

section b - abstracts

1. GENERAL (INCLUDING LAND USE)

9398 **Cattand, P., 1994.** Trypanosomiase humaine africaine: situation épidémiologique actuelle, une recrudescence alarmante de la maladie. [Human African trypanosomiasis: present epidemiological situation, an alarming resurgence of the disease.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 307-310.

Division of Control of Tropical Diseases, WHO, 1211 Geneva 27, Switzerland.

With 20-25,000 new cases notified per year, human African trypano-somiasis attracts less attention from health authorities than other parasitic or tropical diseases. This lack of interest is linked to the fact that it affects only the most isolated and poorest rural populations. Its effect here, though, can be devastating. Data from recent surveys in Zaire show a prevalence of 70% in some villages in the Bundoundou region. The overall prevalence in Zaire is thought to be at least 3-5%, with 8-10 million of the 37 million population exposed to the risk of infection. Other countries also show an alarming upsurge. Action to combat the disease calls for long-term commitment of human resources, materials and equipment. Practical options consist of active surveillance of the populations at risk by mobile teams, passive surveillance by medical centres with appropriate diagnostic facilities, and vector control by means of impregnated traps and screens, the most effective strategy being to use all three options simultaneously.

9399 **Cloudsley-Thompson, J.L., 1992.** Okavango the jewel that hangs by a thread. *Environmental Conservation*, **19** (4): 355-357.

Department of Biology, University College London, Gower Street, London WC1E 6BT, UK.

The rich animal and plant life of the Okavango delta, and threats to its conservation, are discussed. Lack of water and the presence of tsetse were regarded in Botswana as obstacles to economic progress. Game slaughter, chopping and burning natural vegetation and insecticide spraying were therefore carried out as control measures. Now that tsetse have been virtually eliminated from the Okavango delta, there is a real threat that cattle will enter the region for food and water, although it is not good cattle country, leading to overgrazing and desertification.

9400 **Frezil, J.-L. and Cuisance, D., 1994.** Trypanosomiasis, maladies d'avenir: leurs perspectives et leurs

inconnues. [Trypanosomiasis, diseases of the future: prospects and uncertainties.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 391-393.

Frezil: Centre ORSTOM, B.P. 5045, 34032 Montpellier Cedex, France.

Despite considerable progress, much remains unknown about the trypanosomiasis and their epidemiology. Questions that need to be addressed are reviewed under the following headings: course of the disease, infection of the vector, the animal reservoir, the trypanosome in man, the origin of epidemics, vector characteristics, vector control and vaccine research. Given the vast scope of potential research, coordinated action and research targets are needed.

9401 **Jabbah, M.A., Reynolds, L. and Francis, P.A., 1995.**

Sedentarisation of cattle farmers in the derived savannah region of south-west Nigeria: results of a survey. *Tropical Animal Health and Production*, **27** (1): 55-64.

Jabbah: ILRI, Socio-economic Sciences Division, P.O. Box 5689, Addis Ababa, Ethiopia.

A survey was conducted to assess the process and extent of sedentarisation among Fulani cattle owners in the derived savanna zone of south-west Nigeria where the level of tsetse challenge has been declining as a result of land clearance for agriculture, changing climatic patterns and tsetse control programmes. The results, based on the responses of 66 randomly selected cattle owners, indicated an on-going process of settlement with an increasing number becoming mixed livestock/crop farmers. Most of the cattle owned were non-trypanotolerant Zebu. As the period of settlement increased, herd size became smaller and herd composition changed from pure Zebu to a mixture of Zebu and crosses between Zebu and trypanotolerant breeds. When questioned on cattle health profiles, 69% of informants mentioned specific diseases; over half of these cited a combination of trypanosomiasis, streptothricosis and helminthosis, while the rest mentioned one of these.

9402 **Kuzoe, F., 1994.** Orientations actuelles de la recherche sur la trypano-somiose africaine. [Current orientations of research on African trypano-somiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 390.

TDR, WHO, 1211 Geneva 27, Switzerland.

