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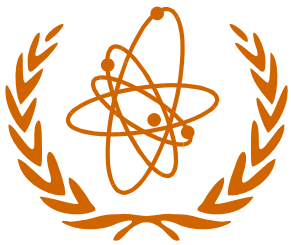

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SECTION A - NEWS

PAAT TECHNICAL AND SCIENTIFIC SERIES: 3

Integrating the Sterile Insect Technique as a Key Component of Area-wide Tsetse and Trypanosomiasis Intervention: PAAT Technical and Scientific Series No. 3

This handbook is published by FAO in 2001, with joint support from FAO, WHO, IAEA and OAU. The authors are U. Feldman and J. Hendrichs, Insect and Pest Control Section, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, IAEA, Vienna, Austria.

The magnitude of the problem presented by trypanosomiasis and its vector, the tsetse fly, is reviewed. Past and present efforts to control tsetse and trypanosomiasis are summarized, with recognition that in most circumstances several methods of control may have to be used, in order to establish viable agricultural systems. Trypanocidal drugs are widely used, but suffer from several disadvantages. They are expensive for the peasant farmer to buy, especially if diagnosis is involved. Unsupervised use of these drugs leads to underdosing, and hence to increasing resistance by the parasite. Fake drugs are on sale. The prospects of new effective drugs coming on stream are poor. Trypanotolerant cattle have merits, although they too are at risk in heavier disease challenge areas, and when under stress through use for draught or because of malnutrition. Insecticides when applied to cattle, or to artificial devices (traps, targets), can suppress tsetse populations in most situations. Whether community participation in such schemes can outlast external funding support remains a problem to be tackled. While large control measures mainly based on the use of insecticide delivered from the air or from the ground have been used in the recent past, such measures are somewhat out of favour due to environmental concerns and technical difficulties of treating all pockets of the fly habitat. Nevertheless, some such methods will probably have to be used in conjunction with SIT, and this anticipated integrated mode of control forms the subject of much of the handbook.

The sterile insect technique is defined and explained. Examples of the successful use of the SIT against the screw worm fly and other target species are given, as well as a summary of the partially successful efforts against the tsetse in various locations, such as Zanzibar. The mass rearing requirements of tsetse are compared with those of the screw worm fly, and it is pointed out that blood, the only food of tsetse, is locally available, and once made sterile is a satisfactory food medium for rearing the fly in artificial colonies. The low reproductive rate of the tsetse is seen as an advantage in field campaigns, as it takes much longer time for partially suppressed populations to recover than is the case for insects that have a very high reproductive rate (such as the screw worm fly); the slow recovery would give greater opportunity for the SIT method to take effect. Regarding the rate of tsetse advance or infiltration into a new area, figures depend on the species involved. The process can be likened to a gradual flooding from infested areas to previously non-infested areas; sudden jumps of fly from one area to a non-adjacent area

such as is commonplace for the screw worm, probably does not normally occur. Work in progress on barriers to tsetse advance using insecticide treated cloth screens might well benefit from ongoing studies on gene flow between adjacent populations. Decisions on the strategic location of tsetse barriers will benefit from the application of Geographic Information Systems. The logistic challenges of a SIT campaign against tsetse are considered to be considerable but manageable.

It is possible to list the conditions under which the opportunities for the use of tsetse SIT are greatest. A full list cannot be given here, but it includes places where the target population is isolated in ecological islands, where tsetse-infested areas of difficult topography are out of reach, or where tsetse-infested wildlife reserves and agricultural areas are in proximity and threaten one another. A number of possible target areas are listed, including the Ethiopian valley systems, peri-urban systems in West Africa, the *Glossina fuscipes fuscipes* belt around much of Lake Victoria, and the Okovango delta in Botswana. Detailed assessments have to be conducted before any such campaign is started.

The SIT has some environmental advantages over other methods of control. For instance, the release of sterile males of a given species, targets that particular species and no other. No predator or parasite is known to be dependent upon the tsetse for its food, so that tsetse eradication is not harming other species directly. If game reserves are seen by farmers to help the survival of tsetse, the farmers might welcome the destruction of the reserves; if however, the flies have been eradicated, this factor is removed, although there may be other pressures on the wild life.

The handbook warns against a piecemeal approach to control, as measures against the fly are more effective the larger the area that is tackled. Arguing for a large effort, the example is given of the screw worm eradication campaign, in which nearly US$1 billion was spent over the years 1957 to 2000, resulting in benefits to the previously affected countries of US$1.165 billion annually. Recurrent expenditures resulting from trypanosomiasis are often high, so that making the effort and expenditure to control the disease rather than to simply contain it, has economic advantages in the long run.

Technical aspects of SIT requiring attention include the need to target several economically important species, implying that several breeding colonies will be needed where there are several tsetse species transmitting trypanosomiasis. Improving existing barrier techniques requires continued study. Mass-rearing of flies is an area needing technical improvement and cost-cutting, most probably by automating several of the existing labour-intensive activities. The food, blood, could be supplied by contract; likewise private companies could be contracted to release the sterilized flies from the air.

In sketching out a plan of action, the advancement, promotion and implementation of SIT are seen as requiring efforts in the areas of (i) Awareness, support and funding issues, (ii) Technical issues, and (iii) Normative issues.

In conclusion, the handbook anticipates sustainable results from area-wide integrated tsetse eradication with an SIT component.

BOOK SERIES ON PARASITES

World Class Parasites: Volume 1, The African Trypanosomes

A new series of books has been launched by Kluwer Academic Publishers [kluwer@wkap.com], dealing with parasites. This series, called World Class Parasites, is written for researchers, students and scholars, and deals with problems of global significance caused by these organisms. Each of the series is focused on a parasite or group of parasites that have had an impact on human health and agriculture, and against which we have as yet an inadequate defence.

The first volume in the series was published in 2001; it is called *The African Trypanosomes,* 176 pp. This is edited by S.J. Black (University of Massachusetts, Amherst, MA) and J.R. Seed (University of North Carolina, Chapel Hill, NC), who contribute a Preface and an Epilogue.

There are twelve articles as follows (authors' names given): D. Molyneux, *African Trypanosomiasis. Failure of Science and Public Health* [see 12136]; M. Gilbert et al., *The Programme against African Trypanosomiasis Information System (PAATIS)* [see 12135]; J.J. McDermott et al., *Effects of Climate, Human Population and Socio-Economic Changes on Tsetse-Transmitted Trypanosomiasis to 2050* [see 12143]; S. Askoy, *Tsetse Vector Based Strategies for Control of African Trypanosomiasis* [see 12141]; P. Büscher, *Diagnosis of Human and Animal Trypanosomiasis* [see 12150]; J.R. Seed and D.W. Boykin, *Chemotherapy of African Trypanosomiasis* [see 12165]; J.M. Mansfield, T.H. Davis and M.E. Dubois, *Immunology of African Trypanosomiasis – New Paradigms, Newer Questions* [see 12154]; J. Naessens, D.J. Grab and M. Selighem, *Identifying the Mechanisms of Trypanotolerance in Cattle* [see 12157]; N.B. Murphy and T. Olijhoek, *Trypanosome Factors Controlling Population Size and Differentiation Status* [see 12146]; D. Nolan et al., *The Endocytic Machinery of Bloodstream Stage African Trypanosomes* [see 12193]; J.E. Donelson, *The Genome of the African Trypanosome* [see 12168]; S.J. Black, N.B. Murphy and D.P. Nolan, *Towards a Trypanosomiasis Vaccine* [see 12158]. These various contributions are the subject of entries in Section B – Abstracts appearing later, under the respective entry numbers, in this issue of *Tsetse and Trypanosomiasis Information Quarterly*.

