet season and a decline in the dry season. No new country records were found.

13312 **Mireji, P.O., Mabveni, A.M., Dube, B.N., Ogembo, J.G., Matoka, C.M. & Mangwiro, T.N.C., 2003.** Field responses of tsetse flies (Glossinidae) and other Diptera to oils in formulations of deltamethrin. *Insect Science and its Application*, **23** (4): 317–323.

Mireji: Department of Biological Sciences, University of Zimbabwe, P. O. Box MP 167, Mount Pleasant, Harare, Zimbabwe. [Mireji@yahoo.com]

Investigations were conducted to establish field responses of *Glossina pallidipes*, *G. morsitans morsitans*, muscoids and tabanids to castor, raw linseed, paraffin and

chlorinated paraffin oils in deltamethrin suspension concentrate (sc) formulation, through randomized Latin square experiments. Tsetse landing responses on targets treated with 400 ml/m^2 of any of the oils in 2 g/m^2 deltamethrin formulation were significantly lower than on non-oil-containing deltamethrin formulations, for both *G. pallidipes* and *G. m. morsitans*. The landing response indices, relative to the control formulation without oil, were 0.60, 0.70, 0.61 and 0.41 in *G. pallidipes* and 0.92, 0.82, 0.75 and 0.42 in *G. m. morsitans* for paraffin, chlorinated paraffin, castor and raw linseed oils respectively. *Glossina pallidipes* and *G. m. morsitans* landing responses were inversely proportional to raw linseed oil concentrations. None of the oils significantly affected muscoid or tabanid landing response, or tsetse fly resting persistence on the targets. The reduced tsetse fly response to targets treated with any of the oils can be attributed to adverse effect of the oil treatments on the tsetse fly olfactory responses to the targets. Since the oil formulations reduce target efficiency by reducing tsetse responses to the targets, application of the oil formulations on targets deployed in *G. pallidipes* and *G. m. morsitans* control programmes is not recommended.

13313 **Muzari, M.O. & Hargrove, J.W., 2005.** Artificial larviposition sites for field collections of the puparia of tsetse flies *Glossina pallidipes* and *G. m. morsitans* (Diptera: Glossinidae). *Bulletin of Entomological Research*, **95** (3): 221–229.

Muzari: National Institute of Health Research, Box CY573, Causeway, Harare, Zimbabwe.

At Rekomitjie Research Station, Zambezi Valley, Zimbabwe, the tsetse fly species *Glossina pallidipes* and *G. morsitans morsitans* deposit their larvae in warthog burrows in August–November. Artificial burrows, made from 200 litre steel drums, were used to sample these flies and to collect their puparia. Sand-filled plastic trays in the burrows served as a substrate for larval deposition. The sand was covered with *c.* 2 cm of leaf litter after it was shown that only 3 percent of larvae were deposited on bare sand if both substrates were available. Other burrow modifications – artificially shading the burrow entrance, increasing the relative humidity inside the burrow, or reducing the size of the burrow entrance – significantly decreased deposition rates. The use of burrows in the hot season resulted in a reduction in the temperature experienced by the puparium towards an assumed optimum level of 26 degrees C. Artificial burrows maintained a mean temperature of 28.5 degrees C during October–November 1998, *c.* 2.5 degrees C cooler than ambient; earlier work has shown that natural burrows can be *c.* 5 degrees C cooler than ambient at these times. This may explain why natural burrows in full sunlight were used for larviposition, whereas artificial burrows were used only when they were in deep shade, and why significantly higher proportions of *G. pallidipes* were found in natural (66 percent) than in artificial burrows (34 percent). Better-insulated artificial burrows might produce more puparia with higher proportions of *G. pallidipes*. Burrows become waterlogged during the rains and may be too cool for optimum puparial development during the rest of the year. The percentages of *G. m. morsitans* in catches of females from artificial burrows, refuges and odour-baited traps were 34, 26 and <10 percent respectively. Traps are biased in favour of *G. pallidipes*; artificial burrows may show a

bias in favour of *G. m. morsitans* that is a function of temperature. Artificial warthog burrows provide a convenient way of studying the puparial stage in tsetse and for the first time facilitate the capture of females as they deposit their larvae.

13314 **Ouma, J.O., Marquez, J.G. & Krafsur, E.S., 2005.** Macrogeographic population structure of the tsetse fly, *Glossina pallidipes* (Diptera : Glossinidae). *Bulletin of Entomological Research*, **95** (5): 437–447.

Krafsur: Department of Entomology, Iowa State University, Ames, IA 50011, USA.

Tsetse flies are confined to sub-Saharan Africa where they occupy discontinuous habitats. In anticipation of area-wide control programmes, estimates of gene flow among tsetse populations are necessary. Genetic diversities were partitioned at eight microsatellite loci and five mitochondrial loci in 21 *Glossina pallidipes* populations. At microsatellite loci, Nei's unbiased gene diversity averaged over loci was 0.659 and the total number of alleles was 214, only four of which were shared among all populations. The mean number of alleles per locus was 26.8. Random mating was observed within but not among populations (fixation index F_{ST}=0.18) and 81 percent of the genetic variance was within populations. Thirty-nine mitochondrial variants were detected. Mitochondrial diversities in populations varied from 0 to 0.85 and averaged 0.42, and F_{ST}=0.51. High levels of genetic differentiation were characteristic, extending even to subpopulations separated by tens and hundreds of kilometres, and indicating low rates of gene flow.

3. TSETSE CONTROL (INCLUDING ENVIRONMENTAL SIDE EFFECTS)

[See also **28**: nos. 13288, 13299, 13319]

13315 **Bastiaensen, P., Kouagou, N.T., Gnofam, M., Batawui, K., Napala, A. & Hendrickx, G., 2004.** Adoption d'une nouvelle technique de contrôle de la mouche tsétsé par des éleveurs du nord du Togo: considérations socio-économiques. [Acquisition of a new tsetse fly control technique by farmers of the north of Togo: socio-economic aspects.] *Bulletin of Animal Health and Production in Africa*, **52** (3): 142–158.

Hendrickx: Projet régional FAO de lutte contre la trypanosomose animale, Direction nationale, B.P. 114, Sokodé, Togo.

This document comments on an approach of integrated AAT control through vector control (tsetse control), a technique which requires concerted action and the cooperation of the farmers. The results recorded between 1997 and 1999 showed that the method was never 100 percent accepted (between 3 percent and 67 percent). The organisation of livestock owners in time (synchronisation) and space (adherence) was problematic. Cattle numbers, as well as economic constraints, forced stockholders to adapt the technology in terms of lower frequency of treatment, a weaker synchronisation and/or a smaller

coverage of the herd. Factors such as the importance of animal traction, the relationships between stockholders, their knowledge of the disease and of the insecticides available, as well as the importance farmers attach to tick control and the health status of their animals were important in determining acceptance of the control method. General veterinary expenses decreased by 43 percent, cattle numbers increased by 28 percent. The latter was a result of increased trading and influx of cattle herds into the controlled areas. This campaign has hardly been an overall success, but offers nevertheless an interesting insight into socio-cultural and economic mechanisms which contribute to the farmers' decision to accept or reject a new technology.

13316 **Riehle, M.A. & Jacobs-Lorena, M., 2005.** Using bacteria to express and display anti-parasite molecules in mosquitoes: current and future strategies. *Insect Biochemistry and Molecular Biology*, **35** (7): 699–707.

Riehle: Department of Molecular Microbiology & Immunology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA.

Vector-borne diseases impose enormous health and economical burdens throughout the world. Unfortunately, as insecticide and drug resistance spread, these burdens will increase unless new control measures are developed. Genetically modifying vectors to be incapable of transmitting parasites is one possible control strategy and much progress has been made towards this goal. Numerous effector molecules have been identified that interfere with parasite development in its insect vectors, and techniques for transforming the vectors with genes encoding these molecules have been established. While the ability to generate refractory vectors is close at hand, a mechanism for replacing a wild vector population with a refractory one remains elusive. This review examines the feasibility of using bacteria to deliver the anti-parasitic effector molecules to wild vector populations. The first half briefly examines paratransgenic approaches currently being tested in both the triatomine bug and tsetse fly. The second half explores the possibility of using midgut bacteria to control malaria transmission by *Anopheles* mosquitoes.

13317 **Schofield, C.J. & Patterson, J.S., 2005.** Preparing for tsetse eradication. *South African Journal of Science*, **101** (3–4): 116.

Schofield: Department of Infectious and Tropical Disease, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK.

13318 **Vale, G.A. & Torr, S.J., 2005.** User-friendly models of the costs and efficacy of tsetse control: application to sterilizing and insecticidal techniques. *Medical and Veterinary Entomology*, **19** (3): 293–305.

Vale: 93 Chase, Mount Pleasant, Harare, Zimbabwe

An interactive programme, incorporating a deterministic model of tsetse populations, was developed to predict the cost and effect of different control techniques applied singly or together. Its value was exemplified by using it to compare: (i) the sterile insect technique (SIT), involving weekly releases optimized at three sterile males for each wild male, with (ii) the use of insecticide-treated cattle (ITC) at 3.5/km^2. The isolated pre-treatment population of adults was 2 500 males and 5 000 females/km^2. If the population was reduced by 90 percent, its growth potential was 8.4 times per year. However, the population expired naturally when it was reduced to 0.1 wild male/km^2 due to difficulties in finding mates, so that control measures could then be stopped. This took 187 days with ITC and 609 days with SIT. If ITC was used for 87 days to suppress the population by 99 percent, subsequent control by SIT alone took 406 days; the female population increased by 48 percent following the withdrawal of ITC and remained above the immediate post-suppression level for 155 days; the vectorial capacity initially increased seven times and remained above the immediate post-suppression level for 300 days. Combining SIT and ITC after suppression was a little faster than ITC alone, provided the population had not been suppressed by more than 99.7 percent. Even when SIT was applied under favourable conditions, the most optimistic cost estimate was 20–40 times greater than for ITC. Modelling non-isolated unsuppressed populations showed that tsetse invaded ~8 km into the ITC area compared to ~18 km for SIT. There was no material improvement to be obtained by using a 3 km barrier of ITC to protect the SIT area. In general, tsetse control by increasing deaths is more appropriate than reducing births, and SIT is particularly inappropriate. User-friendly models can assist the understanding and planning of tsetse control. The model, freely available via http://www.tsetse.org, allows further exploration of control strategies with user-specified assumptions.

4. EPIDEMIOLOGY: VECTOR-HOST AND VECTOR-PARASITE INTERACTIONS

[See also **28**: nos. 13298, 13299, 13309, 13316, 13330, 13334]

13319 **Aksoy, S. & Rio, R.V.M., 2005.** Interactions among multiple genomes: tsetse, its symbionts and trypanosomes. *Insect Biochemistry and Molecular Biology*, **35** (7): 691–698.

Aksoy: Department of Epidemiology and Public Health, Yale University School of Medicine, 60 College St., 606 LEPH, New Haven, CT 06510, USA.

Insect-borne diseases exact a high public health burden and have a devastating impact on livestock and agriculture. To date, control has proved to be exceedingly difficult. One such disease that has plagued sub-Saharan Africa is caused by the protozoan African trypanosomes (*Trypanosoma* spp.) and transmitted by tsetse flies. This presentation describes the biology of the tsetse fly and its interactions with trypanosomes as well as its symbionts. Tsetse can harbour up to three distinct microbial symbionts,

including two enterics (*Wigglesworthia glossinidia* and *Sodalis glossinidius*) as well as facultative *Wolbachia* infections, which influence host physiology. Recent investigations into the genome of the obligate symbiont *Wigglesworthia* have revealed characteristics indicative of its long co-evolutionary history with the tsetse host species. Comparative analysis of the commensal-like *Sodalis* with free-living enterics provides examples of adaptations to the host environment (physiology and ecology), reflecting genomic tailoring events during the process of transitioning into a symbiotic lifestyle. From an applied perspective, the extensive knowledge accumulated on the genomic and developmental biology of the symbionts coupled with our ability to both express foreign genes in these microbes *in vitro* and repopulate tsetse midguts with these engineered microbes now provides a means to interfere with the host physiological traits which contribute to vector competence promising a novel tool for disease management.

13320 **Dagnogo, M., Traore, G. & Souleymane, F., 2004.** Determination of sleeping sickness transmission risk areas from trypanosome infection rates of tsetse flies in Daloa, Côte d'Ivoire. *International Journal of Tropical Insect Science*, **24** (2): 170–176.

Dagnogo: Université d'Abobo Adjamé, UFR SN, 02 BP 801 Abidjan 02, Côte d'Ivoire.

A study was carried out for four years in the forest area of Daloa in Côte d'Ivoire to assess the rate of trypanosome infection in tsetse, and thereby the trypanosomiasis infection risk. In different *Glossina* biotopes, 18 908 *Glossina palpalis palpalis* were caught with Vavoua traps and were dissected. The most widespread species of trypanosomes infecting the *Glossina* was *Trypanosoma congolense* (7.63 percent) followed by *T. vivax* (4.50 percent). *Trypanosoma brucei*, the trypanosome responsible for animal and human African trypanosomiasis (HAT), was found only in 34 of the tsetse flies collected, and it had a very low infection rate (0.18 percent). Although infected tsetse flies were captured in all habitats examined, the infection rate was relatively higher along footpaths (0.44 percent), in farms (0.20 percent) and around forested water springs (0.27 percent) compared to the edge of villages (0.06 percent) and forest borders (0.05 percent). Among the 34 tsetse flies infected with *T. brucei*, only 0.05 percent had parasites exclusively in their salivary glands. Our results suggest that footpaths, plantations of coffee and cocoa and forested water springs are potential biotopes where the risk of infection by *T. brucei* is most important. The anthropophily of *Glossina* associated with the relatively high number of parasites in these sites could be the reason why the disease is endemic in Daloa today. In our study, female *Glossina* were infected more frequently with trypanosomes (0.14 percent) than males (0.04 percent) and generally, females lived longer than males. It is likely that the longevity of females, which carry parasites, is the major cause for the endemicity of HAT in this locality.