Two recent events are likely to influence resources available for further research on African trypanosomiasis. Firstly, the World Development Report (1993) used the global burden of disease to determine

the relative importance of various diseases. The epidemic propensity of African trypanosomiasis, which makes it one of the important public health problems in sub-saharan Africa, has not been taken into consideration. Secondly, in response to diminishing resources and from strategic considerations, TDR has undergone restructuring since January 1994. To enable available resources to be optimally utilised, limited and focused priorities have been drawn for each target disease. Thus, for African trypanosomiasis, the search for an effective and inexpensive chemotherapeutic agent, which would also be effective against other parasites, thus increasing its market potential, is a high priority. Much progress has been achieved in the development of tools for the control of African trypanosomiasis, but their integration into health care systems, which could improve surveillance of the population at risk, has been slow. Therefore, the development of cost effective methods of surveillance is a high priority. Finally, studies on the molecular mechanisms underlying pathogenesis of African trypanosomiasis, which could potentially lead to developing intervention strategies, is also a high priority. Outside TDR, research on African trypanosomiasis will continue, but to what extent it will be influenced by TDR priorities remains to be seen.

9403 **Pender, J. and Rosenberg, J., 1995.** *Impact of tsetse control on land use in the semi-arid zone of Zimbabwe. Phase 1: classification of land use by remote sensing imagery.* Chatham, UK; Natural Resources Institute (NRI Bulletin no. 66). v + 38 pp; 16 colour plates; 1 map. (ISBN 0-85954-430-3.)
NRI, Central Avenue, Chatham Maritime, Chatham, Kent ME4 4TB, UK.

In areas of Africa affected by trypanosomiasis, tsetse control is a major component of rural development activities. As part of an international programme of work to evaluate the environmental and socio-economic impacts of tsetse control in southern Africa, its effects on land use and vegetation change over a 20-year period are being assessed using satellite imagery. The study area covers approximately 8500 km² south of Lake Kariba in Zimbabwe, and Phase 1 of the research programme used Landsat TM imagery and aerial photography to define baseline vegetation and land-use classes. Black and white aerial photography for 1990 and a Landsat TM image for 19 February 1992 were used for the analysis. Bands 2, 3 and 4 were contrast-

stretched to achieve maximum variation between spectral signatures and photographs prepared for ground truthing. Fieldwork was carried out in both the wet (February 1993) and dry (June 1993) seasons. More than 300 field sites were fixed using a global positioning system, and data were collected on geology, soil type, drainage and topography. All data coverages were incorporated in an ARC/INFO geographical information system (GIS). As with previous work, the study showed that in regions of sparse vegetation, such as semi-arid and arid zones, vegetation classification from satellite imagery is strongly influenced by the soil background and the time of year the imagery was taken. Geological and topographic factors are also influential and, hence, manual classification of the satellite image was necessary with considerable reliance on ground survey data. Fifteen land-use/vegetation classes were derived, four of which relate to human land use, bare soil and the effects of fire (16% of the land cover). *Colophospermum mopane* and a mosaic of *C. mopane* and *Julbernardia globiflora* woodlands were the predominant natural vegetation (54%) in the study area. Landsat TM and MSS imagery for seven years between 1972 and 1993 have been selected for Phase 2 of the study, which will quantify land use and vegetation changes in relation to the history of tsetse control operations in the area.

9404 **Raadt, P. de, 1994.** Horizon 2000: quelle perspective pour la trypano-somiose africaine? [Towards year 2000: what prospects for human African trypanosomiasis?] (Editorial.) *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 301-302.

Division of Control of Tropical Diseases, WHO, 1211 Geneva 27, Switzerland.