The Preface points out that in the cause of containment and control of disease such as trypanosomiasis, scientists can accurately describe the field situation, advocate the effective use of existing strategies of parasite and vector control, improve scientist to scientist communication and improve lines of contact with administrative and funding agencies, so as to foster further parasitological research and the implementation of the results. The articles cover these areas.

The Epilogue takes the opportunity to discuss how far Professor Molyneux's complaints are being met by new developments, and the editors point especially to PAATIS and the future trypanosomiasis risk assessment programme as steps in the direction of formulating a more coherent policy for combating the disease. The overview of the subject as given by Volume 1 is admitted to be less than comprehensive, as topics such as tsetse attractants and trap technology, the molecular basis for human resistance to

infections with *T. b. brucei, T. congolense and T. vivax*, and the characterization of metabolic and transport processes that are critical for trypanosome survival, are omitted. Including these topics in later volumes of the World Class Parasites series is not ruled out.

PLANS FOR TSETSE CONTROL IN ETHIOPIA

OAU PATTEC initiatives in Ethiopia

The Lancet reports (Nita Bhalla, 2002, "Pan African group takes lead against the tsetse fly" *Lancet*, **359**: 686) how the OAU has launched a new campaign to control the tsetse fly. The plan is to release millions of sterilized male flies that will mate with healthy normal female flies in the field, causing them to be sterilized themselves. The fly population will thus be progressively reduced by this Sterile Insect Technique (SIT) with benefits to the people and livestock under threat from trypanosomiasis. John Kabayo, regional co-ordinator of the Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) is quoted as saying that it is no accident that the concentration of much of the world's most acute poverty is in regions of sub-Saharan Africa infected with trypanosomiasis. WHO estimates that close to half a million people are affected by human trypanosomiasis; concerning agriculture, the UK government estimates that Africa loses US$4.5 billion annually due to the tsetse fly.

Noting that trypanosomiasis was eradicated from the island of Zanzibar, with benefits to milk and beef production there, Ethiopia has started on a tsetse eradication programme in certain southwestern areas including the Omo Valley, using the SIT, as in Zanzibar. Technical support comes from the International Atomic Energy Agency (IAEA) but the cost of the campaign is to come from the Ethiopian government. The plan is to release ten million sterile male tsetse flies starting next year. First positive results from the campaign will be the clearance of tsetse-infested land, and will be seen in two years; the whole campaign will take 15 years.

However, there have been words of caution expressed by some. John McDermott (epidemiologist, International Institute for Livestock Research, Nairobi) says that the eradication of tsetse fly is a complex issue. It would have helped the technique that Zanzibar was an island and the risk of reinvasion low; other earlier attempts to use SIT in Nigeria and mainland Tanzania, failed because of the difficulty of isolating vast mainland areas.

Nevertheless, several countries have started breeding flies and identifying areas that could be targeted, and the OAU PATTEC taskforce has plans to help other affected countries in similar ways.

TRYPANOSOMIASIS CONTROL EFFORTS IN UGANDA

Ugandan veterinarians counter cattle-borne HAT

Recent publications in the scientific press implicating infected cattle in the recent outbreaks of HAT in parts of Uganda have spurred the Ugandan veterinary authorities to stop such cattle movements before the cattle have been treated, Charles Wendo reports in *Lancet*, 2002, **359**:239. The Director of Animal Resources, Dr. William Olaho Mukhani, is quoted as saying that in areas where trypanosomiasis is endemic, veterinary officials will not issue movement permits to traders before their cattle had been treated. Farmers would meet the cost of treatment. A dose costs US$0.50 to US$1, while the average price of cattle is US$100. The crux of the problem is the loss of cattle to rustlers, and the subsequent attempts by farmers in Soroti in the east of Uganda, to replace these losses by bringing in cattle from other parts of the country. By this traffic in cattle, human-infective strains of trypanosomes have been introduced into places previously free of infection. Some 60 cases of sleeping sickness per year are reported from the area, but this is thought to underestimate the true incidence of the disease. The Ministry of Health has praised the cooperation of the veterinary workers.

STRATEGY FOR TSETSE CONTROL, MALI AND BURKINA FASO

Integrated control of animal trypanosomiasis to create a tsetse fly free zone

In Mali and Burkina Faso the two most important tsetse species are the palpalis group flies *Glossina palpalis gambiensis* and *G. tachinoides*. These fly species cause problems by their transmission of trypanosomiasis to the resident cattle population and thereby greatly reducing the productivity of the national herd, and elimination of the disease by removal of the vector flies from designated zones is seen as a major step towards the elimination of hunger and alleviation of poverty in the affected area.

The governments of these two countries have signed a document that outlines a strategy to create tsetse free zones; the document is co-signed by IAEA, endorsing the initiative. The techniques expected to be used to create these tsetse free zones are the sterile insect technique, traps, insecticide impregnated cloth screens, the pour-on technique and sequential aerosol application of insecticides. All these different methods will be integrated to achieve the desired end. The geographical unit will be the catchment area or 'primary river system' and special efforts will be directed to surveying by various means how far each unit is isolated from neighbouring ones. High resolution satellite imagery, tsetse population dynamics, patterns of distribution and the information available from genetic markers, are the main sources of information which will guide management in assessing the effective isolation of target areas. Fly barriers will be erected at points of likely migration of flies from one river system to another.

It is anticipated that the project will benefit from the existing rearing facilities that cultures *G. p. gambiensis*, at the CIRDES center in Bobo Dioulassou; expansion of these

facilities will allow the release of 30,000 sterile males per week in to the target areas (see Insect Pest Control Newsletter, Joint FAO/IAEA Division).

SECTION B- ABSTRACTS

1. GENERAL (INCLUDING LAND USE)

12134 **Cook, G.C., 2002.** Charles Wilberforce Daniels, FRCP (1862-1927): underrated pioneer of tropical medicine. *Acta Tropica*, **81** (3): 237-250.

Cook: Wellcome Trust Centre for the History of Medicine at UCL, 183 Euston Road, London NW1 2BE, UK.

Charles Wilberforce Daniels was a major pioneer in the early days of the newly-formed medical specialism – tropical medicine. At the London School of Tropical Medicine of which he was a leading stalwart, he took an active part in research, teaching and administration, but like others in the new discipline he spent a great deal of time at various tropical locations: Fiji, British Guiana (where he made important observations on various forms of filariasis), east Africa and Malaya. However, his most important research contribution was arguably confirmation of Ronald Ross' 1898 discovery of the complete life-cycle of avian malaria, in Calcutta.

12135 **Gilbert, M., Jenner, C., Pender, J., Rogers, D., Slingenbergh, J. and Wint, W., 2001.** The Programme against African Trypanosomiasis Information System (PAATIS). In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp.11-24. Kluwer Academic Publishers, Dordrecht.