13321 **Malele, I., Craske, L., Knight, C., Ferris, V., Njiru, Z., Hamilton, P., Lehane, S., Lehane, M. & Gibson, W., 2003.** The use of specific and generic primers to identify trypanosome infections of wild tsetse flies in Tanzania by PCR. *Infection, Genetics and Evolution*, **3** (4): 271–279.

Gibson: School of Biological Sciences, University of Bristol, Bristol BS8 1UG, UK

The accurate identification of trypanosome species and subspecies remains a challenging task in the epidemiology of human and animal trypanosomiasis in tropical Africa. Currently, there are specific PCR tests to identify about ten different species, subspecies or subgroups of African tsetse-transmitted trypanosomes. These PCR tests have been used here to identify trypanosomes in four species of tsetse (*Glossina brevipalpis*, *G. pallidipes*, *G. swynnertoni*, *G. morsitans morsitans*) from two areas of Tanzania. PCR using species-specific primers was performed on 1 041 dissection-positive proboscides, giving an overall positive identification in 254 (24 percent). Of these, 61 proboscides (24 percent) contained two or more trypanosomes. The trypanosome with the greatest overall prevalence at both field sites was *Trypanosoma simiae* Tsavo, which was identified in a total of 118 infected tsetse proboscides (46 percent). At Pangani, *T. godfreyi* was found in *G. pallidipes* but not in *G. brevipalpis*, suggesting that these flies might have different susceptibility to this trypanosome or might have fed on a different range of hosts. A high proportion (about 75 percent) of trypanosome infections remained unidentified. To investigate the identity of these unidentified samples, we used primers complementary to the conserved regions of trypanosomal small subunit ribosomal RNA (ssu rRNA) genes to amplify variable segments of the gene. Amplified DNA fragments were cloned, sequenced and compared with ssu rRNA genes on the database of known trypanosome species. In this way, we have tentatively identified two new trypanosomes: a trypanosome related to *Trypanosoma vivax* and a trypanosome related to *T. godfreyi*. The *T. godfreyi*-related trypanosome occurred frequently in the Tanzanian field samples and appears to be widespread. Molecular identification of these two new trypanosomes should now facilitate their isolation and full biological characterisation.

13322 **de la Rocque, S., 2003.** Épidémiologie des trypanosomoses africaines. Analyse et prévision du risque dans des paysages en transformation. [Epidemiology of African trypanosomes. Analysis and forecasting of risk in changing landscapes]. *Courrier de l'Environnement de l'INRA*, **49**: 80–86.

de la Rocque: CIRAD, BP 5035, 34032 Montpellier cedex 1, France. [stephane.de_la_rocque@cirad.fr]

In the course of work on trypanosomiasis in Sideradougou, Burkino Faso, in 1996, two species of tsetse were captured, *Glossina tachinoides* and *G. palpalis gambiensis*. Notes were made on the epidemiology of this agro-pastoral area, with reference to grazing areas, potential transmission sites for the disease, environmental dynamics and health risks.

13323 **Schukken, Y.H., van Schaik, G., McDermott, J.J., Rowlands, G.J., Nagda, S.M., Mulatu, W. & d'Ieteren, G.D.M., 2004.** Transition models to assess risk factors for new and persistent trypanosome infections in cattle – analysis

of longitudinal data from the Ghibe Valley, Southwest Ethiopia. *Journal of Parasitology*, 90 (6): 1279–1287.

Schukken: Department of Population Medicine and Diagnostic Sciences, S3119 Schurmann Hall, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA. [yhs@cornell.edu]

The objective of this study was to apply transition models to distinguish between factors associated with both incident and persistent trypanosome infections. Data collected from 1 561 cattle were analyzed from a long-term study involving eight herds in which both trypanosome infections (a total of 56 931 cattle sampling-months) and tsetse (*Glossina* spp.) challenge were monitored monthly from March 1986 to March 1998. Both pour-on and insecticide-target tsetse control programmes and mass treatment with diminazene aceturate before tsetse control were associated with significant decreases in both incidence and persistence of trypanosome infection relative to noncontrol periods, as were seasonal and sex effects. The magnitudes of the effects were, however, often different for new and persistent infections. For persistence of infection, there were two trends. In general, the duration of infection increased during the study, despite the regular treatment with diminazene aceturate. The transition model had two major benefits. The first was to identify an increasing duration of infections with time, taking into account other factors associated with increasing infection risk. The second was to highlight different patterns in the effects of certain factors on new and persistent trypanosome infections.

13324 **Van den Bossche, P., Ky-Zerbo, A., Brandt, J., Marcotty, T., Geerts, S. & De Deken, R., 2005.** Transmissibility of *Trypanosoma brucei* during its development in cattle. *Tropical Medicine and International Health*, **10** (9): 833–839.

Van den Bossche: Department of Veterinary Medicine, Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium. [pvdbossche@itg.be]

Recent outbreaks of *Trypanosoma brucei rhodesiense* sleeping sickness in Soroti District of eastern Uganda have demonstrated the important role cattle can play as reservoirs of this parasite. To clarify the epidemiological importance of the cattle reservoir, experiments were conducted to determine the ease with which *T. brucei* is transmitted during the course of its development in Friesian cattle. The development of *T. brucei* in cattle is characterized by an acute phase with high levels of parasitaemia and a decline in PCV. The acute phase is followed by a chronic phase during which the PCV remains low but stable and the parasitaemia is low. Parasites are often difficult to detect using parasitological diagnostic tools during this chronic phase. Challenge of chronically infected cattle with *T. congolense* results in a sudden increase in the *T. brucei* parasitaemia. Despite significant differences in parasitaemia, the proportion of tsetse flies that developed metacyclic infections after a first bloodmeal on the infected cattle did not differ significantly between the acute and chronic phases or the phase of mixed *T. b.*

brucei/*T. congolense* infection. This suggests that, throughout the observation period, the parasitaemia was above the threshold above which infection rates of tsetse are independent of the parasitaemia. The repercussions of the research findings for the understanding of the epidemiology, spread and the control of *T. b. rhodesiense* sleeping sickness are discussed.

5. HUMAN TRYPANOSOMIASIS

(a) SURVEILLANCE

13325 **Chappuis, F., Loutan, L., Simarro, P., Lejon, V. & Büscher, P., 2005.** Options for field diagnosis of human African trypanosomiasis. *Clinical Microbiology Reviews*, **18** (1): 133–146.

Chappuis: Travel and Migration Medicine Unit, Geneva University Hospital, 24 rue Micheli-du-Crest, 1211 Geneva 14, Switzerland. [francois.chappuis@hcuge.ch]

Human African trypanosomiasis (HAT) due to *Trypanosoma brucei gambiense* or *T. b. rhodesiense* remains highly prevalent in several rural areas of sub-Saharan Africa and is lethal if left untreated. Therefore, accurate tools are absolutely required for field diagnosis. For *T. b. gambiense* HAT, highly sensitive tests are available for serological screening but the sensitivity of parasitological confirmatory tests remains insufficient and needs to be improved. Screening for *T. b. rhodesiense* infection still relies on clinical features in the absence of serological tests available for field use. Ongoing research is opening perspectives for a new generation of field diagnostics. Also essential for combating both forms of HAT is accurate determination of the disease stage because of the high toxicity of melarsoprol, the drug most widely used during the neurological stage of the illness. Recent studies have confirmed the high accuracy of raised immunoglobulin M levels in the cerebrospinal fluid for the staging of *T. b. gambiense* HAT, and a promising simple assay (LATEX/IgM) is being tested in the field. Apart from the urgent need for better tools for the field diagnosis of this neglected disease, improved access to diagnosis and treatment for the population at risk remains the greatest challenge for the coming years.

13326 **Chappuis, F., Stivanello, E., Adams, K., Kidane, S., Pittet, A. & Bovier, P.A., 2004.** Card agglutination test for trypanosomiasis (CATT) end-dilution titer and cerebrospinal fluid cell count as predictors of human African trypanosomiasis (*Trypanosoma brucei gambiense*) among serologically suspected individuals in Southern Sudan. *American Journal of Tropical Medicine and Hygiene*, **71** (3): 313–317.

Chappuis: Médecins Sans Frontières, Swiss Section, Rue de Lausanne 78, 1203 Geneva, Switzerland. [francois.chappuis@hcuge.ch]

The diagnosis of human African trypanosomiasis (HAT) due to *Trypanosoma brucei gambiense* relies on an initial serologic screening with the card agglutination test for trypanosomiasis (CATT) for *T. b. gambiense*, followed by parasitologic confirmation in most endemic areas. Unfortunately, field parasitologic methods lack sensitivity and the management of serologically suspected individuals (i.e., individuals with a positive CATT result but negative parasitology) remains controversial. In Kajo-Keji County in southern Sudan, we prospectively collected sociodemographic and laboratory data of a cohort of 2 274 serologically suspected individuals. Thirty-three percent (n = 749) attended at least one follow-up visit and HAT was confirmed in 64 (9 percent) cases. Individuals with lower initial CATT-plasma (CATT-P) end-dilution titres had lowest risks (10.4 and 13.8/100 person-years for 1:4 and 1:8 titres, respectively) that significantly increased for higher dilutions: relative risks = 5.1 and 4.6 for 1:16 and 1:32 titres, respectively. The cumulative yearly risk was also high (76 percent) in individuals found with 11–20 cells in the cerebrospinal fluid, but this involved only eight patients. Adjustment for potential confounders did not affect the results. In conclusion, treatment with pentamidine should be considered for all serologically suspected individuals with a CATT-P end-dilution titre ≥1:16 in areas of a moderate to high prevalence of HAT.

13327 **Fèvre, E.M., Picozzi, K., Fyfe, J., Waiswa, C., Odiit, M., Coleman, P.G. & Welburn, S.C., 2005.** A burgeoning epidemic of sleeping sickness in Uganda. *Lancet*, **366** (9497): 745–747.

Fèvre: Centre for Tropical Veterinary Medicine, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Roslin, Midlothian EH25 9RG, UK. [Eric.Fevre@ed.ac.uk]

The epidemic of *Trypanosoma brucei rhodesiense* sleeping sickness in eastern Uganda, which began in 1998 as a result of movements of the livestock reservoir of the parasite, has continued to spread. An additional 133 000 people have been put at risk of infection in Kaberamaido, another newly affected district. The few resources committed to control interventions in Soroti district have failed to contain the epidemic. The high prevalence of the parasite in cattle presents a significant risk for transmission to human beings and further spread of this neglected zoonotic disease. Targeted interventions are urgently needed to control epidemics and reduce the high mortality resulting from sleeping sickness.

13328 **Lutumba, P., Robays, J., Bilenge, C.M.M., Mesu, V.K.B.K., Molisho, D., Declercq, J., Van der Veken, W., Meheus, F., Jannin, J. & Boelaert, M., 2005.** Trypanosomiasis control, Democratic Republic of Congo, 1993-2003. *Emerging Infectious Diseases*, **11** (9): 1382–1388.

Boelaert: Institute of Tropical Medicine, Antwerp, Belgium.

In the Democratic Republic of Congo (DRC), human African trypanosomiasis (HAT) reached unprecedented levels in the 1990s. To assess recent trends and evaluate control efforts, we analyzed epidemiological and financial data collected by all agencies

involved in HAT control in DRC from 1993 to 2003. Funds allocated to HAT control and to the screening of populations, doubled from 1993 to 1997 and from 1998 to 2003. The number of cases detected decreased from 26 000 new cases per year in 1998 to 11 000 in 2003. Our analysis shows that HAT control in DRC is almost completely dependent on international aid and that sudden withdrawal of such aid in 1990 had a long-lasting effect. Since 1998, control efforts intensified because of renewed donor interest, including a public-private partnership, and this effort led to a major reduction in HAT incidence. To avoid re-emergence of this disease, such efforts should be sustained.

13329 **MacLean, L., Chisi, J.E., Odiit, M., Gibson, W.C., Ferris, V., Picozzi, K. & Sternberg, J.M., 2004.** Severity of human African trypanosomiasis in East Africa is associated with geographic location, parasite genotype, and host inflammatory cytokine response profile. *Infection and Immunity*, **72** (12): 7040–7044.

Sternberg: School of Biological Sciences, University of Aberdeen, Zoology Building, Aberdeen AB24 2TZ, UK. [j.sternberg@abdn.ac.uk]

The mechanisms underlying virulence in human African trypanosomiasis are poorly understood, although studies with experimental mice suggest that unregulated host inflammatory responses are associated with disease severity. We identified two trypanosomiasis foci with dramatically different disease virulence profiles. In Uganda, infections followed an acute profile with rapid progression to the late stage (meningoencephalitic infection) in the majority of patients (86.8 percent). In contrast, infections in Malawi were of a chronic nature, in which few patients progressed to the late stage (7.1 percent), despite infections of several months' duration. All infections were confirmed to be *Trypanosoma brucei rhodesiense* by testing for the presence of the serum resistance-associated (*SRA*) gene, but trypanosomes isolated from patients in Uganda or Malawi were distinguished by an *SRA* gene polymorphism. The two disease profiles were associated with markedly different levels of tumour necrosis factor alpha (TNF-α) and transforming growth factor β (TGF-β) in plasma. In Uganda but not Malawi early-stage TNF-α was elevated, while in Malawi but not Uganda early-stage TGF-β was elevated. Thus, rapid disease progression in Uganda is associated with TNF-α-mediated inflammatory pathology, whereas in the milder disease observed in Malawi this may be ameliorated by counterinflammatory cytokines. These differing host responses may result either from differing virulence phenotypes of northern and southern trypanosomes or from immune response polymorphisms in the different host populations.