Trypanosomiasis is no longer seen as a major public health problem, either in the majority of endemic countries or internationally. However, the most important aspect of sleeping sickness is its epidemic potential. Recent epidemics in Sudan and Uganda have been caused by population displacements, with refugees taking trypanosomiasis to new areas. Another epidemic, in Busoga, Uganda, resulted from a fundamental change in land use from cotton monoculture to livestock and food crop production, particularly *Lantana camara*, a preferred resting site of tsetse. A third epidemic, in Zaire, resulted from disruptions to surveillance by mobile teams. These worrying developments should be taken as a warning of the danger where national health

services are already stretched to their limits. Some of the problems and ideas which are research priorities were considered at a Round Table held in Limoges during the Second Congress of Tropical Neurology (21-23 September 1994). The texts of papers presented were published in a special issue of *Bulletin de la Société de Pathologie exotique* and are abstracted in this issue of *TTIQ* (see nos. 9398, 9400, 9402, 9405, 9426, 9430, 9432-9434, 9436, 9438, 9440-9443, 9471, 9473, 9474, 9476, 9480, 9486).

9405 **Stanghellini, A., Gampo, S. and Sicard, J.-M., 1994.** Rôle des facteurs environnementaux dans la recrudescence actuelle de la trypanosomiase humaine africaine. [The role of environmental factors in the present resurgence of human African trypanosomiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 303-306.

Service d'Epidémiologie et des Grandes Endémies, Ministère de la Santé, B.P. 1066, Brazzaville, Congo. The major target for the prevention of human African trypanosomiasis is a decrease in the parasite reservoir. This requires detection of patients and their treatment, and prevention of contact between humans and vectors. The environmental factors that could favour outbreaks of trypanosomiasis are reviewed. Political will is reflected in decision-making and mobilisation of resources. However, choice of priorities is often based on technical criteria which do not favour trypanosomiasis, and problems on the borders of affected states restrict the implementation of coordinated control activities. Internal political disturbances and local conflicts lead to mismanagement of health care services and to population migration to infected areas without access to medical care. As well as political and economic factors, human behaviour, perceptions of risk by the authorities, quality of technical personnel and disease perception by the population are important factors.

9406 **Stuth, J.W. and Kamau, P.N., 1990.** Influence of woody plant cover on dietary selection by goats in an *Acacia senegal* savanna of East Africa. *Small Ruminant Research*, **3** (3): 211-225.

Department of Range Science, Texas A & M University, College Station, TX 77843, USA.

A warning is given that, when contemplating bush removal of woody plants, for example for tsetse control, consideration should be given to the role that large *Acacia* trees can play in stabilising protein intake of goats and other domestic or wild browsers.

9407 **Travassos Santos Dias, J.A., 1989 [1992].** A luta contra as tripanos-somoses em Moçambique e a importancia dos estudos florísticos como suporte dos reconhecimentos glossinicos. [Trypanosomiasis control in Mozambique and the importance of botanists in tsetse surveys.]

Garcia de Orta, Série de Zoologia, **16** (1-2): 239-244.

Centro de Zoologia, Instituto de Investigação Científica Tropical, Rua da Junqueira, 14-1300 Lisbon, Portugal.

From 1910, several government departments were involved in trypanosomiasis control in Mozambique. In 1945, the Missao de Combate as Tripanossomiases was created with four divisions (medical, veterinary, entomological and research) to deal with all aspects of the disease. The problem of tsetse fly surveys is considered, and the important contribution of botanists from other government departments is gratefully acknowledged. A list is given of all those educated to university level who worked in the MCT.

9408 **White, L., 1995.** Tsetse visions: narratives of blood and bugs in colonial Northern Rhodesia, 1931-9. *Journal of African History*, **36** (2): 219-245.

National Humanities Center, Research Triangle Park, NC 27709, USA.

This article looks at different kinds of historical sources – colonial science and African rumours – and argues that both can be used to reconstruct the history of changing colonial policies, and African responses to them, for tsetse and game control in the Northern Province of Northern Rhodesia in the 1930s. These sources and the arguments developed from them can be read as separate and distinct historical narratives, but nevertheless each articulates a specific relationship between African farmers, shifting cultivation and wild animals. Each history discloses a vision of how best to control a dreaded disease, and each history describes a separate and distinct landscape in which Africans, insects and wild animals might best live together. Moreover, each source reveals the close links between African ideas about the forcible extraction of vital fluids and European ideas about sleeping sickness, insect vectors and deforestation.