Gilbert: Laboratoire de Biologie animale et cellulaire, CP 160/12, Free University of Brussels, av. F.D.Roosevelt 50, B-1050 Brussels, Belgium.

The Programme against Animal Trypanosomiasis (PAAT) was set up in 1995. It is managed by a joint secretariat to which FAO, OAU/IBAR, IAEA and WHO are contributors. The present paper describes the PAAT-Information System (PAATIS), which is intended to assist taking decisions relating to selection of tsetse control areas and control strategy, and to provide information on tsetse and trypanosomiasis. It will be packaged electronically and distributed for wide evaluation and eventual modification.

12136 **Molyneux, D.H., 2001.** African trypanosomiasis: Failure of science and public health. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp.1-10. Kluwer Academic Publishers, Dordrecht.

Molyneux: Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK.

It is argued that much work on trypanosomiasis concentrates more on the biochemistry and host-parasite relations, rather than specifically on disease control

measures. It is urged that the massive public health problem of sleeping sickness should be countered by ensuring that we use existing diagnostic and vector control tools cost-effectively within sustainable public health systems; science should be given a final chance to produce effective new drugs against trypanosomiasis.

2. TSETSE BIOLOGY

(a) REARING OF TSETSE FLIES

(b) TAXONOMY, ANATOMY, PHYSIOLOGY, BIOCHEMISTRY

12137 **Kimura, T., Carlson, D.A. and Mori, K., 2001.** Synthesis of all the stereoisomers of 13,17-dimethyl-1-tritriacontene and 13,17-dimethyl-1-pentatriacontene, the contact sex pheromone components of the female tsetse fly, *Glossina austeni*. *European Journal of Organic Chemistry*, **17**: 3385-3390.

Mori: Department of Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka 1-3, Shinjuku-ku, Tokyo 162-8601, Japan.

All of the stereoisomers of 13,17-dimethyl-1-tritriacontene and 13,17-dimethyl-1-pentatriacontene, the contact sex pheromone components of the female tsetse fly (*Glossina austeni*), were synthesized starting from the enantiomers of the protected syn- and anti-2,6-dimethylheptane-1,7-diol, which were prepared from the enantiomers of methyl 3-hydroxy-2-methylpropanoate and methyl phenyl sulfone.

12138 **Yan, J., Cheng, Q., Li, C.-B. and Aksoy, S., 2002.** Molecular characterization of three gut genes from *Glossina morsitans morsitans*: *cathepsin B*, *zinc-metalloprotease* and *zinc-carboxypeptidase*. *Insect Molecular Biology*, **11** (1): 57-65.

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

(c) DISTRIBUTION, ECOLOGY, BEHAVIOUR, POPULATION STUDIES

12139 **Dransfield, R.D. and Brightwell, R., 2001.** Trap efficiency for *Glossina pallidipes* (Diptera: Glossinidae) at Nguruman, south-west Kenya. *Bulletin of Entomological Research*, **91** (6): 429-444.

Dransfield: 5 The Square Cottages, Burwash, East Sussex, TN19 7EF, UK. [thebobs@mistral.co.uk]

An incomplete ring of electric nets was evaluated as a means of estimating trap efficiency for *Glossina* spp. This methodology assumes flies approach the trap directly, and then enter, or leave directly in random directions. These results showed that the ratio of the number of flies intercepted on the outside of the electric nets to the number on the inside was lower than predicted by this single-approach behavioural model. Moreover, an incomplete ring of nets around a trap reduced trap catch more than the model predicted. These inconsistencies were greater early in the day, and greater for females than for males. It is suggested that flies may make several approaches to a trap before entering or departing. This mixes arriving and departing flies on each side of the electric nets. Use of a complete ring of nets around a trap to estimate trap efficiency entails fewer behavioural assumptions. Catches at a complete ring around a trap were compared to catches in a trap without nets, replicated in a cross-over design. The efficiency of an odour-baited NG2G trap was estimated to be 58% for males and 37% for females. Biconical traps were much less efficient. Both trap types were less efficient in the early morning, suggesting entry response is temperature dependent. The NG2G trap was more efficient for non-teneral nulliparous females than for other ages. For both trap types there was little difference between mean fat content of approaching and trapped males, but the mean fat content of trapped females was lower than that of approaching females.

12140 **Krafsur, E.S., 2002.** Population structure of the tsetse fly *Glossina pallidipes* estimated by allozyme, microsatellite and mitochondrial gene diversities. *Insect Molecular Biology*, **11** (1): 37-45.

Krasfur: Department of Entomology, Iowa State University, Ames, Iowa, 50011-3222, USA. [ekrafsur@iastate.edu]

Diversities at nuclear and mitochondrial loci were examined in eleven natural populations of *Glossina pallidipes* from east and southern Africa. Alleles in each class of loci are assumed to be selectively neutral. Allozyme gene diversities (heterozygosities) averaged over eight loci were 0.146 among seven Kenya populations and 0.201 among four southern African populations. Microsatellite diversity averaged over three loci was 0.250 in Kenya and only 0.218 in southern Africa. Mitochondrial diversities averaged 0.504 in Kenya and only 0.156 in southern Africa. Mitochondrial and microsatellite diversities in the populations were strongly correlated with each other, but uncorrelated with allozyme diversities. In contrast to the allozyme diversities, mitochondrial and microsatellite variation indicated a severe and prolonged reduction in population size in southern Africa. Genetic distances among populations increased with the geographical distances between them. Allozyme diversities in southern populations were conserved. Genetic differentiation at allozyme loci among populations was greatly damped when compared with the other markers. The foregoing can be explained if allozyme diversities were maintained by balancing selection. Three main points emerged: genetic data confirm the historical evidence that southern *G. pallidipes* populations experienced a severe and prolonged bottleneck; allozyme variation was conserved in the bottlenecked populations; and gene flow among populations is surprisingly restricted.

3. TSETSE CONTROL (INCLUDING ENVIRONMENTAL SIDE EFFECTS)

[See also: **25** no. 12139]

12141 **Aksoy, S., 2001.** Tsetse vector based strategies for control of African trypanosomiasis. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 39-49. Kluwer Academic Publishers, Dordrecht.

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

The symbiotic bacteria that naturally live within the tsetse fly body can be made to express foreign genes. Such symbionts reside in the same tissues as trypanosomes for which the tsetse is a vector, and could be used by means of anti-trypanosome gene products to disrupt parasite differentiation or establishment in the gut.

12142 **Maniania, N.K., 2002.** A low-cost contamination device for infecting adult tsetse flies, *Glossina* spp., with the entomopathogenic fungus *Metarhizium anisopliae* in the field. *Biocontrol Science and Technology*, **12** (1): 59-66.