13330 **Odiit, M., Coleman, P.G., Liu, W.C., McDermott, J.J., Fèvre, E.M., Welburn, S.C. & Woolhouse, M.E.J., 2005.** Quantifying the level of under-detection of *Trypanosoma brucei rhodesiense* sleeping sickness cases. *Tropical Medicine and International Health*, **10** (9): 840–849.

Odiit: London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK.

To formally quantify the level of under-detection of *Trypanosoma brucei rhodesiense* sleeping sickness (SS) during an epidemic in Uganda, a decision tree (under-detection) model was developed. Concurrently, in order to quantify the subset of undetected cases that sought health care but were not diagnosed, a deterministic (subset) model was developed. The values of the under-detection model parameters were estimated from previously published records of the duration of symptoms prior to presentation and the ratio of early to late stage cases in 760 SS patients presenting at LIRI hospital, Tororo, Uganda during the 1988–1990 epidemic of SS. For the observed early to late stage ratio of 0.47, we estimate that the proportion of under-detection in the catchment area of LIRI hospital was 0.39 (95 percent CI 0.37–0.41) i.e. 39 percent of cases are not reported. Based on this value, it is calculated that for every one reported death of SS, 12.0 (95 percent CI 11.0–13.0) deaths went undetected in the LIRI hospital catchment area, i.e. 92 percent of deaths are not reported. The deterministic (subset) model constructed on the possible routes that might be taken by an SS infection to diagnosis or death, within the health system or not, showed that of a total of 73 undetected deaths, 62 (CI 60–64) (85 percent) entered the healthcare system but were not diagnosed, and 11 (CI 11–12) died without seeking health care from a recognized health unit. The measure of early to late stage presentation provides a tractable measure to determine the level of rhodesiense SS under-detection and to gauge the effects of interventions aimed at increasing treatment coverage.

13331 **Oury, B., Jamonneau, V., Tibayrenc, M. & Truc, P., 2004.** Characterization of *Trypanosoma brucei gambiense* stocks isolated from humans by RAPD fingerprinting in Côte d'Ivoire: another evidence for multiple infections. *African Journal of Biotechnology*, **3** (1): 94–98.

Truc: Institut de Recherche pour le Développement (IRD), Unité de recherche 165 "Génétique et Evolution des Maladies Infectieuses" UMR CNRS/IRD 2724, BP 64501 34394 Montpellier Cedex 5, France.

Trypanosoma brucei gambiense was isolated twice from each of 23 patients in Côte d'Ivoire. Genetic characterization using RAPD (Random Primed Amplified Polymorphic DNA) showed additional variability within a given isoenzyme profile (zymodeme), confirming that this fingerprinting method has a higher discriminative power (faster molecular clock) than isoenzymes. RAPD confirmed also the evidence of multiple infections by different genotypes in the same patient despite a low genetic variability among *Trypanosoma brucei gambiense* stocks. The involvement of this phenomenon in treatment failure is discussed.

13332 **Stewart, M.L., Krishna, S., Burchmore, R.J.S., Brun, R., de Koning, H.P., Boykin, D.W., Tidwell, R.R., Hall, J.E. & Barrett, M.P., 2005.** Detection of arsenical drug resistance in *Trypanosoma brucei* with a simple fluorescence test. *Lancet*, **366** (9484): 486–487.

Barrett: University of Glasgow, Division of Infection and Immunity, Institute of Biomedical and Life Sciences, The Joseph Black Building, Glasgow G12 8QQ, UK. [m.barrett@bio.gla.ac.uk]

The resurgence of human African trypanosomiasis (HAT), coupled with an increased incidence of drug resistance, is of concern. We report a quick, simple, and sensitive test for identification of parasites resistant to melarsoprol, the main drug used to treat late stage HAT. Resistant parasites are defective in a plasma membrane transporter responsible for drug uptake. The same transporter carries the fluorescent diamidine DB99 (2,5-bis-(4-amidinophenyl)-3,4-dimethylfuran) into trypanosomes. The two DNA-containing structures in the trypanosome, the nucleus and the kinetoplast, begin to fluoresce within 1 min of introduction of DB99, unless the trypanosome is drug resistant.

13333 **Truc, P., Jamonneau, V. & Guegan, J.F., 2005.** Confirmation of the use of latex IgM on cerebrospinal fluid for improving stage determination of human African trypanosomiasis. *African Journal of Biotechnology*, **4** (6): 517–521.

Truc: Institut de Recherche pour le Développement, UR177 "Trypanosomoses Africaines", Campus international de Baillarguet, IRD/CIRAD, TA 207/G 34 398 Montpellier Cedex 5, France. [truc@ird.fr]

The clinical evolution of the chronic form of human African trypanosomiasis starts with the haematolymphatic or first stage (P1). The meningoencephalitic or second stage (P2) begins when trypanosomes reach the cerebrospinal fluid (CSF). The classical stage determination method is based on CSF cell count, CSF protein concentration and/or the presence of trypanosomes detected in CSF. However, their cut-off values and the sensitivity of detection of trypanosomes in CSF remains doubtful while the appropriate treatment depends on this determination of disease stage. Thus, the classical stage determination was reconsidered using new serological tests, and results were compared to clinical data. Thirty eight patients diagnosed with African trypanosomiasis between 1996 and 1998 in Côte d'Ivoire, were classified into four clinical groups according to the observed degree of severity of neuropsychiatric signs. Based on multivariate analysis evaluating the relevance of the new serological tests, it was confirmed that latex IgM CSF was cheap, easy to perform under field conditions, and might improve the stage determination of the disease.

(b) PATHOLOGY AND IMMUNOLOGY

13334 **Blum, J., Beck, B.R., Brun, R. & Hatz, C., 2005.** Clinical and serologic responses to human 'apathogenic' trypanosomes. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **99** (10): 795–797.

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We describe a female patient suffering from a benign self-healing febrile disease with strongly positive serology for *Trypanosoma brucei*. The patient showed a clinical picture with similarities to that of human African trypanosomiasis (HAT). HAT due to *T. b. gambiense* and *T. b. rhodesiense* were ruled out. We performed serologic tests because the patient was worried about HAT after receiving tsetse bites. The possibilities of an infection with human 'apathogenic' trypanosomes such as *T. b. brucei*, *T. congolense* or *T. vivax* are discussed.

13335 **Köhler, W. & Köhler, M., 2002.** Zentralblatt für Bakteriologie – 100 years ago: Sleeping sickness – Intoxication or infectious disease? *International Journal of Medical Microbiology*, **292** (3–4): 141–147.

Köhler: Adolf-Reichwein-Str. 26, D-07745 Jena, Germany.

13336 **Mansfield, J.M. & Paulnock, D.M., 2005.** Regulation of innate and acquired immunity in African trypanosomiasis. *Parasite Immunology*, **27** (10–11): 361–371.

Mansfield: Department of Bacteriology, University of Wisconsin-Madison, Madison, WI 53706, USA. [jmm@bact.wisc.edu]

African trypanosomes are well known for their ability to avoid immune elimination by switching the immunodominant variant surface glycoprotein (VSG) coat during infection. However, antigenic variation is only one of several means by which trypanosomes manipulate the immune system of their hosts. In this article, the role of parasite factors such as GPI anchor residues of the shed VSG molecule and the release of CpG DNA, in addition to host factors such as IFN-γ, in regulating key aspects of innate and acquired immunity during infection is examined. The biological relevance of these immunoregulatory events is discussed in the context of host and parasite survival.

13337 **Matovu, E., Stewart, M.L., Geiser, F., Brun, R., Mäser, P., Wallace, L.J.M., Burchmore, R.J., Enyaru, J.C.K., Barrett, M.P., Kaminsky, R., Seebeck, T. & de Koning, H.P., 2003.** Mechanisms of arsenical and diamidine uptake and resistance in *Trypanosoma brucei*. *Eukaryotic Cell*, **2** (5): 1003–1008.

De Koning: Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow G12 8QQ, UK.

Sleeping sickness, caused by *Trypanosoma brucei* spp., has become resurgent in sub-Saharan Africa. Moreover, there is an alarming increase in treatment failures with melarsoprol, the principal agent used against late-stage sleeping sickness. In *T. brucei*, the uptake of melarsoprol as well as diamidines is thought to be mediated by the P2 aminopurine transporter, and loss of P2 function has been implicated in resistance to these agents. The trypanosomal gene *TbAT1* has been found to encode a P2-type transporter when expressed in yeast. Here we investigate the role of *TbAT1* in drug uptake and drug resistance in *T. brucei* by genetic knockout of *TbAT1*. *TbAT1*-null

trypanosomes were deficient in P2-type adenosine transport and lacked adenosine-sensitive transport of pentamidine and melaminophenyl arsenicals. However, the null mutants were only slightly resistant to melaminophenyl arsenicals and pentamidine, while resistance to other diamidines such as diminazene was more pronounced. Nevertheless, the reduction in drug sensitivity might be of clinical significance, since mice infected with *TbAT1*-null trypanosomes could not be cured with 2 mg of melarsoprol/kg of body weight for four consecutive days, whereas mice infected with the parental line were all cured by using this protocol. Two additional pentamidine transporters, HAPT1 and LAPT1, were still present in the null mutant, and evidence is presented that HAPT1 may be responsible for the residual uptake of melaminophenyl arsenicals. High-level arsenical resistance therefore appears to involve the loss of more than one transporter.

13338 **Nikolskaia, O., Lee, S.H., Paul, K., Barat, N., Dumler, J.S., Kim, Y.V., Kim, K.S. & Grab, D.J., 2004.** Interaction of GFP-labeled human infective African trypanosomes with human brain microvascular endothelial cells (HBMEC). *Molecular Biology of the Cell*, **15** (Suppl.): 463a.

Grab: Pediatric Infectious Diseases, John Hopkins University, Baltimore MD, USA.

Experimental details are given of a laboratory model for studying the entry of trypanosomes into epithelial cells of the human blood brain barrier, using fluorescent microscopy.

(c) TREATMENT

[See also **28**: nos. 13293, 13332, 13337]

13339 **Chappuis, F., Udayraj, N., Stietenroth, K., Meussen, A. & Bovier, P.A., 2005.** Eflornithine is safer than melarsoprol for the treatment of second-stage *Trypanosoma brucei gambiense* human African trypanosomiasis. *Clinical Infectious Diseases*, **41** (5): 748–751.

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Patients with second-stage human African trypanosomiasis treated with eflornithine (n = 251) in 2003 in Kiri, southern Sudan, had an adjusted relative risk of death of 0.2 and experienced significantly fewer cutaneous and neurological adverse effects than did patients who were treated with melarsoprol in 2001 and 2002 (n = 708).

13340 **Dardonville, C., 2005.** Recent advances in antitrypanosomal chemotherapy: patent literature 2002-2004. *Expert Opinion on Therapeutic Patents*, **15** (9): 1241–1257.

Dardonville: CSIC, Juan Cierva 3, Madrid, Spain.

Sleeping sickness and Chagas' disease (African and American trypanosomiases, respectively) are protozoan parasitic diseases threatening millions of people in sub-Saharan Africa and Latin America. Trypanosomiases are among the most neglected diseases in the world, desperately lacking financial support for investigation. The current chemotherapy of both diseases is poor and suffers from intolerable side effects and low efficacy in many cases. A review of the patent literature from 2002 to early 2005 claiming molecules with anti-trypanosomal activity afforded 36 entries, equally shared between industry and acadaemia. Among the targets validated against trypanosomes, patents dealing with protease inhibitors were the most represented (16 patents). Other targets claimed in the patent literature included membrane architecture (sterol biosynthesis inhibitors, protein farnesyltransferase inhibitors), DNA (DNA binders, tubulin inhibitors) and pyrimidine metabolism (cytidine triphosphate [CTP] synthetase inhibitors). Natural products were also a great source of trypanocidal lead compounds (9 patents). A few patents claiming compounds with antitrypanosomal activity, but disclosing no specific target, were also encountered.

13341 **Likeufack, C.L., Tongue, L.K. & Truc, P., 2003.** *In vitro* activity of commercial formulation and active principle of trypanocidal drugs against bloodstream forms of *Trypanosoma brucei gambiense*. *African Journal of Biotechnology*, **2** (11): 474–476.

Truc: Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale (OCEAC), Départment de Recherche et de Lutte contre la Trypanosomose humaine africaine, BP 288, Yaounde, Cameroon. [truc@iccnet.cm]

The *in vitro* trypanocidal activities of four commercial formulations Ornidyl®, Pentamidine isethionate®, Germanin® and Lampit® and their corresponding active principles (Dl-difluoromethylornithine, pentamidine isethionate, suramine and 5-nitrofuran) were compared against *Trypanosoma brucei gambiense*. Differences of minimum inhibitory concentration (MIC) were observed between Ornidyl® and Dl-difluoromethylornithine and between Lampit® and 5-nitrofuran. For RO 15 strain and the comparison of Ornidyl®/DFMO, the MIC when using the commercial drug was more than twice the MIC value obtained with the active principle. For all three trypanosome strains, MICs were identical for Lampit® and 5-nitrofuran but the MIC with the commercial formulation was twice the MIC obtained with the active principle. The active principles, rather than commercial formulations, should be used for standardization of *in vitro* assay protocols.