9409 **Williams, B., Campbell, C. and Williams, R., 1995.** Broken houses: science and development in the African savannahs. *Agriculture and Human Values*, **12** (2): 29-38.

B. Williams: Epidemiology Research Unit, P.O. Box 4584, Johannesburg, South Africa.

Some of the problems that arise in relation to development projects are considered, focusing on the savanna regions of Africa and, in particular, on the control of tsetse flies. A detailed case study is presented of a project designed to enable a Maasai community in Kenya to carry out their own tsetse fly control using traps. The complex set of relationships and power structures that mediate the actions of the players in development (scientists, local communities, governmental and non-governmental institutions, and development agencies) are examined. The purpose of the paper is not to present solutions to complex and difficult problems but rather to raise questions that should provide a framework for a debate concerning the role of science and technology in the development process.

2. tsetse biology

(a) REARING OF TSETSE FLIES

(b) TAXONOMY, ANATOMY, PHYSIOLOGY, BIOCHEMISTRY

9410 **Baruffi, L., Malacrida, A.R., Feldmann, V., Gomulski, L.M., Torti, C. and Gasperi, G., 1994.** Biochemical and molecular markers in studies of the tsetse genome. (Meeting abstract.) *Parassitologia*, **36** (Suppl. 1): 13.

Baruffi: Dipartimento di Biologia Animale, Università di Pavia, Pavia, Italy.

9411 **Dale, C., Toleman, M., Welburn, S.C., Crampton, J.C. and Maudlin, I., 1995.** Stable plasmid transformation of *Glossina* midgut symbionts (RLO). (Meeting abstract no. C3-404.)

Journal of Cellular Bio-chemistry, **1995** (Suppl. 21A): 223.

Dale: Tsetse Research Group, Department of Veterinary Medicine, University of Bristol, Bristol BS18 7DU, UK. Isolation and characterisation of extra-chromosomal DNA from cultured midgut symbionts from seven species/subspecies of tsetse has shown that all strains of symbionts contain a complex array of large plasmid-like molecules. A unique vector was developed by combining a symbiont plasmid origin of replication with a kanamycin resistance gene from the transposon Tn902. This vector is non-conjugative and is highly stable both in laboratory strains of *Escherichia coli* and *Glossina* symbionts and can thus be used as a shuttle vector for gene transfer between these two bacteria. The presence of *Glossina* symbionts has been shown to have a profound effect upon establishment and maturation of trypanosome infections in tsetse and, with a view to manipulating this relationship to generate refractory flies, we have engineered a unique cloning site into this vector to

allow the introduction and expression of foreign genes within these symbionts.

9412 **Goes van Naters, W.M. van der, 1995.** Taste hairs on the legs of tsetse flies and their function. (Meeting abstract no. 312.) *Chemical Senses*, **20** (6): 795.

Department of Animal Physiology, University of Groningen, P.O. Box 14, 9750 AA Haren (Gn), Netherlands.

The sense organs which mediate feeding behaviour are being studied with the aim of prolonging the contact time between insect and screen. At least two tarsal sensilla on each leg of *Glossina fuscipes fuscipes* respond to human sweat. The spike activity from the chemosensory cells in these sensilla is recorded by placing an electrode over the tips of the hairs. Sweat excites two or three cells in each sensillum as does one of its solutes, uric acid. Other components of sweat which are effective stimuli include isoleucine, leucine, phenylalanine, tryptophan, tyrosine and valine. From the spike trains it is clear that these amino acids stimulate the same cell in each sensillum. Dose-response curves show that the cells are most sensitive to phenylalanine (threshold dose at $\sim 10^{-8}$ M). In behavioural studies the flies will not respond to a paper surface treated with the electrophysiologically effective stimuli. Sensory stimuli of other modalities, such as heat, do induce feeding behaviour on a paper surface. However, in conjunction with heat, the tastants enhance the feeding activity of the flies to a level far above the response to heat alone. The effect appears to be maximal after 2 days of food deprivation (more than four times the response to heat alone). For fly species studied so far, including house flies, the taste quality of the surface is the prime stimulus to trigger extension of the proboscis. In contrast, taste in tsetse flies has a subsidiary, though important, function as a synergistic agent.