Maniania: ICIPE, P.O.Box 30772, Nairobi, Kenya. [nmaniania@icipe.org]

A low-cost device for infecting adult tsetse fly, *Glossina fuscipes fuscipes*, with the entomopathogenic fungus *Metarhizium anisopliae* was designed and tested in the field. Tsetse flies that are attracted to the trap entered the contamination device and ultimately became infected with the fungus. Traps exposed to the sun attracted more flies than did the ones placed in the shade. The time spent by single flies in the contamination device varied between 5-189 s, and the subsequent number of conidia collected varied between 1.6 x 10^5 conidia and 40.5 x 10^5 conidia per fly, and largely depended on the behaviour of individual flies. Dry conidia of *M. anisopliae* in the device retained their viability for 31 days in the field, and efficacy against *G. fuscipes* was not affected.

12143 **McDermott, J.J., Kristjanson, P.M., Kruska, R.L., Reid, R.S., Robinson, T.P., Coleman, P.G., Jones, P.G. and Thornton, P.K., 2001.** Effects of climate, human population and socio-economic changes on tsetse-transmitted trypanosomiasis to 2050. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 25-38. Kluwer Academic Publishers, Dordrecht.

McDermott: ILRI, P.O.Box 30709, Nairobi, Kenya.

The impact of climate change, human population growth and control activities on tsetse distribution and on the risk of trypanosomiasis in sub-Saharan Africa are followed to 2050. Overall, areas under risk will contract, especially in the semi-arid and sub-humid zones of western Africa. The situation in humid central and western Africa will be less altered. Sleeping sickness is expected to remain a major problem if control measures are not put in place.

4 EPIDEMIOLOGY: VECTOR-HOST AND VECTOR PARASITE INTERACTIONS

12144 **De la Rocque, S., Michel, J.F., De Wispelaere, G. and Cuisance, D., 2001.** New tools for animal trypanosomosis study: Remote sensing and geographical information system to highlight the sites of transmission. *Parasite*, **8** (3): 171-195.

De la Rocque: CIRAD-EMVT, campus de Baillarguet, TA 30 F, 34398 Montpellier Cedex 5, France.

Recent studies in a rangeland area of Burkina Faso showed that riparian tsetse flies (*Glossina tachinoides* and *G. palpalis gambiensis*) were found along the main rivers, but depending on their location, had different hosts and were not infected by the same trypanosomoses. There were different epidemiological situations within a distance of a few kilometres, and local assessment of the trypanosome risk thus called for a global approach taking account of the environmental and human factors involved in the interfaces between hosts and vectors. Various types of information concerning entomology, parasitology, ecology, land occupation and animal production systems were fed into a Geographical Information System. High spatial resolution remote sensing tools and original modelling methods were used to detect the valley landscapes most favourable to tsetse flies, and to describe land use by herds. The impact of trypanosomes appeared to depend largely on animal movements, watering practices and the degree of contact with riparian tsetse flies. Linking these types of information revealed the most dangerous sites in epidemiological terms, which in this case represented some 18 % of the network initially surveyed.

12145 **MacLeod, A., Tait, A., and Turner, C.M.R., 2001.** The population genetics of *Trypanosoma brucei* and the origin of human infectivity (vol **356**, pg 1035, 2001). (Corrections are made to the earlier Figure 1.) *Philosophical Transactions of the Royal Society of London, Series B – Biological Sciences*, **356** (1416): 1975.

MacLeod: Wellcome Centre of Molecular Parasitology, Anderson College, University of Glasgow, 56 Dumbarton Rd, Glasgow G11 6NU, UK. [gvwa08@udcf.gla.ac.uk]

12146 **Murphy, N.B. and Olijhoek, T., 2001.** Trypanosome factors controlling population size and differentiation status. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 113-126. Kluwer Academic Publishers, Dordrecht.

Murphy: ILRI, P.O.Box 30709, Nairobi, Kenya.

In the African trypanosome life cycle, growth differentiation and population size of trypanosomes in the tsetse fly and in the mammalian host, are under close control. Recent work has shown that a low molecular weight factor is released by bloodstream forms which causes the trypanosomes to cease division. The same factor also acts on metacyclic forms, blocking their infectivity for mammals. Some of the effects on the living trypanosome cell have been traced.

12147 **Tait, A., Masiga, D., Ouma, J., MacLeod, A., Sasse, J., Melville, S., Lindegard, G., McIntosh, A. and Turner, M., 2002.** Genetic analysis of phenotype in *Trypanosoma brucei*: a classical approach to potentially complex traits. *Philosophical Transactions of the Royal Society of London, Series B – Biological Sciences*, **357** (1417) 89-99.

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The genome of the African trypanosome, *Trypanosoma brucei*, is currently being sequenced, raising the question of how the data generated can be used to determine the function of the large number of genes that will be identified. There is a range of possible approaches, and in this paper we discuss the use of a classical genetic approach coupled with positional cloning based on the ability of trypanosomes to undergo genetic exchange. The genetics of these parasites is essentially similar to a conventional diploid Mendelian system with allelic segregation and an independent assortment of markers on different chromosomes. Data are presented showing that recombination occurs between markers on the same chromosome allowing the physical size of the unit of recombination to be determined. Analysis of the available progeny clones from a series of crosses shows that, in principal, large numbers of progeny can readily be isolated from existing cryopreserved products of mating and, taking these findings together, it is clear that genetic mapping of variable phenotypes is feasible. The available phenotypes for analysis are outlined and most are relevant to the transmission and pathogenesis of the parasite. Genetic maps from two crosses are presented based on the use of the technique of AFLP; these maps comprise 146 and 139 markers in 30 and 21 linkage groups respectively. Segregation distortion is exhibited by some of the linkage groups and the possible reasons for this are discussed. The general conclusion, from the results presented, is that a genetic-mapping approach is feasible and will, in the future, allow the genes determining a number of important traits to be identified.

12148 **Truc, P., Ravel, S., Jamonneau, V., N'Guessan, P. and Cuny, G., 2002.** Genetic variability within *Trypanosoma brucei gambiense*: evidence for the circulation of different genotypes in human African trypanosomiasis patients in Côte d'Ivoire. *Transactions of the Royal Society of Tropical Medicine and Hygeine*, **96** (1): 52-55.

Truc: Institut de Recherche pour le Développement, Départment Sociétés et Santé, UR 035 'Trypanosomoses Africaines', OCEAC, BP 288, Yaoundé, Cameroon. [truc@iccnet,cem]

For 23 Ivoirian patients infected by *Trypanosoma brucei gambiense*, isolation and genetic characterization using PCR and microsatellite primers were performed (in 1996-99) using two different isolates (A and B) from each patient. When using TBDAC 1/2, seven genotypes were observed, and DNAs A and B for two patients were different. This might be the first evidence of the presence of two different genotypes of *T. b. gambiense* group I in the same patient.

5. HUMAN TRYPANOSOMIASIS

(a) SURVEILLANCE

12149 **Bisser, S., Lejon, V., Preux, P.M., Bouteille, B., Stanghellini, A., Jauberteau, M.O., Büscher, P. and Dumas, M., 2002.** Blood-cerebrospinal fluid barrier and intrathecal immunoglobulins compared to field diagnosis of central nervous system involvement in sleeping sickness. *Journal of the Neurological Sciences*, **193** (2): 127-135.