6. ANIMAL TRYPANOSOMIASIS

(a) SURVEY AND DISTRIBUTION

[See also **28**: nos. 13323, 13328]

13342 **Maikaje, D.B., 2002.** An outbreak of biting flies and bovine trypanosomosis in Kaura L.G.A., Kaduna State, Nigeria. *West African Journal of Biological Sciences*, **13**: 56–65.

Maikaje: Department of Biological Sciences, Nigerian Defence Academy, PMB 2109, Kaduna, Nigeria.

Dry and rainy seasons surveys were carried out in Kaura Local Government Area of Kaduna State to verify a newspaper report of outbreaks of tsetse flies leading to a mass exodus of Fulanis and their livestock from the area. The most abundant tsetse species caught with the biconical and NiTse traps was *Glossina palpalis* followed by *G. tachinoides*. Other biting flies caught were *Stomoxys calcitrans*, *Haematotopa* spp. and *Tabanus* spp. More biting flies were caught during the rainy season than during the dry season. The prevalence of bovine trypanosomosis determined parasitologically and with the ELISA were 17.3 percent and 49.4 percent respectively in the dry season and 53.0 percent and 63.5 percent respectively during the rainy season. Single *Trypanosoma brucei* infections were the most commonly observed, followed by single and mixed *T. congolense* and *T. vivax* infections in the cattle examined during these surveys in Kaura LGA. During a pilot study in this area, complete cure of all trypanosome-infected cattle was achieved with diminazene aceturate treatment and large numbers of biting flies were caught with biconical and NiTse traps. These observations suggest that the use of these measures may effectively control bovine trypanosomosis and its vectors and enhance livestock development and growth in Kaura LGA.

13343 **Okoli, I.C., 2003.** Incidence and modulating effects of environmental factors on trypanosomosis, peste des petit ruminants (PPR) and bronchopneumonia of West African dwarf goats in Imo State, Nigeria. *Livestock Research for Rural Development*, **15** (9): article 6.

Okoli: Tropical Animal Health and Production Research Laboratory, Department of Animal Science and Technology, Federal University of Technology, PMB 1526, Owerri, Imo State, Nigeria. [dr_charleso@yahoo.com]

Clinical records of natural infections of trypanosomiasis, peste des petit ruminants (PPR) and bronchopneumonia among West African Dwarf (WAD) goats brought for treatment at government veterinary clinics in Imo State, Nigeria were scrutinized for three years (1999–2001) in order to determine disease trends and modulating effects of

rainfall, relative humidity and mean daily air temperature on disease occurrence. Of the 26 763 such cases, 14 824 (55.4 percent) were due to trypanosomiasis, while 25.09 percent (6 714) and 19.5 percent (5 225) were accounted for by bronchopneumonia and PPR respectively, indicating a significantly lower treatment figure for PPR. Overall, treatment figures across four seasons stayed above 6 000 cases per season. However, the 4 375 (29.5 percent) cases of trypanosomiasis recorded during early dry season were significantly higher than those of other seasons. Treatment means for PPR (22.8 percent) during late wet season and late dry season figures for bronchopneumonia (33.5 percent) were significantly higher than those of other seasons. Simple correlation matrix of mean monthly disease occurrence showed that trypanosomiasis and bronchopneumonia tended to vary together 41.0 percent of the times while for PPR and bronchopneumonia it was 44.0 percent indicating a moderate association between these diseases. Occurrence of trypanosomiasis became lower during the heavy rainfall, high humidity and lower daily air temperature months (July to September) while more cases of PPR and bronchopneumonia were recorded during the dry months of December to January. Contrary to published reports, trypanosomiasis remained the most common of the diseases encountered in WAD goats treated at Imo State veterinary clinics.

13344 **Waiswa, C., 2005.** Porcine trypanosomiasis in Southeastern Uganda: prevalence and assessment of therapeutic effectiveness. *Bulgarian Journal of Veterinary Medicine*, **8** (1): 59–68.

Waiswa: Department of Veterinary Medicine, Faculty of Veterinary Medicine, Makerere University, P.O Box 7062, Kampala, Uganda.

This study aimed at investigating the prevalence of trypanosomiasis and the usefulness of diminazene aceturate and isometamidium chloride in the treatment of pigs infected with *Trypanosoma brucei* subgroup. Whole blood was collected from pigs kept in two disease endemic areas with riverine and open savannah environments. The prevalence of trypanosomiasis was recorded at 8.1 percent in the riverine environment as compared to the 2.1 percent in the open savannah environment and the infections in the former were significantly higher. All pigs that received a treatment of isometamidium chloride (Samorin®) at 1 mg/kg body weight did not show relapse when followed up to one month post treatment using microscopy. However, relapses were recorded among pigs treated with diminazene aceturate (Berenil®) at a dose rate of 7 mg/kg body weight and no relapses were recorded in those treated with 14 mg/kg body weight. From this investigation, it is apparent that the trypanosome prevalence among pigs kept under the riverine environment is higher than those kept under the open savannah. In addition, 1 mg/kg and 14 mg/kg isometamidium chloride and diminazene aceturate respectively should be adopted for the treatment of trypanosome infections among the pigs in the trypanosomiasis endemic areas.

(b) PATHOLOGY AND IMMUNOLOGY

13345 **Naessens, J., Kitani, H., Momotani, E., Sekikawa, K., Nthale, J.M. & Fuad Iraqi, 2004.** Susceptibility of TNF-α-deficient mice to *Trypanosoma*

congolense is not due to a defective antibody response. *Acta Tropica*, **92** (3): 193–203.

Naessens: International Livestock Research Institute, Genetic Resistance to Disease, POB 30709, Nairobi, Kenya. [j.naessens@cgiar.org]

C57BL/6 mice deficient in one or two copies of the gene for tumour necrosis factor alpha (TNF-α) were more susceptible to *Trypanosoma congolense* infection than their resistant, wild-type counterparts. The number of TNF-α genes was correlated with the capacity to control parasitaemia and with survival time. Absence of TNF-α resulted in a diminished capacity to form germinal centres in lymph nodes and spleen. Since germinal centres are involved in antibody production and affinity maturation, the susceptibility of the TNF-α-deficient mice could have been due to this secondary defect. Despite the lack of the germinal centres, the antibody responses to internal and exposed trypanosome antigens and to non-trypanosome antigens were not significantly different. Also the relative avidities measured in infected sera did not significantly differ between the two mouse strains. These data suggest that the role of TNF-α in control of *T. congolense* was not due to its role in the development of an antibody response.

13346 **Turay, A.A., Nwobu, G.O., Okogun, G.R.A., Igwe, C.U., Adeyeye, K., Aghatise, K.E., Okpala, H.O. & Tatfeng, Y.M., 2005.** A comparative study on the susceptibility of male and female albino mice to *Trypanosoma brucei brucei*. *Journal of Vector Borne Diseases*, **42** (1): 15–20.

Okogun: Department of Medical Laboratory Science, Faculty of Pathological Sciences, College of Medicine, Ambrose Alli University, PMB 14 Ekpoma, Edo State, Nigeria. [graokogun@yahoo.com]

Trypanosomiasis has remained a major set-back in the development of livestock farming in tropical Africa. There is thus the need for ascertaining the trypanotolerant levels of domestic animal breeds and possible improvement in them. In this study, levels of trypanotolerance in animals were compared between sexes using albino mice infected with a Nigerian strain of *Trypanosoma brucei brucei* at a 50 percent mouse lethal dose (MLD_{50}). The male mice showed unrestrained parasite growth with a prepatent period (PP) of two days and a mean survival period (MSP) of six days corresponding to a gradual decrease in packed cell volume (PCV), body weight, diet response and white blood cells (WBC) count to the time of death. Their female counterparts showed a PP of three days and MSP of ten days with a similar PCV gradient but a refractory WBC count. There was no significant difference in the differential leucocytes count in the two sexes. However, the eosinophil count was significantly higher in the infected animals. It was found that female albino mice exercised more parasite restraint than their male counterparts. The result suggests that the female animals may be more trypanotolerant hence may be more useful in protein production in trypanosomiasis endemic areas. However, further research using large domestic breeds like goats and sheep may be required to confirm the hypothesis.

13347 **Wållberg, M. & Harris, R.A., 2005.** Co-infection with *Trypanosoma brucei brucei* prevents experimental autoimmune encephalomyelitis in DBA/1 mice through induction of suppressor APCs. *International Immunology*, **17** (6): 721–728.

Wållberg: Applied Immunology Unit, Centre for Molecular Medicine L8:04, Karolinska Institute, SE-17176 Stockholm, Sweden.

The immune system has co-evolved with the infectious agents that challenge it, and in response pathogens have developed different mechanisms to subvert host immunity. A wealth of evidence suggests that infections are important components in the development of a functional immune system, and understanding the modulation of the host immune system by pathogens may offer new therapeutic strategies in a non-infectious setting. We investigated how infection with the protozoan parasite *Trypanosoma brucei brucei* (*Tbb*) modulates the autoimmune response to recombinant myelin oligodendrocyte glycoprotein (rMOG) in DBA/1 mice. Mice harbouring a *Tbb* infection did not develop experimental autoimmune encephalomyelitis (EAE) induced by immunization with rMOG in CFA, an animal model for the human autoimmune disease multiple sclerosis. Additionally, mice infected with the parasite at the time of immunization or 1 week later developed less severe EAE than uninfected controls. Protected mice displayed a markedly diminished rMOG-specific proliferation and IFNγ production in lymph node cells and had correspondingly low titres of serum anti-rMOG IgG. Antigen-presenting cells (APCs) from spleens of *Tbb*-infected mice presented rMOG less efficiently to rMOG-specific T cells *in vitro* than did splenic APCs from uninfected mice and could also inhibit antigen-specific proliferation in control *in vitro* cultures. This suppressive effect is at least in part due to increased release of IL-10. Transfer of splenic APCs from *Tbb*-infected mice into mice immunized with rMOG-CFA 7 days previously abrogated disease significantly. These findings indicate that infections can prevent autoimmunity and that APCs might be used as immunomodulants.

(c) TRYPANOTOLERANCE

[See also **28**: nos. 13345, 13355]

13348 **Dhollander, S., Bos, J., Kora, S., Sanneh, M., Gaye, M., Leak, S., Berkvens, D. & Geerts, S., 2005.** Susceptibility of West African Dwarf goats and WAD × Saanen crosses to experimental infection with *Trypanosoma congolense*. *Veterinary Parasitology*, **130** (1–2): 1–8.

Dhollander: International Trypanotolerance Centre, PMB 14, Banjul, The Gambia.

West African Dwarf goats (WADs) and their Saanen crosses were experimentally infected with *Trypanosoma congolense*. No significant differences were found between trypanosome parasitaemia and antibody response of the crossbred and WAD goats. Neither the WAD goats nor the Saanen crosses were able to control the drop in PCV

following trypanosome infection. The level of anaemia caused by the trypanosome infection was similar in the two breeds during the trial. Based on these findings, no difference in tolerance or susceptibility to *T. congolense* could be demonstrated between the WAD goats and their Saanen crosses. Although the weight of all goats increased during the trial, the crosses gained significantly more weight than the WAD goats. The trypanosome infection reduced the growth rate of both breeds, but this reduction was not statistically significant. Crossbreeding trypanotolerant WADs with trypanosusceptible Saanen goats might, therefore, be an effective means of increasing productivity.

13349 **Koudandé, O.D., Arendonk, J.A.M. van & Iraqi, F., 2005.** Marker-assisted introgression of trypanotolerance QTL in mice. *Mammalian Genome*, 16 (3): 112–119.

Arendonk: Animal Breeding and Genetics Group, Wageningen Institute of Animal Sciences, Wageningen University, P.O. Box 338, 6700 AH Wageningen, Netherlands. [Johan.vanArendonk@wur.nl]

A marker-assisted introgression (MAI) experiment was conducted to use genetic markers to transfer each of the three trypanotolerance quantitative trait loci (QTL) from a donor mouse strain, C57BL/6, into a recipient mouse strain, A/J. We used a backcross strategy that consisted of selecting two lines, each carrying two of the donor QTL alleles through the backcross (BC) phase. At the fourth BC generation, single-carrier animals were selected for the production of homozygous animals in the intercross phase. The QTL regions (QTLR) were located on chromosomes MMU1, MMU5, and MMU17. Groups of mice with different genotypes and the parental lines were subjected to a challenge with *Trypanosoma congolense*. The results show that trypanotolerance QTL was successfully moved into the recipient background genotype, yielding a longer survival time. The mean estimated survival time was 57.9, 49.5, and 46.8 days for groups of mice carrying the donor QTL on MMU1, MMU5, and MMU17 on A/J background. The mean estimated survival time was 29.7 days for the susceptible A/J line and 68.8 days for the resistant C57BL/6 line. The estimated QTLR effects are close to 30 percent smaller than those in the original mapping population which result was likely caused by the difference in the background on which the effects of QTLR are tested. This is the first report of successful marker-assisted introgression of QTL in animals. It is experimental proof of the use of genetic markers for marker-assisted introgression in animal breeding.

13350 **Magona, J.W., Walubengo, J. & Odimim, J.J., 2004.** Differences in susceptibility to trypanosome infection between Nkedi Zebu and Ankole cattle, under field conditions in Uganda. *Annals of Tropical Medicine and Parasitology*, **98** (8): 785–792.