9413 **Goes van Naters, W.M. van der, Bootsma, L., Otter, C.J. den and Belemtougri, R.G., 1996.** Search for tsetse attractants: a structure-activity study on 1-octen-3-ol in *Glossina fuscipes fuscipes* (Diptera: Glossinidae). *Journal of Chemical Ecology*, **22** (3): 343-355.

Goes van Naters: Department of Animal Physiology, University of Groningen, P.O. Box 14, 9750 AA Haren (Gn), Netherlands.

Trapping tsetse flies belonging to the *palpalis* group still relies totally upon luring by visual cues even though odour-baited trapping is used effectively

against the *morsitans*-group species. Forty-three percent of the antennal olfactory cells of *G. f. fuscipes*, a member of the *palpalis* group, respond to 1-octen-3-ol. For this species we report a structure-activity relationship between 1-octen-3-ol analogues, in which carbon chain length and the configuration of the hydroxyl and π -bond moieties are varied, and biological activity. Although the optimum chain length for all cells sensitive to 1-octen-3-ol is eight and most cells give lower responses when the hydroxyl function is omitted, there is a clear division into two groups. One group is diverse and represents cells that appear indifferent to the presence or position of the π bond; many will respond to such disparate structures as acetone and 3-methylphenol as well as to 1-octen-3-ol. In the other group, the structural requirements for the stimulus are more stringent; the cells appear to be specifically tuned to 1-octen-3-ol. Their thresholds are three orders of magnitude lower than those of the former group. The existence of two clusters points to a functional division in the olfactory sense. We suggest that the latter low-threshold group is involved in host detection from a distance while the former diverse group is involved in host discrimination at close range. Trap harvests with 1-octen-3-ol as a bait may have been disappointing because the appropriate mixture for generating a landing response on the traps is still lacking.

9414 **Lehane, M.J., Allingham, P.G. and Weglicki, P., 1996.**

Composition of the peritrophic matrix of the tsetse fly, *Glossina morsitans morsitans*. *Cell and Tissue Research*, **283** (3): 375-384.

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

The three-layered peritrophic matrix of *G. m. morsitans* is shown, by histochemistry, to be formed of a mixture of glycosaminoglycans, glycoproteins and chitin. In all three layers the glycosaminoglycans contain GlcNAc-hexuronic and Gal-GlcNAc moieties, together with chitin. Glycosaminoglycans in layer 3 are sulphated and sulphated sites have a mean interspace distance of 53 nm, similar to the spacing of fixed charge sites in glomerular basement membrane, suggesting a role for these sites in the filtration properties of the peritrophic matrix. O-linked oligosaccharides are present in all three layers. Layer 1 contains the widest variety of glycoprotein oligosaccharide constructs GlcNAc and α linked GalNAc possibly as

GalNAc α 1,3GalNAc, the latter apparently distal to Gal β 1-4GlcNAc. Lectin binding suggests that layer 2 contains GalNAc α 1,3Gal β 1,3GlcNAc and that layer 3 contains GalNAc and Gal β 1,4GlcNAc. The evidence for N-linked oligosaccharides is more equivocal. Two-dimensional electrophoresis showed that the peritrophic matrix contains a range of proteins, most of which require relatively harsh treatment for their solubilisation.

9415 **Maudlin, I., 1996.** Tsetse trypanosome interactions. (Meeting abstract no. 54.) *Journal of Eukaryotic Microbiology*, **43** (1): 10A.

Tsetse Research Group, University of Bristol, Langford House, Langford, Bristol BS18 7DU, UK.