Bisser: Institut d'Epidemiologie Neurologique et de Neurologie Tropicale (IENT), Faculté de Médecin 2, rue du Docteur Raymond Marcland, 87025 Limoge Cedex, France. [ient@unilim.fr]

Diagnosis of central nervous system (CNS) involvement in sleeping sickness is crucial in order to give an appropriate treatment regimen. Neurological symptoms occur late, therefore field diagnosis is based on white blood cell count, total protein concentration and presence of trypanosomes in cerebrospinal fluid (CSF). More sensitive and specific parameters are now available. Blood-CSF barrier (B-CSFB) dysfunction, intrathecal total and specific immunoglobulin synthesis were evaluated in 95 patients with and without obvious meningoencephalitis, and compared to field criteria. B-CSFB dysfunction is a rather late event in the course of CNS involvement and correlates with the presence of trypanosomes, neurological signs and intrathecal polyspecific and specific immune response. IgM intrathecal response and particularly IgM antibody index are early markers of CNS invasion. We showed that 29% of patients with CSF abnormalities but without trypanosome detection in the field had no neuro-immunological response. In contrast, patients with normal CSF according to field diagnosis showed an intrathecal immune response in 31% of the cases. Field diagnosis can therefore fail to determine

neurological involvement but can also provide false positive results. Improved criteria including B-CSFB dysfunction and IgM detection are needed in order to provide an adapted treatment regimen.

12150 **Büscher, P., 2001.** Diagnosis of human and animal African trypanosomiasis. In *The African Trypanosomes*, (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed) pp. 51-63. Kluwer Academic Publishers, Dordrecht.

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

Considerable success has been obtained in the development of diagnostic tests based on the detection of antibodies, some of which tests are already in use in the rural tropics. Molecular diagnostic methods have great potential for the detection of human and animal African trypanosomiasis, being highly sensitive and specific. They should be brought to bear on the needs of those working in the field, by making such methods more robust and by tackling the problem of cost.

12151 **Magnus, E., Lejon, V., Bayon, D., Buyse, D., Simarro, P., Verloo, D., Vervoort, T., Pansaerts, R., Büscher, P. and Van Meirvenne, N., 2002.** Evaluation of an EDTA version of CATT/*Trypanosoma brucei gambiense* for serological screening of human blood samples. *Acta Tropica*, **81** (1): 7-12.

Magnus: Department of Parasitology, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium. [emagnus@itg.be]

CATT/*Trypanosoma brucei gambiense*, a direct card agglutination test designed for field surveys on human African trypanosomosis, is currently used with freshly collected heparinized blood samples. When testing serum samples, it had been observed earlier that, at lower sample dilutions, a complement-mediated inhibition phenomenon may cause false negative test results. This can be avoided by adding an anticomplementary agent such as di-sodium ethylenediaminetetraacetate dihydrate (EDTA) to the reaction. As the sensitivity of the blood assay might be improved in the same way, this possibility has been examined under both laboratory and field conditions, by adding EDTA to the test buffer or, as an anticoagulant, to the blood samples. The CATT-EDTA versions proved up to 7% more sensitive but also 1-2% less specific than the current test. CATT buffer supplemented with EDTA remained stable for at least 2 years at +45^{o}C.

(b) PATHOLOGY AND IMMUNOLOGY

12152 **LaCount, D.J. and Donelson, J.E., 2001.** RNA interference in The African Trypanosomes. (Editorial review.) *Protist*, **152** (2): 103-111.

Donelson: Department of Biochemistry, University of Iowa, Iowa City, Iowa 52242, USA. [john-donelson@uioma.edu]

12153 **Lonsdale-Eccles, J.D. and Grab, D.J., 2002.** Trypanosome hydrolases and the blood-brain barrier. *Trends in Parasitology*, **18** (1): 17-19.

Lonsdale-Eccles: Centre for Biophysical Sciences and Engineering, University of Alabama at Birmingham, AL 35294, USA.

African trypanosomes cross the blood-brain barrier, but how they do so remains an area of speculation. We propose that proteases, such as the trypanopains and oligopeptidases that are released by trypanosomes, could mediate in this process. The trypanosomes also possess cell-surface-associated acid phosphatases that could play a role in invasion similar to that in advancing cancer cells. Such enzymes, perhaps acting in concert, have the potential to cause tissue degradation and ease the passage of the trypanosomes through various tissues in the host, including the blood-brain barrier.

12154 **Mansfield, J.M., Davis, T.H. and Dubois, M.E., 2001.** Immunobiology of African trypanosomiasis: New paradigms, newer questions. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 79-96. Kluwer Academic Publishers, Dordrecht.

Mansfield: Department of Bacteriology, 1925 Willow Drive/FRI Building, University of Wisconsin-Madison, Madison, WI 53706 USA.

With the aim of providing new perspectives on the immunology of African sleeping sickness, the subject is reviewed with particular reference to recent findings concerning the variant surface glycoprotein specific Ab response, and the agents providing tissue-specific protection against trypanosomes. The topics of "antigen pattern" recognition of the VSG coat by B cells, and the role of the trypanosome T lymphocyte triggering factor, are addressed.

(c) TREATMENT

[See also **25**: no. 12165]

12155 **Burchmore, R.J.S., Ogbunude, P.O.J., Enanga, B. and Barrett, M.P., 2002.** Chemotherapy of human African trypanosomiasis. (Review). *Current Pharmaceutical Design*, **8** (4): 257-267.

Burchmore: Institute of Biochemical and Life Sciences, Division of Infection and Immunity, University of Glasgow, Glasgow, UK.

Human African trypanosomiasis or sleeping sickness is resurgent. The disease is caused by subspecies of the parasitic haemoflagellate, *Trypanosoma brucei*. Infection starts with the bite of an infected tsetse fly (*Glossina* spp.). Parasites move from the site of infection to the draining lymphatic vessels and blood stream. The parasites proliferate within the bloodstream and later invade other tissues including the central nervous system. Once they have established themselves within the CNS, a progressive breakdown of neurological function accompanies the disease. Coma precedes death during this late phase. Two forms of the disease are recognised, one caused by *Trypanosoma brucei rhodesiense*, endemic in Eastern and Southern Africa, in which parasites rapidly invade the CNS causing death within weeks if untreated. *Trypanosoma b. gambiense*, originally described in West Africa, but also widespread in Central Africa, proliferates more slowly and can take several years before establishing a CNS-involved infection. Many countries are in the midst of epidemics caused by gambiense-type parasites. Four drugs have been licensed to treat the disease; two of them, pentamidine and suramin, are used prior to CNS involvement. The arsenic-based drug, melarsoprol, is used once parasites are established in the CNS. The fourth, eflornithine, is effective against late stage disease caused by *T. b. gambiense*, but is ineffective against *T. b. rhodesiense*. Another drug, nifurtimox is licenced for South American trypanosomiasis but also been used in trials against melarsoprol-refractory late stage disease. This review focuses on what is known about modes of action of current drugs and discusses targets for future drug development.

6. ANIMAL TRYPANOSOMIASIS

(a) SURVEY AND DISTRIBUTION

[See also: **25** no. 12150]

12156 **Nkinin, S.W., Njiokou, F., Penchenier, L., Grébaut, P., Simo, G. and Herder, S., 2002.** Characterization of *Trypanosoma brucei* s.l. subspecies by isoenzymes in domestic pigs from the Fontem sleeping sickness focus of Cameroon. *Acta Tropica*, **81** (3): 225-232.