Magona: Livestock Health Research Institute, P.O. Box 96, Tororo, Uganda.

A cross-sectional study was conducted in tsetse-infested areas of Soroti district in Uganda, with the aim of assessing the response of the Nkedi Zebu and Ankole breeds of

cattle to trypanosome infection. Overall, 1 215 Nkedi Zebu and 260 Ankole cattle kept under similar levels of tsetse challenge were examined for trypanosome infection, using the Buffy-coat technique and haematocrit centrifugation, and had their packed-cell volumes (PCV) measured. As expected, the infected cattle, whether of the Nkedi Zebu (26.7 percent *v*. 29.6 percent) or Ankole breeds (24.9 percent *v*. 29.1 percent), had significantly lower mean PCV than the uninfected. In the Nkedi Zebu cattle, the prevalence of trypanosome infection was lower (7.9 percent *v*. 10.8 percent) and the overall mean PCV was significantly higher (29.4 percent *v*. 28.7 percent) than in the Ankole. Compared with the Ankole, Nkedi Zebu cattle appear to be less susceptible to (detectable) trypanosome infection and to the trypanosome-attributable lowering of their PCV.

13351 **Maillard, J.C., Berthier, D., Thevenon, S., Piquemal, D., Chantal, I. & Marti, J., 2005.** Efficiency and limits of the Serial Analysis of Gene Expression (SAGE) method: Discussions based on first results in bovine trypanotolerance. *Veterinary Immunology and Immunopathology*, **108** (1–2 Sp. Issue): 59–69.

Maillard: Cirad-Prise, c/o NIAH, Thuy Phuong, Tu Liem, Hanoi, Vietnam

Post genomic biotechnologies, such as transcriptome analysis, are now efficient enough to characterize the full complement of genes involved in the expression of specific biological functions. One of them is the Serial Analysis of Gene Expression (SAGE) technique. SAGE involves the construction of transcript libraries for a quantitative analysis of the entire set of genes expressed or inactivated at particular stages of cellular activation. Bioinformatic comparisons in hosts and pathogens genomic databases allow the identification of several up- and down-regulated genes, ESTs and unknown transcripts directly involved in the host-pathogen immunological interaction mechanisms. Based on the first results obtained during an experimental *Trypanosoma congolense* infection in trypanotolerant cattle, the efficiency and limits of such a technique, from the data acquisition level to the data analysis level, is discussed in this analysis.

13352 **Maillard, J.C., Berthier, D., Thevenon, S., Quéré, R., Piquemal, D., Manchon, L. & Marti, J., 2004.** Use of the Serial Analysis of Gene Expression (SAGE) method in veterinary research: a concrete application in the study of the bovine trypanotolerance genetic control. *Annals of the New York Academy of Sciences*, 1026 171–182.

Maillard: Cirad-Prise, c/o NIAH, Thuy Phuong, Tu Liem, Hanoï, Vietnam. [maillard@fpt.vn ; maillard@cirad.fr]

New postgenomic biotechnologies, such as transcriptome analyses, are now able to characterize the full complement of genes involved in the expression of specific biological functions. One of these is the Serial Analysis of Gene Expression (SAGE) technique, which consists of the construction of transcript libraries for a quantitative analysis of the entire gene expressed or inactivated at a particular step of cellular

activation. Bioinformatic comparisons in the bovine genomic databases allow the identification of several up- and down-regulated genes, expressed sequence tags, and unknown functional genes directly involved in the genetic control of the studied biological mechanism. The preliminary results in comparing the expressed genes in two total mRNA transcripts libraries obtained during an experimental *Trypanosoma congolense* infection in one trypanotolerant N'Dama cow are discussed. Knowing all the functional genes involved in the trypanotolerance control will permit validation of some results obtained with the quantitative trait locus approach, to set up specific microarrays sets for further metabolic and pharmacological studies, and to design field marker-assisted selection by introgression programmes.

(d) TREATMENT

[See also **28**: nos. 13293, 13332]

7. EXPERIMENTAL TRYPANOSOMIASIS

(a) DIAGNOSTICS

13353 **Cox, A., Tilley, A., McOdimba, F., Fyfe, J., Eisler, M., Hide, G. & Welburn, S., 2005.** A PCR based assay for detection and differentiation of African trypanosome species in blood. *Experimental Parasitology*, **111** (1): 24–29.

Welburn: Centre for Tropical Veterinary Medicine, Royal (Dick) School of Veterinary Medicine, University of Edinburgh, Easter Bush, Roslin, Midlothian EH25 9RG, UK.

Direct PCR analysis of trypanosome infected blood samples in the quantities required for large scale epidemiological study has always been problematic. Current methods for identifying and differentiating trypanosomes typically require several species-specific reactions, many of which rely on mouse passaged samples to obtain quality concentrated genomic DNA. As a consequence important epidemiological information may be lost during the sample preparation stage. Here, we report a PCR methodology that reduces processing and improves on the sensitivity of present screening methods. The PCR technique targets the gene encoding the small ribosomal subunit in order to identify and differentiate all clinically important African trypanosome species and some subspecies. The method is more economical, simple, and sensitive than current screening methods, and yields more detailed information, thereby making it a viable tool for large-scale epidemiological studies.

13354 **Gonzalez, L.E., Garcia, J.A., Nunez, C., Perrone, T.M., Gonzalez-Baradat, B., Gonzatti, M. & Reyna-Bello, A., 2005.** *Trypanosoma vivax*: A novel method for purification from experimentally infected sheep blood. *Experimental Parasitology*, **111** (2): 126–129.

Reyna-Bello: Universidad Simón Rodríguez-IDECYT, Laboratorio de Inmunología, Caracas, Venezuela.

Trypanosoma vivax is the principal aetiological agent of bovine trypanosomosis, a widely disseminated disease in tropical and subtropical regions. Here, we present a simple and reproducible method for the purification of *T. vivax* from experimentally infected and immunosuppressed sheep, using an isopycnic Percoll gradient, followed by DEAE-cellulose chromatography, with an estimated yield of 11–15 percent. This method could be used for the purification of *T. vivax* geographical isolates from various locations and from different natural hosts.

(b) PATHOLOGY AND IMMUNOLOGY

13355 **Abenga, J.N., David, K.M., Ezebuiro, C.O.G., Samdi, S. & Fajinmi, A.O., 2004.** Leucocyte and thrombocyte changes in young dogs infected with *Trypanosoma congolense*. *Journal of Protozoology Research*, **14** (1–2): 8–15.

Abenga: Pathology, Epidemiology and Statistics Division Nigerian Institute for Trypanosomiasis Research, P.M.B. 2077, Kaduna, Nigeria.

Studies were undertaken to determine the effect of infection with *Trypanosoma congolense* on the leucocyte and thrombocyte values of six local puppies. The puppies were of mixed sexes and seven weeks old. Although the puppies became parasitaemic 6 to 7 days post infection (PI), the effect on leucocyte counts were mild as significant leucopenia characterised by neutropenia, ensinopenia, and lymphopenia ($P \leq 0.05$) did not occur until the last four weeks of the 8 week observation period. Infection had more effects on thrombocyte counts as thrombocytopenia occurred from week one PI. The low impact of infection with *T. congolense* on the leucocyte values of infected puppies was attributable to trypanotolerance in the local breed of dogs and low antigenicity of the strain of *T. congolense* used. It is concluded that the ability to resist the development of anaemia may not be the only haematological evidence of trypanotolerance in animals and that further research is needed to determine the true trypanotolerance status of breeds of local dogs in Nigeria and other parts of the West African subregion.

13356 **Abenga, J.N., Ezebuiro, C.O., David, K., Fajinmi, A.O. & Samdi, S., 2005.** Studies on anaemia in Nigerian local puppies infected with *Trypanosoma congolense*. *Veterinarski Arhiv*, **75** (2): 165–174.

Abenga: Pathology, Epidemiology and Statistics Division, Nigerian Institute for Trypanosomiasis Research, Private Mail Bag, 2077 Kaduna, Nigeria.

Investigation into the effect of infection with *Trypanosoma congolense* on the haematology of growing Nigerian local dogs was undertaken using six puppies infected with 1×10^6 of the parasites. Infection resulted in mild anaemia characterized by a slight drop in the packed cell volume (PCV), haemoglobin (Hb) and red blood cells (RBC)

counts which did not occur until the second half of the eight-week observation period. The anaemia was macrocytic normochromic. The mild decrease in the overall erythrocyte values of *T. congolense*-infected young dogs was attributable to trypanotolerance in the local breed of dog. However, the infected group did not attain full erythrocyte values as in the control group, suggesting that similar changes occurring in infected young animals contribute to retarded growth associated with trypanosome infections.

13357 **Ajuwape, A.T.P., Adetosoye, A.I., Ikheloa, J.O., Alaka, O.O., Taiwo, V.O., Talabi, O.A., Otesile, E.B. & Ojo, M.O., 2004.** Pathogenicity of *Mycoplasma capricolum* subspecies c*apricolum* for cattle immunosuppressed with *Trypanosoma congolense*. *Israel Journal of Veterinary Medicine*, **59** (4): 73–77.

Ajuwape: Department of Veterinary Microbiology and Parasitology, University of Ibadan, Ibadan, Nigeria.

The pathogenicity of *Mycoplasma capricolum* subspecies *capricolum* in Red Bororo (RB) bull calves was investigated. Two calves infected with 4.21×106 cells of *Trypanosoma congolense* and later inoculated endobronchially with 1.6×109 CFU/ml of *M. capricolum* subspecies *capricolum* (Tc/Mcc) died 38.0±1.4 days post infection (pi) presenting fibrinous interstitial pneumonia and severe lymphoid depletion in spleen and lymph nodes, while another set of two calves was infected with *Trypanosoma congolense* (Tc) only. The mean PCV values (mPCV) of each of the four Tc-infected RB calves (21.7±2.4 percent, 25.5±2.5 percent, 23.3±3.9 percent and 23.3±2.4 percent) were significantly lower than that of the control (31.1±1.7 percent). The mean rectal temperature (mRT) of each of the four calves (39.6±0.8 degrees C, 40.0±0.5 degrees C, 37.9±0.5 degrees C and 38.1±0.2 degrees C) with Tc and Mcc or Tc infections was significantly higher than that of the control (38.2±0.5 degrees C). In these experimental infections, necropsy examinations revealed oedema, congestion, consolidation and marbling of the lungs. Histopathological changes observed were *inter alia* thickening of the interlobular septae by fibrin and showers of lymphocytes. The spleen showed lymphoid necrosis and haemosiderosis in the red pulp. *Mycoplasma capricolum* subspecies *capricolum* was recovered from the lungs, lymph nodes, kidneys, spleen and liver of the dead calves. The *Trypanosoma congolense* infection induced a state of immunosuppression. In Africa, where cattle are herded along with sheep and goats, this study revealed that *Mycoplasma capricolum* subsp. *capricolum* can indeed cause CBPP-like lesions that may be indistinguishable from CBPP caused by bovine mycoplasmas. It is therefore suggested that thorough laboratory investigation should be carried out along with post mortem examination of suspected CBPP cases to identify the specific *Mycoplasma* species involved. Efforts should be made to immunize cattle, sheep and goats against *M. capricolum* subsp. *capricolum*.

13358 **Berge, B., Chevrier, C., Blanc, A., Rehailia, M., Buguet, A. & Bourdon, L., 2005.** Disruptions of ultradian and circadian organization of core temperature in a rat model of African trypanosomiasis using periodogram techniques on detrended data. *Chronobiology International*, **22** (2): 237–251.

Blanc: Laboratoire de Biologie Animale et Appliquée, 23 Rue Docteur Paul Michelon, F-42023 St Etienne, Cedex 2, France.

Periodogram techniques on detrended data were used to determine the effect of *Trypanosoma brucei brucei* infection on the distribution of the core temperature of rats and on the expression of temperature rhythms. In such an animal model, sudden episodic hypothermic bouts are described. These episodes of hypothermia are used here as marks for the purpose of performing time-based comparisons on temperature organization. The experiment was conducted on ten infected and three control (non-infected) Sprague-Dawley rats reared under a 24 h light-dark cycle. Core temperature was recorded continuously throughout the experiment, until the animals' death. Temperature distributions, analyzed longitudinally for the full duration of the experiment, exhibited a progressive shift from a bimodal to a unimodal pattern, suggesting a weakening of the day/night core temperature differences. After hypothermic events, the robustness of the circadian rhythm substantially weakened, also affecting the ultradian components. The ultradian periods were reduced, suggesting breakdown of temperature generation. Moreover, differences between daytime and nighttime ultradian patterns decreased during illness, confirming the weakening of the circadian component. The results of the experiments show that both core temperature distribution and temperature rhythm were disrupted during the infection. These disruptions worsened after each episode of hypothermia, suggesting an alteration of the temperature regulatory system.

13359 **Büscher, P., Shamamba, S.K.B., Ngoyi, D.M., Pyana, P., Baelmans, R., Magnus, E. & Overmeir, C.V., 2005.** Susceptibility of *Grammomys surdaster* thicket rats to *Trypanosoma brucei gambiense* infection. *Tropical Medicine and International Health*, **10** (9): 850–855.

Büscher: Unit of Parasite Diagnostics, Department of Parasitology, Institute of Tropical Medicine, Antwerp, Belgium.