Tsetse symbionts (RLO) provide a useful carrier for inserting modified molecules into flies and for examining the relationship between lectins and trypanosome surface molecules. Research has concentrated on interference with establishment or maturation of trypanosome infections by manipulating the lectin system through carbohydrate inhibition of lectin activity in the fly gut. Refractoriness can be achieved either by preventing flies from maturing infections or by preventing flies from becoming infected. Two strategies are being adopted: (a) Insertion of a chitinase gene from *Serratia marcescens* into RLO would result in all flies having midgut infections but none maturing through over-production of lectin inhibitory carbohydrates; (b) Insertion of a GlcNAc permease would enable RLO to remove GlcNAc from the fly gut with higher efficiency, potentiating refractoriness. The insertion of catabolic genes for metabolism of chitin into the modified RLO would be expected to offer a selective advantage to the transgenic flies.

(c) DISTRIBUTION, ECOLOGY, BEHAVIOUR, POPULATION STUDIES

[See also **19**: nos. 9407, 9412, 9413, 9427.]

9416 **Mwangalwa, M.I., Dransfield, R.D., Otieno, L.H. and Mbata, K.J., 1995.** The responses of *Glossina fuscipes fuscipes* Newstead to odour attractants and traps. *Journal of African Zoology*, **109** (1): 23-30.

ICIPE, P.O. Box 30772, Nairobi, Kenya.

Studies at Rusinga island in Kenya determined the responses of *G.f. fuscipes* to various host odours and trap types. The odours included: (a) cow urine, (b) human

urine, (c) acetone, (d) 1-octen-3-ol, (e) a mixture of 8 parts 4-methylphenol, 4 parts 1-octen-3-ol, 1 part 3-n-propylphenol, (f) a mixture of 1 part 3-methylphenol, 1 part 4-methylphenol, 2 parts 1-octen-3-ol, (g) a mixture of 3 parts 3-methylphenol, 1 part 1-octen-3-ol, (h) aqueous washings from a monitor lizard (*Varanus niloticus niloticus*), and (i) aqueous washings from a goat. Six types of traps were compared: biconical, NG2B, NG2G, F3, pyramidal and Vavoua. The addition of odour baits to traps did not affect significantly ($P > 0.05$) the catches of male *G. f. fuscipes*. Females were sometimes slightly attracted by acetone and cow urine and repelled by combinations of acetone, cow urine and phenolic fractions. The biconical trap caught consistently more tsetse than the other designs.

9417 **Yu, P., Habtemariam, T., Oryang, D., Obasa, M., Nganwa, D. and Robnett, V., 1996.** Stochastic model of spatial spread and control of tsetse flies (Diptera: Muscidae).

Environmental Entomology, **25** (1): 78-84.

Center for Computational Epidemiology, School of Veterinary Medicine, Tuskegee University, Tuskegee, AL 36088, USA.

A stochastic model is developed to study the spatial spread and control of tsetse flies, *Glossina* spp. In this model, the movement mechanism is described by the travel direction and distance of an individual tsetse fly, birth and death rates are described by probability distributions, and some control measures are considered. The model is used to estimate the straight-line distance travelled in the life span of a fly, and the distance fly populations will spread during a 10-year period. Simulation results indicate that the straight-line distance travelled in the life span of a tsetse fly is < 1.71 km from its birth place. The spread distance for fly populations is ~ 18.7 km by the end of the 10th year based on a 99% confidence prediction limit. Strategies of preventing tsetse flies from advancing to a tsetse-free region are examined. The probabilities that a fly crosses a protective barrier (buffer zone) are obtained for different control methods. The width of a protective barrier required to prevent the tsetse flies from advancing to a tsetse-free region is estimated.

9418 **Ziba, M.M., Murkunyandela, M., Sikiya, S., Chipipa, J.S. and Mwanza, L., 1994.** A comparison of three types of 'M' traps for sampling tsetse fly (Diptera: Glossinidae) populations at South Luangwa game management area, Zambia. *Central African Journal of Medicine*, **40** (8): 212-217.

TDRC, P.O. Box 71769, Ndola, Zambia.