Herder: LRCT/CIRAD-IRD, TA 207/G, Campus International de Baillarguet, 34398 Montpellier Cedex 5, France. [herder@mpl.ird.fr]

Though it has been established that domestic animals (especially the pig) are potential reservoir hosts for *Trypanosoma brucei gambiense* in West Africa, there is little data to this effect concerning Central Africa. Instead, some previous authors report the absence of *Trypanozoon* type trypanosomes in domestic animals in Cameroon. Thirty-two domestic pigs were sampled by KIVI (kit for in vitro isolation) of trypanosomes in the northern region (Bechati) of the Fontem sleeping sickness focus of Cameroon. Twenty-one of these were found positive, from 15 of which 17 isolates were successfully obtained. Isoenzyme characterization revealed that isolates from 4 of the 15 pigs

belonged to zymodemes associated with *T. brucei gambiense* group 1. The prevalence of this disease in the local human population is, however, very low. It is evident from this study that the domestic pig may be a potential reservoir host for *T. brucei gambiense* in the Fontem focus. There is, however, need for an extensive study on domestic animals in Cameroon and other neighbouring countries for a better comprehension of the epidemiology of sleeping sickness within the Central African region.

(b) PATHOLOGY AND IMMUNOLOGY

[See also: **25** no.12154]

(c) TRYPANOTOLERANCE

12157 **Naessens, J., Grab, D.J. and Sileghem, M., 2001.** Identifying the mechanisms of trypanotolerance in cattle. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 97-111. Kluwer Academic Publishers, Dordrecht.

Naessens: ILRI, P.O.Box 30709, Nairobi, Kenya.

N'Dama and other trypanotolerant breeds remain productive under challenge from trypanosomes. Research on the mechanisms of such trypanotolerance could lead to new avenues for disease control. Comparison of responses in trypanotolerant and trypanosusceptible cattle breeds, and in mouse models, reveals two separate mechanisms at work, and further insights are expected to follow from genetic studies.

(d) TREATMENT

[See also: **25** no. 12165]

7. EXPERIMENTAL TRYPANOSOMIASIS

(a) DIAGNOSTICS

(b) PATHOLOGY AND IMMUNOLOGY

12158 **Black, S.J., Murphy, N.B. and Nolan, D.P., 2001.** Towards a trypanosomiasis vaccine. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 159-174. Kluwer Academic Publishers, Dordrecht.

Black: Department of Veterinary and Animal Sciences, University of Massachusetts, Paige Laboratory, Amherst, MA 01003, USA.

The development of a vaccine against trypanosomiasis will depend on knowledge of the trypanosome habitat in the mammalian host, of various nutrients and growth factors, and of trypanocidal and trypanostatic agents. Antibodies are regarded as the most promising area, and on-going research is outlined which offers some promise of further progress.

(c) CHEMOTHERAPEUTICS

12159 **Bravo, B.J.A., Sauvain, M., Gimenez, T.A., Balanza, E., Serani, L., Laprévote, O., Massiot, G. and Lavaud, C., 2001.** Trypanocidal withanolides and withanolide glycosides from *Dunalia brachyacantha*. *Journal of Natural Products*, **64** (6): 720-725.

Lavaud: Laboratoire de Pharmacolognosie, UMR 6013 CNRS, Bâtiment 18, BP 1039, 51097 Reims, Cedex 2, France. [catherine.lavaud@univ-reims.fr]

12160 **Gull, K., 2002.** The cell biology of parasitism in *Trypanosoma brucei*: Insights and drug targets from genomic approaches? (Review.) *Current Pharmaceutical Design*, **8** (4): 241-256.

Gull: School of Biological Sciences, University of Manchester, 2.205 Stopford Building, Oxford Road, Manchester M13 9PT, UK. [k.gull@man.ac.uk]

The African trypanosome, *Trypanosoma brucei*, exhibits a complex, digenetic life cycle that alternates between the tsetse fly vector and the mammalian host. The life cycle is characterised by a complex series of cell type differentiations and variations in metabolism. In addition the trypanosome exhibits a particular cell biology that has become adapted for its role as a parasite. This article places some of these areas in a framework that considers the role of cellular processes in parasitism. I rehearse some conclusions from recent studies and provide hypotheses and suggestions for future work. Areas debated include: cell surface protein expression, cell differentiation, endomembrane trafficking and protein targeting, the cytoskeleton, flagellum functions in motility, attachment and plasma membrane differentiation, organelle specialisations, control of cell cycle, parasite/host, parasite/parasite and parasite/vector interactions. The review also focusses on the likely impact of the genome project and reverse genetics in providing greater insight to these cellular processes and how, if coordinated with some élan by scientists and funding agencies, this may provide novel targets for future drug development.

12161 **Hatada, S., Seed, J.R., Barker, C., Hajduk, S.L., Black, S. and Maeda, N., 2002.** No trypanosome lytic activity in the sera of mice producing human haptoglobin-related protein. [*T. brucei*.] (Short communication.) *Molecular and Biochemical Parasitology*, **119** (2): 291-294.

Maeda: Department of Pathology and Laboratory Medicine, CB 7525, The University of North Carolina, Chapel Hill, NC 27599-7525, USA. [nobuyo@med.inc.edu]

12162 **Magez, S., Stijlemans, B., Caljon, G., Eugster, H.-P. and De Baetselier, P., 2002.** Control of experimental *Trypanosoma brucei* infections occurs independently of lymphotoxin-α induction. *Infection and Immunity*, **70** (3): 1342-1351.

Magez: Department of Immunology, Parasitology and Ultrastructure, Vlaams Interuniversitair Instituut voor Biotechnologie, Vrije Universiteit Brussel, Paardenstraat 65, B-1640 Sint Genesius Rode, Belgium.

Trypanosome infections are marked by severe pathological features, including anemia, splenomegaly, and suppression of T-cell proliferation. We have used lymphotoxin-α-deficient (LT-$\alpha^{-/-}$) mice, as well as LT-α-tumor necrosis factor-double-deficient (LT-$\alpha^{-/-}$TNF$^{-/-}$) mice, to analyze the contributions of these related cytokines in both induction of trypanosomosis-associated immunopathology and infection control. Moreover, as the cytokine-deficient mice used have no detectable lymph nodes and lack germinal-centre formation upon immune stimulation, we have analyzed the functional importance of both the lymph nodes and spleen during experimental *Trypanosoma brucei* infections. First, we show that the absence of LT-α does not significantly alter early trypanosomosis development or pathology but does result in better control of late-stage parasitemia levels and slightly prolonged survival. This increased survival of infected LT-$\alpha^{-/-}$ mice coincides with the appearance of increased chronic-stage anti-trypanosome immunoglobulin M (IgM)-IgG2a serum titres that are generated in the absence of functional peripheral lymphoid tissue and do not require germinal-centre formation. Second, we show that splenectomized mice control their parasitemia to the same extent as fully immune-competent littermates. Finally, using LT-$\alpha^{-/-}$TNF$^{-/-}$ double-deficient mice, we show that in these mice *T. brucei* infections are very well controlled during the chronic infection stage and that infection-induced pathology is minimized. Together, these findings indicate that while increased IgM-IgG2a anti-trypanosome antibody titres (generated in the absence of LT-α, peripheral lymph nodes, and germinal-centre formation) coincide with improved parasitemia control, it is TNF that has a major impact on trypanosomosis-associated immunopathology.