Human African trypanosomiasis is caused by *Trypanosoma brucei gambiense* and *T. b. rhodesiense*. Historically, a treatment relapse rate of about 5 percent is observed in patients treated with melarsoprol, an arsenical derivative used for treatment of both *gambiense* and *rhodesiense* second stage sleeping sickness. More recently, relapse rates up to 30 percent are noted in *gambiense* sleeping sickness foci in Angola, Sudan and Uganda. Accordingly, WHO established a Network on Treatment Failure and Drug Resistance in Sleeping Sickness. One of its objectives is to improve isolation of *T. b. gambiense* from relapsing cases for research on drug resistance mechanisms. *Trypanosoma b. gambiense* isolation techniques suffer from low success rates and long periods needed to adapt the parasite to its new host. Usually, rodents are inoculated with patient's blood or cerebrospinal fluid and sub-passaged until the strain becomes sufficiently adapted to yield high parasitaemia within few days after inoculation. Until now, the best recipient for *T. b. gambiense* is *Mastomys natalensis*, with a success rate of about 50 percent. In this study, *Grammomys surdaster* (formerly *Thamnomys surdaster*) was investigated as a potential recipient for isolation of *T. b. gambiense*. Comparative

experimental infections of Swiss mice, Wistar rats and *G. surdaster* thicket rats with *T. b. gambiense* clearly show that this trypanosome grows faster in *G. surdaster*. Inoculation of the same rodent species with patient's blood and cerebrospinal fluid in Kinshasa (R.D. Congo) confirms the observation that the thicket rats are more susceptible to *T. b. gambiense* infection than typical laboratory rodents.

13360 **Chevrier, C., Canini, F., Darsaud, A., Cespuglio, R., Buguet, A. & Bourdon, L., 2005.** Clinical assessment of the entry into neurological state in rat experimental African trypanosomiasis. *Acta Tropica*, **95** (1): 33–39.

Chevrier: Centre de recherches du service de santé des armées, Département des Facteurs Humains, 24 avenue des Maquis du Grésivaudan, BP 87, 38702 La Tronche, France.

Human African trypanosomiasis, caused by *Trypanosoma brucei gambiense* or *T. b. rhodesiense*, evolves in two stages: the haemolymphatic stage and the meningo-encephalitic stage, the latter featuring numerous neurological disorders. In experimental models infected with diverse *T. brucei* sub-species, body weight (BW) loss, drop in food intake (FI), and hypo-activity after an asymptomatic period suggest the occurrence of a similar two-stage organization. In addition to daily measurement of BW and FI, body core temperature (T_{co}) and spontaneous activity (SA) were recorded by telemetry in *T. b. brucei*-infected rats. After a 10- to 12-day symptom-free period, a complex clinical syndrome suddenly occurred. If the animal survived the crisis, the syndrome recurred at approximately 5-day intervals until death. The syndrome consisted of a drop in FI and BW, a sharp decrease in T_{co} and a loss of SA, suggesting a rapid alteration of the central nervous system functioning. Such events confirm the existence of a two-stage disease development in experimental trypanosomiasis. The entry into the second stage is marked by the occurrence of the first crisis, with tracking of the BW being essential and often sufficient for its determination.

13361 **Drennan, M.B., Stijlemans, B., Abbeele, J. van den, Quesniaux, V.J., Barkhuizen, M., Brombacher, F., Baetselier, P. de, Ryffel, B. & Magez, S., 2005.** The induction of a type 1 immune response following a *Trypanosoma brucei* infection is MyD88 dependent. [Mice] *Journal of Immunology*, **175** (4): 2501–2509.

Drennan: Immunology of Infectious Disease Medical Research Council/University of Cape Town Unit, Institute of Infectious Disease and Molecular Medicine, Health Science Faculty, University of Cape Town, Cape Town, South Africa.

The initial host response toward the extracellular parasite *Trypanosoma brucei* is characterized by the early release of inflammatory mediators associated with a type 1 immune response. In this study, we show that this inflammatory response is dependent on activation of the innate immune system mediated by the adaptor molecule MyD88. In the present study, MyD88-deficient macrophages are nonresponsive toward both soluble

VSG (variant-specific surface glycoprotein), as well as membrane-bound VSG purified from *T. brucei*. Infection of MyD88-deficient mice with either clonal or nonclonal stocks of *T. brucei* resulted in elevated levels of parasitemia. This was accompanied by reduced plasma IFN-γ and TNF levels during the initial stage of infection, followed by moderately lower VSG-specific IgG2a Ab titers during the chronic stages of infection. Analysis of several TLR-deficient mice revealed a partial requirement for TLR9 in the production of IFN-γ and VSG-specific IgG2a Ab levels during *T. brucei* infections. These results implicate the mammalian TLR family and MyD88 signaling in the innate immune recognition of *T. brucei*.

13362 **Sallau, A.B., Nok, A.J., Ndams, I.S. & Balogun, E.O., 2004.** Role of sialic acids in the midguts of *Trypanosoma congolense* infected *Culex pipiens pipiens* mosquitoes. *African Journal of Biotechnology*, **3** (8): 405–408.

Balogun: Department of Biochemistry, Ahmadu Bello University, Zaria, Nigeria.

Free and total sialic acid concentrations were determined in the midgut extracts of *Culex pipiense pipiense* mosquitoes infected with *Trypanosoma congolense*. The mean total sialic acid concentrations were found to be 1.5 to 2 fold higher than the mean free sialic acid concentrations in the midgut extracts of all the groups of the *T. congolense* infected *C. p. pipiense*. Infusion of 10 mg/ml galactose and 10 mg/ml lactose did not change the pattern of this difference but resulted to 1.3 to 1.4 fold decrease in the total sialic acid concentration. The relevance of these findings to the role of sialic acids in the midgut of *T. congolense* infected *C. p. pipiense* mosquitoes is discussed.

(c) CHEMOTHERAPEUTICS

13363 **Ansede, J.H., Voyksner, R.D., Ismail, M.A., Boykin, D.W., Tidwell, R.R. & Hall, J.E., 2005.** *In vitro* metabolism of an orally active O-methyl amidoxime prodrug for the treatment of CNS trypanosomiasis. *Xenobiotica*, **35** (3): 211–226.

Ansede: Division of Drug Delivery and Disposition, School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, N. Carolina, USA

13364 **Anthony, J.P., Fyfe, L. & Smith, H., 2005.** Plant active components - a resource for antiparasitic agents? *Trends in Parasitology*, **21** (10): 462–468.

Smith: Scottish Parasite Diagnostic Laboratory, Stobhill Hospital, Glasgow G21 3UW, UK.

Plant essential oils (and/or active components) can be used as alternatives or adjuncts to current antiparasitic therapies. Garlic oil has broad-spectrum activity against *Trypanosoma*, *Plasmodium*, *Giardia* and *Leishmania*, and *Cochlospermum planchonii*

and *Croton cajucara* oils specifically inhibit *Plasmodium falciparum* and *Leishmania amazonensis*, respectively. Some plant oils have immunomodulatory effects that could modify host-parasite immunobiology, and the lipid solubility of plant oils might offer alternative, transcutaneous delivery routes. The emergence of parasites resistant to current chemotherapies highlights the importance of plant essential oils as novel antiparasitic agents.

13365 **Arafa, R.K., Brun, R., Wenzler, T., Tanious, F.A., Wilson, W.D., Stephens, C.E. & Boykin, D.W., 2005.** Synthesis, DNA affinity, and antiprotozoal activity of fused ring dicationic compounds and their prodrugs. *Journal of Medicinal Chemistry*, **48** (17): 5480–5488.

Boykin: Department of Chemistry, Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA 30303-3083, USA.

13366 **Atawodi, S.E., 2005.** Comparative *in vitro* trypanocidal activities of petroleum ether, chloroform, methanol and aqueous extracts of some Nigerian savannah plants. *African Journal of Biotechnology*, **4** (2): 177–182.

Atawodi: Biochemistry Department, Ahmadu Bello University, Zaria, Nigeria. [atawodise@yahoo.com]

Using *Trypanosoma brucei* as test organism, about two hundred extracts of varying polarities obtained from different parts of about forty tropical plants harvested from the savannah vegetational belt of Nigeria, were evaluated for their *in vitro* trypanocidal activities at concentrations of 2 and 4 mg/ml. The proportion of petroleum ether, chloroform, methanol and aqueous extracts that eliminated motility within 60 min at the highest concentration tested were 77, 67, 50 and 47 percent, respectively, while 10, 11, 19 and 14 percent of these extracts were completely non-active under the test condition. Among the plants studied, extracts of *Adenium obesum* (stem bark), *Afrormosia laxiflora* (leaves and stem bark), *Cochlospermum planchoni* (stem bark), *Prosopis africana* (stem and root barks), *Striga* spp. (leaves), *Terminalia avicennioides* (root and stem bark) and *Swartzia madagascariensis* (fruit pulp) exhibited the highest trypanocidal activity. These results suggest that tropical plants could be a very promising source of new generations of trypanocidal agents.

13367 **Baliani, A., Bueno, G.J., Stewart, M.L., Yardley, V., Brun, R., Barrett, M.P. & Gilbert, I.H., 2005.** Design and synthesis of a series of melamine-based nitroheterocycles with activity against trypanosomatid parasites. *Journal of Medicinal Chemistry*, **48** (17): 5570–5579.

Gilbert: Welsh School of Pharmacy, Redwood Building, Cardiff University, King Edward VII Avenue, Cardiff CF10 3XF, UK.

The parasites that give rise to human African trypanosomiasis (HAT) are auxotrophs for various nutrients from the human host, including purines. They have

specialist nucleoside transporters to import these metabolites. In addition to uptake of purine nucleobases and purine nucleosides, one of these transporters, the P2 transporter, can carry melamine derivatives; these derivatives are not substrates for the corresponding mammalian transporters. In this paper, we report the coupling of the melamine moiety to selected nitroheterocycles with the aim of selectively delivering these compounds to the parasites. Some compounds prepared have similar *in vitro* trypanocidal activities as melarsoprol, the principal drug used against late-stage HAT, with 50 percent growth inhibitory concentrations in the submicromolar range. Selected compounds were also evaluated *in vivo* in rodent models infected with *Trypanosoma brucei brucei* and *T. brucei rhodesiense* and showed pronounced activity and in two cases were curative without overt signs of toxicity. Compounds were also tested against other trypanosomatid pathogens, *Leishmania donovani* and *Trypanosoma cruzi*, and significant activity *in vitro* was noted for *T. cruzi* against which various nitroheterocycles are already registered for use.

13368 **Chérigo, L., Polanco, V., Ortega-Barria, E., Heller, M.V., Capson, T.L. & Rios, L.C., 2005.** Antitrypanosomal activity of a novel norlignan purified from *Nectandra lineata*. *Natural Product Research*, **19** (4): 373–377.

Rios: Laboratory of Natural Products, Faculty of Natural and Exact Sciences and Technology, Apdo. 0824, University of Panama, Panama City, Republic of Panama.

13369 **Delespaux, V., Geysen, D., Majiwa, P.A.O. & Geerts, S., 2005.** Identification of a genetic marker for isometamidium chloride resistance in *Trypanosoma congolense*. *International Journal for Parasitology*, **35** (2): 235–243.

Delespaux: Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium.

Isometamidium chloride has remained a very important prophylactic and therapeutic drug against trypanosomosis in cattle since its introduction into the market in the 1950s with, unfortunately, a concomitant development of resistance in trypanosomosis endemic areas. Amplified Fragment Length Polymorphism (AFLP) was used to compare two isogenic clones of *Trypanosoma congolense*. The parent clone, sensitive to isometamidium, has a CD_{50} (the curative dose that gives complete cure in 50 percent of the animals) in the mouse of 0.018 mg/kg and its derivative exposed to increasing doses of isometamidium, has a CD_{50} that is 94-fold higher. Sixty-four combinations of eight Eco RI and eight Mse I primers were used in comparative AFLP analysis to detect subtle genetic differences between the two clones. Thirty-five polymorphic fragments of DNA that were observed only in the resistant clone were purified and then sequenced. The nucleotide sequences were used in searching the GeneDB *T. congolense* database to find surrounding sequences upstream of an open reading frame and downstream to a stop codon. The sequences of the open reading frames were subsequently compared to the sequences in the genomic databases. A predicted gene coding for an 854 amino acids protein was thus identified. The protein

contains a putative ATP binding site, Walker B and LSGG motifs and eight predicted trans-membrane domains. The gene in the resistant strain of *T. congolense* has a triplet insertion coding for an extra lysine. Using polymerase chain reaction-restriction fragment length polymorphism, the insertion was sought in the genomes of 35 *T. congolense* strains isolated from different geographic origins and whose response to isometamidium chloride had been determined through single dose mouse tests. The presence of the insertion, specifying an extra codon, was found to always be present in the genomes of *T. congolense* clones that were resistant to isometamidium chloride.

13370 **Hoet, S., Opperdoes, F., Brun, R. & Quetin-Leclercq, J., 2004.** Natural products active against African trypanosomes: a step towards new drugs. *Natural Product Reports*, **21** (3): 353–364.

Hoet: Laboratoire de Pharmacognosie, Unité d'Analyse Chimique et Physico-Chimique des Médicaments, Université Catholique de Louvain, Av. E. Mounier 72, UCL 72.30-CHAM, B-1200, Brussels, Belgium. [sara.hoet@cham.ucl.ac.be]

13371 **Ismail, M.A., Brun, R., Wenzler, T., Tanious, F.A., Wilson, W.D. & Boykin, D. W., 2004.** Novel dicationic imidazo[1,2-α]pyridines and 5,6,7,8-tetrahydro-imidazo[1,2-α]pyridines as antiprotozoal agents. [mice] *Journal of Medicinal Chemistry*, **47** (14): 3658–3664.