A field trial was conducted between 27 July and 1 August 1992 in Mfuwe, south Luangwa, Zambia, to assess the effectiveness of locally developed 'M' traps for suppressing and sampling the tsetse flies *Glossina pallidipes* and *G. morsitans morsitans*. The tsetse catches in the 'M' traps and the standard F3 traps were collected at 24 h intervals. The highest catches of both tsetse species in the series of 'M' traps were in the M3 trap. The numbers of female flies caught for both species in all the trap types were significantly higher than those for male flies ($P < 0.001$). Trap catches for *G. pallidipes* were uniformly distributed among the M2, M3 and F3 traps. In contrast, there was a significant drop in the M1 catches. For *G. m. morsitans*, the results were not significantly different between the M1 and the M3 catches. Based on the results of this trial, it is recommended adopting the M1 trap, a more cost-effective trap, for suppression, and the M3 trap for sampling of *G. m. morsitans* which is the only species in Kampumbu (our trial suppression area) in the Isoka district of Zambia.

3. tsetse control (including environmental side-effects)

[See also **19**: nos. 9399, 9403, 9406, 9409, 9417.]

9419 **Dejoux, C., 1990.** Conséquences ecotoxicologiques de la lutte anti-vectorielle en pays tropicaux: la situation des milieux lotiques africains.

[Ecotoxicological consequences of vector control in tropical countries: the situation in African lotic ecosystems.] *Science of the Total Environment*, no. 97/98: 799-813.

ORSTOM, 213 rue La Fayette, 75480 Paris Cedex 10, France.

The chemicals used for the control of the vectors of onchocerciasis and trypanosomiasis are described, and published studies of their impact on aquatic ecosystems reviewed. All insecticides used for tsetse control (DDT, dieldrin, endosulfan and the pyrethroids cypermethrin, permethrin and deltamethrin) are toxic to fish and aquatic invertebrates to varying degrees. Endosulfan in particular is highly toxic to fish, causing a high level of mortality even at the reduced dose rates currently used.

9420 **Douthwaite, R.J. and Tingle, C.C.D. (eds), 1994.** *DDT in the tropics: the impact on wildlife in Zimbabwe of ground-spraying for tsetse fly control.*

Chatham, UK; Natural Resources Institute. viii + 195 pp. (ISBN 0-85954-364-1.)

NRI, Central Avenue, Chatham Maritime, Chatham, Kent ME4 4TB, UK.

The environmental impact of DDT used in ground-spraying operations to eradicate tsetse flies from north-western Zimbabwe was assessed in field studies between 1987 and 1991. Fauna monitored included populations of bats, birds, lizards, fish and insects; microbial processes contributing to soil fertility were also checked.

Despite the relatively low application rate, and rapid dissipation of residues, adverse effects on a landscape scale were found in populations of four bird and one lizard species. The comparative scarcity of several bird and terrestrial invertebrate species in sprayed areas may also have been due to DDT. Residue concentrations in at least five bat species posed a significant risk to survival during drought. No significant effects were detected in fish or on soil processes. Effects on the majority of scarcer species are unknown. The effects are reversible, probably within 10-20 years, and are less serious than those caused by habitat loss due to human settlement and elephant damage. In economic terms, the environmental damage cost of using DDT for tsetse fly control was very low. DDT residue burdens in humans were not monitored in this study but the domestic use of DDT for mosquito control is probably a far more important source of exposure in man. The adverse effects of ground-spraying with DDT can be mitigated by alternative control techniques or by substituting deltamethrin, a less persistent insecticide, for DDT. However, if substitution increases costs significantly, wildlife conservation would benefit more from the retention of DDT and investment of savings in projects to manage wildlife habitat than from substitution.

9421 **Mihok, S., Kang'ethe, E.K. and Kamau, G.K., 1995.** Trials of traps and attractants for *Stomoxys* spp. (Diptera: Muscidae). *Journal of Medical Entomology*, **32** (3): 283-289. Mihok: ICIPE, P.O. Box 30772, Nairobi, Kenya.