12163 **Murilla, G.A., Peregrine, A.S., Ndung'u, J.M., Holmes, P.H. and Eisler, M.C., 2002.** The effects of drug-sensitive and drug-resistant *Trypanosoma congolense* infections on the pharmacokinetics of homidium in Boran cattle. *Acta Tropica*, **81** (3): 185-195

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Two groups of five Boran (*Bos indicus*) cattle were infected with one of two populations of *Trypanosoma congolense*; one drug-sensitive (IL1180), and one drug-

resistant (IL3330). The animals were then treated intramuscularly with homidium bromide at a dose rate of 1.0 mg kg^{-1} bodyweight 7 days after trypanosomes were detected in the peripheral blood of all the five animals in each group. Following treatment of cattle infected with drug-sensitive trypanosomes, parasites could no longer be detected in the bloodstream of four out of five cattle after 24 h, and after 48 h for the fifth animal. The animals remained aparasitaemic up to the end of the observation period of 90 days and serum drug concentrations determined by enzyme-linked immunosorbent assay (ELISA) remained above the detection limit of 0.1 ng ml^{-1} for the entire period. Following treatment of cattle infected with drug-resistant trypanosomes, parasites did not disappear from the bloodstream in any of the five animals. The rate of drug elimination was greater in cattle infected with drug-resistant trypanosomes and the drug was no longer detectable approximately 3 weeks after treatment. Non-compartmental pharmacokinetic analysis showed that the values for $t_{½}\beta$ of 75.5 ± 16.9 h, the area under the curve ($AUC_{(0-\infty)}$) of 1.33 ± 0.156 μg h ml^{-1} and the $MRT_{0-\infty}$ of 32.8 ± 4.45 h obtained in cattle infected with the drug-resistant trypanosome population were significantly lower than the values of 424 ± 146 h for $t_{½}\beta$, 1.67 ± 0.233 μg h ml^{-1} for $AUC_{(0-\infty)}$ and 297 ± 159 h for $MRT_{0-\infty}$ obtained in cattle infected with the drug-sensitive population. The persistence of drug-resistant infections in cattle following homidium treatment was associated with more rapid drug elimination than in those in which infections with drug-sensitive parasites were cleared by the drug.

12164 **Nyarko, E., Hara, T., Grab, D.J., Tabata, M. and Fukuma, T., 2002.** Toxic effects of mercury(II), cadmium(II) and lead(II) porphyrins on *Trypanosoma brucei brucei* growth. *Chemico-Biological Interactions*, **139** (2): 177-185.

Tabata: Department of Chemistry, Faculty of Science and Engineering, Saga University, 1 Honjo-machi, Saga 840-8502, Japan. [tabatam@cc.saga-u.ac.jp]

The effects of free mercury(II), cadmium(II) and lead(II) ions and their metalloporphyrin-derivatives on *Trypanosoma brucei brucei* growth in culture were studied. All experiments were conducted in the dark. IC_{50} values on growth obtained in 24-h time-course experiments were 1.5 x 10^{-7}, 2.4 x 10^{-6}, 4.4 x 10^{-6} and 2.6 x 10^{-5} M for mercury(II) porphyrin, cadmium(II) porphyrin, lead(II) porphyrin and free base porphyrin, respectively, while the IC_{50} values for Hg^{2+}, Cd^{2+} and Pb^{2+} were 3.6 x 10^{-6}, 1.5 x 10^{-5} and 1.6 x 10^{-5} M, respectively. These results clearly indicate that the toxicity of the metalloporphyrin complexes of mercury(II), cadmium(II) and lead(II) to *T. b. brucei* parasites was much higher compared to their free metal ions and free base porphyrin at low concentrations. It was also observed after 8 h incubation that the metalloporphyrins were effective in inhibiting the division of the parasites at concentrations >1.25 x 10^{-7} M for mercury(II) porphyrin, concentrations >1.2 x 10^{-6} M for cadmium(II) and lead(II) porphyrins and at concentrations >3.6 x 10^{-6} M for Hg^{2+} ion. These observations were not detected in samples treated with the free metal ions and the free base porphyrin at the same concentrations. Interestingly, trypanosomes treated with metalloporphyrin complexes displayed different morphological features from those cells treated with free

base porphyrin or metal ions. The chemotherapeutic potential or the metalloporphyrins of H_2TMPyP for treatment of African trypanosomiasis is discussed.

12165 **Seed, J.R. and Boykin, D.W., 2001.** Chemotherapy of African trypanosomiasis. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 65-78. Kluwer Academic Publishers, Dordrecht.

Seed: Department of Epidemiology, University of North Carolina, Chapel Hill, NC, 27599 USA.

To answer the need for new trypanocides, it is suggested that screening drugs against the whole animal should be given greater weight, rather than depending primarily on the molecular target approach. Progress in developing analogues of the existing drug pentamidine is outlined, with reference to improving oral bioavailability and better blood-brain transport.

12166 **Tchinda, A.T., Tsopmo, A., Tane, P., Ayafor, J.F., Connolly, J.D. and Sterner, O., 2002.** Vernoguinosterol and vernoguinoside, trypanocidal stigmastane derivatives from *Vernonia guineensis* (Asteraceae). *Phytochemistry*, **58** (4): 371-374.

Connolly: Chemistry Department, The University of Glasgow, G12 8QQ, UK. [joec@chem..gla.ac.uk]

Two bitter stigmastane derivatives, vernoguinosterol (1) and vernoguinoside (2), have been isolated from the stem bark of *Vernonia guineensis* and their structures eludicated using spectroscopic methods. The new compounds exhibit trypanocidal activity.

8. TRYPANOSOME RESEARCH

(a) CULTIVATION OF TRYPANOSOMES

(b) TAXONOMY, CHARACTERISATION OF ISOLATES

12167 **Agbo, E.C., Majiwa, P.A.O., Claassen, E.J.H.M. and Roos, M.H., 2001.** Measure of molecular diversity within the *Trypanosoma brucei* subspecies *Trypanosoma brucei brucei* and *Trypanosoma brucei gambiense* as revealed by genotypic characterization. *Experimental Parasitology*, **99** (3): 123-131.

Agbo: Division of Animal Science, Section for Animal Genomics, ID-Lelystad, Edelhertweg 15, 8200 AB Lelystad, The Netherlands. [e.e.c.agbo@id.wag-ur.nl]

12168 **Donelson, J.E., 2001.** The genome of the African trypanosome. In *The African Trypanosomes* (*World Class Parasites*, Volume 1, eds. S.J.Black & J.R.Seed), pp. 143-158. Kluwer Academic Publishers, Dordrecht.

Donelson: Department of Biochemistry, University of Iowa, Iowa City, Iowa 52242, USA.

Progress in determining the genome of *Trypanosoma brucei* is outlined. The complete sequence determination of chromosomes I and II are nearing completion. It is anticipated that the trypanosome nuclear genome will be arrayed as long transcription units of fifty or more intronless genes. Knowledge of the *T. brucei* genome will help in the work of controlling or eliminating this pathogen.