Ismail: Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA 30303-3083, USA.

13372 **Katete, D.P., McIntosh, R.J. & Lubega, G.W., 2004.** Antibodies to recombinant tubulin can kill trypanosomes in culture. *Molecular Biology of the Cell*, **15** (Suppl.): 463a.

Katete: Veterinary Parasitology and Microbiology, Makarere University, Kampala, Uganda.

An antiserum against recombinant tubulin can kill trypanosomes *in vitro*; the mechanism is still unclear and requires further study as part of the general effort needed towards developing a vaccine against sleeping sickness and/or nagana.

13373 **Kubata, B.K., Nagamune, K., Murakami, N., Merkel, P., Kabututu, Z., Martin, S.K., Kalulu, T.M., Haq Mustakuk, Yoshida, M., Ohnishi-Kameyama, M., Kinoshita, T., Duszenko, M. & Urade, Y., 2005.** *Kola acuminata* proanthocyanidins: a class of anti-trypanosomal compounds effective against *Trypanosoma brucei*. *International Journal for Parasitology*, **35** (1): 91–103.

Kubata: Department of Molecular Behavioral Biology, Osaka Bioscience Institute, 6-2-4 Furuedai, Suita, Osaka 565-0874, Japan.

Human African trypanosomiasis is undergoing an alarming rate of recrudescence in many parts of sub-Saharan Africa. Yet, there is no successful chemotherapy for the disease due to a limited number of useful drugs, side effects and drawbacks of the existing medication, as well as the development of drug resistance by the parasite. Here we describe a new lead anti-trypanosomal compound isolated from *Kola acuminata* (Makasu). We purified a proanthocyanidin by chromatographic procedures and confirmed its homogeneity and structure by Nuclear Magnetic Resonance and Matrix-Assisted Laser Desorption Ionization Time-of-Flight mass spectrometry, respectively. *In vitro*, this compound potently induced growth arrest and lysis of the bloodstream form trypanosomes in a dose- and time-dependent manner. In a mouse model, it exhibited a trypanostatic effect that extended the life of infected, treated animals up to 8 days post-infection against the 4 days for infected, untreated animals. The proanthocyanidin showed a low cytotoxicity against mammalian cells, whereas treated-bloodstream form showed massive enlargement of their flagellar pocket and lysosome-like structures caused by an intense formation of multivesicular bodies and vesicles within these organelles. The observed ultrastructural alterations caused rupture of plasma membranes and the release of cell contents, indicative of a necrotic process rather than a programmed cell death. Interestingly, the proanthocyanidin acted against the bloodstream form but not the procyclic form trypanosomes. This new anti-trypanosomal compound should be further studied to determine its efficacy and suitability as an anti-trypanosomal drug and may be used as a tool to define novel specific drug targets in bloodstream trypanosomes.

13374 **Maikaje, D.B., 2000.** Study on the sensitivity of a *Trypanosoma brucei* isolate from the Kaura Local Government Area to trypanocides. *West African Journal of Biological Sciences*, **11**: 65–70.

Maikaje: Department of Biological Sciences, Nigerian Defence Academy, PMB 2109, Kaduna, Nigeria.

The sensitivity of *Trypanosoma brucei brucei*, the species most commonly isolated from cattle in Kaura LGA of Kaduna State, to Berenil and Samorin at dosages of 7mg/kg and 0.5mg/kg body weight was experimentally investigated in six Red Sokoto goats. The *T. b. brucei* isolate showed high sensitivities to these trypanocides which resulted in complete cure of the goats experimentally infected with it. This observation, which supports similar results obtained from Berenil treatment of natural bovine trypanosomiasis in this LGA, tends to suggest the non-existence of a drug-resistant strain of *T. b. brucei* in this area.

13375 **Maikaje, D.B., 2001.** Preliminary investigations on the therapeutic activities of diminazene and isometamidium on a *Trypanosoma congolense* isolate from the Kaura endemic focus of bovine trypanosomosis. *Academy Journal of Science and Engineering*, **1** (1): 16–24.

Maikaje: Department of Biological Sciences, Nigerian Defence Academy, PMB 2109, Kaduna, Nigeria.

The therapeutic responses of a *Trypanosoma congolense* isolate obtained from the bovine trypanosomosis endemic focus of Kaura Local Government Area, to diminazene aceturate and isometamidium chloride, were investigated. Three goats infected with this trypanosome isolate were completely cured within 24 hours of isometamidium treatment, and remained trypanosomosis-free until the study was completed 10 weeks later. However, there was a lapsed infection in one of two infected goats 17 days after diminazene aceturate treatment cleared the initial parasitaemia within 24 hours. In spite of the clearance of the *T. congolense* parasitaemia in the cured animals by these trypanocides, the declining trend in the values of the clinical parameters observed from the onset of the infection never reversed to normal values even during the ten weeks post-treatment monitoring. Isometamidium chloride at a dosage of 0.5 mg/kg body weight cleared the relapsed infections initially treated with diminazene. The continuous decline in clinical parameters in treated aparasitaemic goats in this study could be attributed to the cytotoxic effects of *T. congolense*-derived substances and/or the effects of confinement of these experimental animals which were used to grazing over long distances in their natural habitats. The initial treatment of trypanosomosis positive cases with the cheap diminazene followed by isometamidium treatment of relapsed cases and vector trapping are suggested for the effective control of bovine trypanosomosis in Kaura LGA.

13376 **Ngamga, D., Yankep, E., Tane, P., Bezabih, M., Ngadjui, B.T., Fomum, Z.T. & Abegaz, B.M., 2005.** Antiparasitic prenylated isoflavonoids from seeds of *Millettia griffoniana*. *Bulletin of the Chemical Society of Ethiopia*, **19** (1): 75–80.

Abegaz: Department of Chemistry, Faculty of Science, University of Botswana, POBox UB00704, Gaborone, Botswana.

Two new prenylated isoflavonoids, namely 7-methoxyebenosin and griffonianone E along with the known calopogonium isoflavone B and 7,2'-dimethoxy-4',5'-methylenedioxy isoflavone were isolated from the seeds of *Millettia griffoniana*. Their structures were assigned on the basis of spectroscopic data. The new compounds exhibit moderate trypanocidal and antiplasmodial activities.

13377 **Nyarko, E., Hara, T., Grab, D.J. & Fukuma, T., 2004.** Trypanocidal effects of Au(III) in the presence of alamarBlue™. An *in vitro* study. *Molecular Biology of the Cell*, **15** (Suppl.): 464a.

Trypanocidal toxicity tests are described involving possible synergy between Au(III) and the proprietary dye alamarBlue.

13378 **Roch, P., Beschin, A. & Bernard, E., 2004.** Antiprotozoan and antiviral activities of non-cytotoxic truncated and variant analogues of mussel defensin. *Evidence-based Complementary and Alternative Medicine*, **1** (2): 167–174.

Roch: Pathogènes et Immunité, UMR Ecosystèmes Lagunaires, Université

de Montpellier 2, cc 093, Place E. Bataillon, 34095 Montpellier Cedex 5, France. [proch@univ-montp2.fr]

13379 **Seebacher, W., Brun, R., Kaiser, M., Saf, R. & Weis, R., 2005.** Synthesis and evaluation of the antitrypanosomal and antiplasmodial activities of new 4-aminobicyclo[2.2.2] octane derivatives. *European Journal of Medicinal Chemistry*, **40** (9): 888–896.

Seebacher: Institute of Pharmaceutical Sciences, Pharmaceutical Chemistry, Karl-Franzens-University, Universitätsplatz 1, A-8010 Graz, Austria.

13380 **Shah, S.T.A., Merkel, P., Ragge, H., Duszenko, M., Rademann, J. & Voelter, W., 2005.** Stereospecific synthesis of chiral 2,3-dihydro-1,4-benzodithiine and methyl-2,3-dihydro-1,4-benzodithiine derivatives and their toxic effects on *Trypanosoma brucei*. *Chembiochem*, **6** (8): 1438–1441.

Voelter: Physiologisch-chemisches Institut der Universität Tübingen, Hoppe-Seyler Strasse 4, 72076 Tübingen, Germany.

13381 **Soeiro, M.N.C., De Souza, E.M., Stephens, C.E. & Boykin, D.W., 2005.** Aromatic diamidines as antiparasitic agents. *Expert Opinion on Investigational Drugs*, **14** (8): 957–972.

Soeiro: Fiocruz MS, Lab Biologia Celular, Instituto Oswaldo Cruz DUBC, Avenida Brasil 4365, BR-21045900 Rio De Janeiro, Brazil.

Parasitic infections are widespread in developing countries and in developed countries are frequently associated with immunocompromised patients. Consequently, such infections are responsible for a significant amount of human mortality, morbidity and economic hardship. A growing consensus has identified the urgent need for the development of new antiparasitic compounds, mostly due to the large number of drug-resistant parasites and the fact that currently available drugs are expensive, highly toxic, require long treatment regimens and frequently exhibit significantly reduced activity towards certain parasite strains and evolutive stages. In this context, the activity of aromatic diamidines has been explored against a widespread range of microorganisms, and the authors' present aim is to review the current status of chemotherapy with these compounds against human parasitic infections.

13382 **Sternberg, J.M., Rodgers, J., Bradley, B., MacLean, L., Murray, M. & Kennedy, P.G.E., 2005.** Meningoencephalitic African trypanosomiasis: Brain IL-10 and IL-6 are associated with protection from neuro-inflammatory pathology. *Journal of Neuroimmunology*, **167** (1–2): 81–89.

Sternberg: School of Biological Sciences, Zoology Building, University of Aberdeen, Aberdeen AB24 2TZ, UK.

The relationship of neuropathology to CNS inflammatory and counter-inflammatory cytokine production in African trypanosome-infected mice was studied using an infection model with a defined disease progression. The initial phase of CNS infection by trypanosomes, where only mild neuropathology is evident, was characterised by high levels of IL-10 and IL-6. In the later phase of CNS infection and in a post-drug treatment model, moderate to severe neuropathology was associated with high levels of IFN-γ and TNF-α. The relationship of these cytokines to neuropathological grade suggests that IL-10 and IL-6 protect the CNS from inflammatory pathology when parasites first enter the brain and the data reconcile previously contradictory clinical measurements of CSF cytokines in meningoencephalitic patients with post-mortem histopathology observations.

13383 **Steverding, D. & Tyler, K.M., 2005.** Novel antitrypanosomal agents. *Expert Opinion on Investigational Drugs*, **14** (8): 939–955.

Steverding: School of Medicine, Health Policy and Practice, University of East Anglia, Norwich NR4 TJ7, Norfolk, UK.

Trypanosomes are the causative agents of Chagas' disease in Central and South America and sleeping sickness in sub-Saharan Africa. The current chemotherapy of the human trypanosomiases relies on only six drugs, five of which were developed > 30 years ago. In addition, these drugs display undesirable toxic side effects and the emergence of drug-resistant trypanosomes has been reported. Therefore, the development of new drugs in the treatment of Chagas' disease and sleeping sickness is urgently required. This article summarises the recent progress in identifying novel lead compounds for antitrypanosomal chemotherapy. Particular emphasis is placed on those agents showing promising, selective antitrypanosomal activity.

13384 **Wurochekke, A.U. & Nok, A.J., 2004.** *In vitro* antitrypanosomal activity of some medicinal plants used in the treatment of trypanosomosis in northern Nigeria. *African Journal of Biotechnology*, **3** (9): 481–483.

Wurochekke: Biochemistry Department, Federal University of Technology, Yola, Nigeria. [wchekke@yahoo.co.uk]

The *in vitro* trypanocidal activity of 13 medicinal plants (*Cassia sieberiana, Ximenia americana, Ziziphus spina-christi, Z. abyssinica, Guiera senegalensis, Maytenus senegalensis, Albizia lebbeck, Cassia siamea, Tamarindus indica, Lawsonia inermis, Balanites aegyptiaca, Khaya senegalensis* and *Vernonia amygdalina*) used by local herdsmen in northern Nigeria for the treatment of trypanosomosis was investigated. Forty-four extracts prepared from the 13 plants were screened for *in vitro* activity against *Trypanosoma brucei brucei*. Four of the extracts (extracts of *G. senegalensis* roots, *T. indica* leaves, and *K. senegalensis* bark) showed activity against the parasite at a minimum concentration of 8.3 mg/ml of blood.

8. TRYPANOSOME RESEARCH

(a) CULTIVATION OF TRYPANOSOMES

(b) TAXONOMY, CHARACTERIZATION OF ISOLATES

[See also **28**: nos. 13321, 13331, 13341, 13353, 13354, 13369]

13385 **Adl, S.M., Simpson, A.G.B., Farmer, M.A., Andersen, R.A., Anderson, O.R., Barta, J.R., Bowser, S.S., Brugerolle, G., Fensome, R.A., Fredericq, S., James, T.Y., Karpov, S., Kugrens, P., Krug, J., Lane, C.E., Lewis, L.A., Lodge, J., Lynn, D.H., Mann, D.G., McCourt, R.M., Mendoza, L., Moestrup, Ø., Mozley-Standridge, S.E., Nerad, T.A., Shearer, C.A., Smirnov, A.V., Spiegel, F.W., & Taylor, M.F.J.R., 2005.** The new higher level classification of eukaryotes with emphasis on the taxonomy of protists. *Journal of Eukaryotic Microbiology*, **52** (5): 399–451

Adl: Department of Biology, Dalhousie University, Halifax, NSB3H 4JI Canada.

A new higher level classification of eukaryotes is presented. Regarding the genus *Trypanosoma*, this is placed within the following successively more inclusive groups: Trypanosomatida Kent, Metakinetoplastida Vickerman, Kinetoplastea Honigberg, Euglenozoa Cavalier-Smith, and Excavata Cavalier-Smith.

13386 **Hamilton, P.B., Stevens, J.R., Gaunt, M.W., Gidley, J. & Gibson, W.C., 2004.** Trypanosomes are monophyletic: evidence from genes for glyceraldehyde phosphate dehydrogenase and small subunit ribosomal RNA. *International Journal for Parasitology*, **34** (12): 1393–1404.

Gibson: School of Biological Sciences, University of Bristol, Bristol BS8 1UG, UK.

The genomes of *Trypanosoma brucei*, *Trypanosoma cruzi* and *Leishmania major* have been sequenced, but the phylogenetic relationships of these three protozoa remain uncertain. We have constructed trypanosomatid phylogenies based on genes for glycosomal glyceraldehyde phosphate dehydrogenase (gGAPDH) and small subunit ribosomal RNA (SSU rRNA). Trees based on gGAPDH nucleotide and amino acid sequences (51 taxa) robustly support monophyly of the genus *Trypanosoma*, which is revealed to be a relatively late-evolving lineage of the family Trypanosomatidae. Other trypanosomatids, including the genus *Leishmania*, branch paraphyletically at the base of the trypanosome clade. On the other hand, analysis of the SSU rRNA gene data produced equivocal results, as trees either robustly support or reject monophyly depending on the range of taxa included in the alignment. We conclude that the SSU rRNA gene is not a reliable marker for inferring deep level trypanosome phylogeny. The gGAPDH results support the hypothesis that trypanosomes evolved from an ancestral insect parasite,

which adapted to a vertebrate/insect transmission cycle. This implies that the switch from terrestrial insect to aquatic leech vectors for fish and some amphibian trypanosomes was secondary. We conclude that the three sequenced pathogens, *T. brucei*, *T. cruzi* and *L. major*, are only distantly related and have distinct evolutionary histories.

13387 **Simo, G. Herder, S., Njiokou, F., Asonganyi, T., Tilley, A. & Cuny, G., 2005.** *Trypanosoma brucei* s.l.: characterisation of stocks from Central Africa by PCR analysis of mobile genetic elements. *Experimental Parasitology*, **110** (4): 353–362.

Simo: Laboratoire de Recherche sur les Trypanosomoses (LRT) OCEAC, P.O. Box 288, Yaoundé, Cameroon.

To better understand the epidemiology of sleeping sickness in the Central African sub-region, notably the heterogeneity of Human African Trypanosomiasis (HAT) foci, the mobile genetic element PCR (MGE-PCR) technique was used to genotype *Trypanosoma brucei s.l.* (*T. brucei s.l.*) isolates from this sub-region. Using a single primer REV B, which detects positional variation of the mobile genetic element RIME, via amplification of flanking regions, MGE-PCR revealed a micro genetic variability between *Trypanosoma brucei gambiense* (*T. b. gambiense*) isolates from Central Africa. The technique also revealed the presence of several *T. b. gambiense* genotypes and allowed the identification of minor and major ubiquitous genotypes in HAT foci. The presence of several *T. b. gambiense* genotypes in HAT foci may explain the persistence and the resurgence phenomena of the disease and also the epidemic and the endemic status of some Central African sleeping sickness foci. The MGE-PCR technique represents a simple, rapid, and specific method to differentiate Central African *T. brucei s.l.* isolates.

13388 **Simonite, T., 2005.** Protists push animals aside in rule revamp. *Nature*, **438** (7064): 8–9.

The article describes new perspectives on how the various types of eukaryotes should be classified. A group of protistologists have put forward the view that eukaryotes should be divided into six kingdoms, of which four are for protists, another group for animals and fungi (Opisthokonta), and a sixth group for plants (Archaeplastida). For the protists, one group (Amoeobazoa) comprises amoebae and slime moulds; another is Rhizaria; the third and fourth are termed Chromalveolata and Excavata. The last two are the most controversial of the groupings.

(c) LIFE CYCLE, MORPHOLOGY, BIOCHEMICAL AND MOLECULAR STUDIES

[See also **28**: nos. 13362, 13369, 13378]

13389 **Aitcheson, N., Talbot, S., Shapiro, J., Hughes, K., Adkin, C., Butt, T., Sheader, K. & Rudenko, G., 2005.** VSG switching in *Trypanosoma brucei*:

antigenic variation analysed using RNAi in the absence of immune selection. *Molecular Microbiology*, **57** (6): 1608–1622.

Rudenko: Peter Medawar Building, Pathogen Research, South Parks Road, University of Oxford, Oxford OX1 3SY, UK.

13390 **Albert, M.A., Haanstra, J.R., Hannaert, V., Van Roy, J., Opperdoes, F.R., Bakker, B.M. & Michels, P.A.M., 2005.** Experimental and *in silico* analyses of glycolytic flux control in bloodstream form *Trypanosoma brucei*. *Journal of Biological Chemistry*, **280** (31): 28306–28315.

Michels: Research Unit for Tropical Diseases, Christian de Duve Institute of Cellular Pathology, ICP-TROP 74.39, Université Catholique de Louvain, Ave. Hippocrate 74, B-1200 Brussels, Belgium. [michels@bchm.ucl.ac.be]

13391 **Aphasizhev, R., 2005.** RNA uridylyltransferases. [Review] *Cellular and Molecular Life Sciences*, **62** (19–20): 2194–2203.

Aphasizhev: Department of Microbiology and Molecular Genetics, B240-Medical Sciences I, University of California, Irvine, California 92697, USA.

13392 **Archuleta, L., Dunham, A., Rains, J. & Fry, D., 2005.** Differential tethering of log phase *Trypanosoma brucei* onto chemically distinct surfaces. *ISIS International Symposium on Interdisciplinary Science*, **755**: 185-189.

Archuleta: Northwestern State University, Natchitoches, Louisiana, USA.

13393 **Atrih, A., Richardson, J.M., Prescott, A.R. & Ferguson, M.A.J., 2005.** *Trypanosoma brucei* glycoproteins contain novel giant poly-*N*-acetyllactosamine carbohydrate chains. *Journal of Biological Chemistry*, **280** (2): 865–871.

Ferguson: University of Dundee School of Life Sciences, Wellcome Trust Biocentre, Dow St., Dundee DD1 5EH, Scotland, United Kingdom. [M.a.j.ferguson@dundee.ac.uk]

13394 **Banerjee, S.K., Kessler, P.S., Saveria, T. & Parsons, M., 2005.** Identification of trypanosomatid PEX19: functional characterization reveals impact on cell growth and glycosome size and number. *Molecular and Biochemical Parasitology*, **142** (1): 47–55.

Parsons: Seattle Biomedical Research Institute, 307 Westlake Avenue N., Seattle, WA 98109, USA.

13395 **Barth, S., Hury, A., Liang, X.H. & Michaeli, S., 2005.** Elucidating the role of H/ACA-like RNAs in trans-splicing and rRNA processing via RNA interference silencing of the *Trypanosoma brucei* CBF5 pseudouridine synthase. *Journal of Biological Chemistry*, **280** (41): 34558–34568.

Michaeli: Faculty of Life Sciences, Bar-Ilan University, Ramat-Gan 52900, Israel. [michaes@mail.biu.ac.il]

13396 **Beitz, E., 2005.** Aquaporins from pathogenic protozoan parasites: structure, function and potential for chemotherapy. *Biology of the Cell*, **97** (6): 373–383.

Beitz: Department of Pharmaceutical Chemistry, University of Tübingen, Morgenstelle 8, D-72076 Tübingen, Germany. [eric.beitz@uni.tuebingen.de]

13397 **Benz, C., Nilsson, D., Andersson, B., Clayton, C., & Guilbride, D.L., 2005.** Messenger RNA processing sites in *Trypanosoma brucei*. *Molecular and Biochemical Parasitology*, **143** (2): 125–134.

Andersson: Centre for Genomics and Bioinformatics, Karolinska Institutet, Berzelius väg 35, S-171 77 Stockholm, Sweden.

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African trypanosomes cause human sleeping sickness and livestock trypanosomiasis in sub-Saharan Africa. We present the sequence and analysis of the 11 megabase-sized chromosomes of *Trypanosoma brucei*. The 26-megabase genome contains 9 068 predicted genes, including ~900 pseudogenes and ~1 700 *T. brucei*-specific genes. Large subtelomeric arrays contain an archive of 806 variant surface glycoprotein (VSG) genes used by the parasite to evade the mammalian immune system. Most *VSG* genes are pseudogenes, which may be used to generate expressed mosaic genes by ectopic recombination. Comparisons of the cytoskeleton and endocytic trafficking systems with those of humans and other eukaryotic organisms reveal major differences. A comparison of metabolic pathways encoded by the genomes of *T. brucei*, *T. cruzi*, and *Leishmania major* reveals the least overall metabolic capability in *T. brucei* and the greatest in *L. major*. Horizontal transfer of genes of bacterial origin has contributed to some of the metabolic differences in these parasites, and a number of novel potential drug targets have been identified.

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Kermode: Department of Pharmacology and Toxicology, University of

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After 100 years of research, only a small number of laboratory strains of *Trypanosoma equiperdum* exists, and the history of most of the strains is unknown. No definitive diagnosis of dourine can be made at the serological or molecular level. Only clinical signs are pathognomonic and international screening relies on an outdated cross-reactive serological test (the complement-fixation test) from 1915, resulting in serious consequences at the practical level. Despite many characterization attempts, no clear picture has emerged of the position of *T. equiperdum* within the *Trypanozoon* group. In this article, we highlight the controversies that exist regarding *T. equiperdum*, and the overlap that occurs with *Trypanosoma evansi* and *Trypanosoma brucei brucei*. By revisiting the published data, from the early decades of discovery to the recent serological- and molecular-characterization studies, a new hypothesis arises in which *T. equiperdum* no longer exists as a separate species and in which current strains can be divided into *T. evansi* (the historical mistake) and *Trypanosoma brucei equiperdum* (the master of disguise). Hence, dourine is a disease caused by specific host immune responses to a *T. b. equiperdum* or *T. evansi* infection.

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The question is posed: Why do the three trypanosomatid species *Trypanosoma brucei*, *T. cruzi* and *Leishmania major*, generate so much interest from scientists? The answer is largely, but only partly, that these are responsible for severe diseases in many

parts of the warmer parts of the world. Additionally, these organisms are especially amenable to laboratory culture and study, and have unique features to do with their genetics and metabolic pathways, RNA editing and anchoring of proteins to membranes. The traditional pharmaceutical industry will not become involved in the vital task of transforming laboratory findings on suitable drug targets, into clinical successes. The idea is floated that perhaps the situation needs research institutes dedicated to "diseases of the poor". Funding by donors such as the governments of the wealthier nations, and others, is needed to respond to these dangerous pathogens.

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Whole-genome sequencing of the protozoan pathogen *Trypanosoma cruzi* revealed that the diploid genome contains a predicted 22 570 proteins encoded by genes, of which 12 570 represent allelic pairs. Over 50 percent of the genome consists of repeated sequences, such as retrotransposons and genes for large families of surface molecules, which include trans-sialidases, mucins, gp63s, and a large novel family (>1 300 copies) of mucin-associated surface protein (MASP) genes. Analyses of the *T. cruzi*, *T. brucei*, and *Leishmania major* (Tritryp) genomes imply differences from other eukaryotes in DNA repair and initiation of replication and reflect their unusual mitochondrial DNA. Although the Tritryp lack several classes of signalling molecules, their kinomes contain a large and diverse set of protein kinases and phosphatases; their size and diversity imply previously unknown interactions and regulatory processes, which may be targets for intervention

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A comparison of gene content and genome architecture of *Trypanosoma brucei*, *T. cruzi*, and *Leishmania major*, three related pathogens with different life cycles and disease pathology, revealed a conserved core proteome of about 6 200 genes in large syntenic polycistronic gene clusters. Many species-specific genes, especially large surface antigen families, occur at nonsyntenic chromosome-internal and subtelomeric regions. Retroelements, structural RNAs, and gene family expansion are often associated with syntenic discontinuities that – along with gene divergence, acquisition and loss, and rearrangement within the syntenic regions – have shaped the genomes of each parasite. Contrary to recent reports, the analyses reveal no evidence that these species are descended from an ancestor that contained a photosynthetic endosymbiont.

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Barry: The Anderson College, University of Glasgow, 56 Dumbarton Rd, Glasgow, G11 6NU, UK. [j.d.barry@bio.gla.ac.uk]

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Leishmania species cause a spectrum of human diseases in tropical and subtropical regions of the world. We have sequenced the 36 chromosomes of the 32.8-megabase haploid genome of *Leishmania major* (Friedlin strain) and predict 911 RNA genes, 39 pseudogenes, and 8 272 protein-coding genes, of which 36 percent can be ascribed a putative function. These include genes involved in host-pathogen interactions, such as proteolytic enzymes, and extensive machinery for synthesis of complex surface glycoconjugates. The organization of protein-coding genes into long, strand-specific, polycistronic clusters and lack of general transcription factors in the *L. major*, *Trypanosoma brucei*, and *T. cruzi* (Tritryp) genomes suggest that the mechanisms regulating RNA polymerase II-directed transcription are distinct from those operating in other eukaryotes, although the trypanosomatids appear capable of chromatin remodeling. Abundant RNA-binding proteins are encoded in the Tritryp genomes, consistent with active posttranscriptional regulation of gene expression.

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