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

[See also: **25** nos. 12146, 12148, 12158, 12160, 12168]

12169 **Abbott, J.J., Ford, J.L. and Phillips, M.A., 2002.** Substrate binding determinants of *Trypanosoma brucei* gamma-glutamylcysteine synthetase. *Biochemistry*, **41** (8): 2741-2750.

Phillips: Department of Pharmacology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9041. [Margaret.Phillips@UTSouthwestern.edu]

12170 **Ajayi, W.U., Chaudhuri, M. and Hill, G.C., 2002.** Site-directed mutagenesis reveals the essentiality of the conserved residues in the putative diiron active site of the trypanosome alternative oxidase. [*T. brucei brucei*]. *Journal of Biological Chemistry*, **277** (10): 8187-8193.

Hill: School of Medicine, Department of Microbiology, Meharry Medical College, Nashville, Tennessee 37208, USA.

12171 **Aphasizhev, R., Sbicego, S., Peris, M., Jang, S.H., Aphasizheva, I., Simpson, A.M., Rivlin, A. and Simpson, L., 2002.** Trypanosome mitochondrial 3′ terminal uridylyl transferase (TUTase): The key enzyme in U-insertion/deletion RNA editing. [*T. brucei.*] *Cell*, **108** (5): 637-648.

Simpson: Department of Microbiology, Immunology and Molecular Genetics, University of California, Los Angeles, California 90095, USA.

12172 **Böhme, U. and Cross, G.A.M., 2002.** Mutational analysis of the variant surface glycoprotein GPI-anchor signal sequence in *Trypanosoma brucei*. *Journal of Cell Science*, **115** (4): 805-816.

Cross: Laboratory of Molecular Parasitology, The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.

12173 **Bütikofer, P., Vassella, E., Boschung, M., Renggli, C.K., Brun, R., Pearson, T.W. and Roditi, I., 2002.** Glycosylphosphatidylinositol-anchored surface molecules of *Trypanosoma congolense* insect forms are developmentally regulated in the tsetse fly. *Molecular and Biochemical Parasitology*, **119** (1): 7-16.

Bütikofer: Institute of Biochemistry and Molecular Biology, University of Bern, Bühlstrasse 28, 3012 Bern, Switzerland. [peter.buetikofer @mci.unibe.ch]

12174 **Bütikofer, P., Vassella, E., Mehlert, A., Ferguson, M.A.J. and Roditi, I., 2002.** Characterisation and cellular localisation of a GPEET procyclin precursor in *Trypanosoma brucei* insect forms. *Molecular and Biochemical Parasitology*, **119** (1): 87-95.

Bütikofer: Institute of Biochemistry and Molecular Biology, University of Bern, Bühlstrasse 28, 3012 Bern, Switzerland. [peter.buetikofer@mci.unibe.ch]

12175 **Cano, M.I.N., Blake, J.J., Blackburn, E.H. and Agabian, N., 2002.** A *Trypanosoma brucei* protein complex that binds G-overhangs and co-purifies with telomerase activity. *Journal of Biological Chemistry*, **277** (2): 896-906.

Cano: Departmento de Genética e Evolução, Instituto de Biologia, Universidade Estadual de Campinas (UNICAMP), CP 6109, Campinas, São Paulo, 13083-970, Brazil. [micano@unicamp.br]

12176 **Chánez-Cárdenas, M.E., Fernández-Velasco, D.A., Vázquez-Contreras, E., Coria, R., Saab-Rincón, G. and Pérez-Montfort, R., 2002.** Unfolding of triosephosphate isomerase from *Trypanosoma brucei*: Identification of intermediates and insight into the denaturation pathway using tryptophan mutants. *Archives of Biochemistry and Biophysics*, **399** (2): 117-129.

Pérez-Montfort: Instituto de Fisiología Celular, UNAM, Apartado Postal 70242, 04510 México D.F., Mexico. [rmontfor@ifisiol.unam.mx]

12177 **Daunes, S. and D'Silva, C., 2002.** Glutathione derivatives active against *Trypanosoma brucei rhodesiense* and *T. brucei brucei* in vitro. *Antimicrobial Agents and Chemotherapy*, **46** (2): 434-437.

D'Silva: Department of Chemistry and Materials, The Manchester Metropolitan University, Manchester M1 5GD, UK. [C.DSilva@mmu.ac.uk]

12178 **Dutoya, S., Gibert, S., Lemercier, G., Santarelli, X., Baltz, D., Baltz, T. and Bakalara, N., 2001.** A novel C-terminal kinesin is essential for maintaining functional acidocalcisomes in *Trypanosoma brucei*. *Journal of Biological Chemistry*, **276** (52): 49117-49124.

Bakalara: Laboratoire d'Immunologie et Parasitologie Moleculaire, B.P.12 Universite Bordeaux II, 146 rue Leo-Saignat, 33. [bakalara@hippocrate.u-bordeaux2.fr]

12179 **Fairlamb, A.H., 2002.** Metabolic pathway analysis in trypanosomes and malaria parasites. *Philosophical Transactions of the Royal Society of London, Series B – Biological Sciences*, **357** (1417): 101-107.

Fairlamb: Division of Biological Chemistry and Molecular Microbiology, University of Dundee, Dundee DD1 5EH, UK. [a.h.fairlamb @dundee.ac.uk]

12180 **Fang, J. and Beattie, D.S., 2002.** Novel FMN-containing rotenone-insensitive NADH dehydrogenase from *Trypanosoma brucei* mitochondria: Isolation and characterization. *Biochemistry*, **41** (9): 3065-3072.

Beattie: Department of Biochemistry and Molecular Pharmacology, West Virginia University School of Medicine, Morgantown, West Virginia 26506-9142, USA. [dbeattie@hsc.wvu.edu]

12181 **Gerrits, H., Mussmann, R., Bitter, W., Kieft, R. and Borst, P., 2002.** The physiological significance of transferrin receptor variations in *Trypanosoma brucei*. *Molecular and Biochemical Parasitology*, **119** (2): 237-247.

Borst: The Netherlands Cancer Institute, Division of Molecular Biology and Center for Biomedical Genetics, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands. [pborst@nki.nl]

12182 **Hara, T., Yasuda, K. and Fukuma, T., 2002.** Effective gene transfer into *Trypanosoma brucei* bloodstream forms by particle bombardment. *Molecular and Biochemical Parasitology*, **119** (1): 117-119.

Fukuma: Department of Parasitology, Kurume University School of Medicine, 67 Asahi-Machi, Kurume, Fukuoka 830-0011, Japan. [tfukuma@med.kurume-u.ac.jp]

12183 **Hendriks, E.F., Robinson, D.R., Hinkins, M. and Matthews, K.R., 2001.** A novel CCCH protein which modulates differentiation of *Trypanosoma brucei* to its procyclic form. *EMBO Journal*, **20** (23): 6700-6711.

Matthews: School of Biological Science, 2-14 Stopford Building, University of Manchester, Oxford Road, Manchester M13 9PT, UK. [keith.matthews@man.ac.uk]

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