Five blue and black cloth traps designed for tsetse were tested for their ability to catch *Stomoxys* spp. in Kenya. Significantly greatest catches were obtained with Vavoua traps, which then were used to compare odour baits at Nairobi Park. Acetone, lactic acid and animal urine (cow, buffalo, waterbuck, camel) or dung (rhinoceros, elephant, hippopotamus) did not increase catches. However, 1-octen-3-ol dispensed at 0.2-2.0 mg/h increased catches up to 3.7-fold. Vavoua traps were highly specific for Stomoxyinae, with 80% of the

catch consisting of 11 different taxa of *Stomoxys* as well as genera such as *Prostomoxys*, *Haematobosca*, *Stygeromyia* and *Rhinomusca*. During periods of peak seasonal abundance, up to 3000 *Stomoxys* per day were collected in an octenol-baited Vavoua trap. These high catches suggest that Vavoua traps may be of practical use for fly control in isolated settings at a relatively low cost.

9422 **Swallow, B., 1995.** Tsetse: Ethiopian success. *African Farming and Food Processing*, 1995 (July/August): 21. ILRI, P.O. Box 30709, Nairobi, Kenya.

A tsetse control programme coordinated by ILRI in the Ghibe valley, southwest Ethiopia, using cypermethrin 'high-cis' pour-on is described. During the first 2 years, treatments were given free of charge. All livestock owners living between the villages of Gullele and Tolley were invited to bring animals for treatment and 97% of cattle owners volunteered some time during the 2 years. The density of tsetse flies (*Glossina pallidipes*, *G. morsitans* and *G. fuscipes*) gradually declined, as did the prevalence of trypanosomiasis in the 100 cattle monitored each month. When participating farmers were asked to pay for treatment in December 1992 on a cost-recovery basis, initially few farmers responded. However, use of pour-on quickly rebounded and surpassed former levels, indicating that benefits far outweigh costs. In 1994, 900 households in 90 villages located in an area of 250 km² participated, with up to 4700 animals being treated during any month. More animals are brought for treatment in the wet season (June to August), partly because farmers have more money available then and partly because tsetse are perceived to be more common in the wet season.

9423 **Tingle, C.C.D., 1995.** Some effects of DDT used to control tsetse fly on woodland invertebrates in Zimbabwe. *Acta Zoologica Fennica*, no. 196: 361-363. NRI, Central Avenue, Chatham Maritime, Chatham, Kent ME4 4TB, UK.

The persistence of residues from discriminative spraying of DDT and their impact on fauna other than the target tsetse fly were investigated by sampling bark and soil and through the use of pitfall traps in sprayed and unsprayed woodland. Residues persisted in hot spots, constituting a risk for non-target wildlife. No major differences were found in the relative abundance or diversity of epigeal invertebrates in sprayed areas, and any effect of DDT on faunal composition of trap catches was found to be secondary

to natural, annual variation. However, certain insects, particularly ants (*Camponotus* spp.), were important in carrying DDT residues into the food chain, causing population decline in two species of woodland birds, the white-headed black chat (*Thamnolaea arnoti*) and the red-billed wood hoopoe (*Phoeniculus purpureus*).

9424 **Tingle, C.C.D. and Grant, I.F., 1995.** Effect of DDT selectively applied for tsetse fly (*Glossina* spp.) control on litter decomposition and soil fauna in semi-arid mopane woodland in Zimbabwe. *Acta Zoologica Fennica*, no. 196: 364-368.

NRI, Central Avenue, Chatham Maritime, Chatham, Kent ME4 4TB, UK.

Leaf litter decomposition during the dry season was measured using nylon litter bags of differing mesh aperture in woodland sprayed to control tsetse fly in Zimbabwe, to assess the impact of DDT on the functioning of the soil biota. Decomposition of buried leaf litter was most rapid in large mesh bags (4000 μm), which allowed access to most detritivorous invertebrates, with up to 60% disappearing after 6 months. Decomposition rates in 600 μm and 64 μm bags were significantly lower (30-38%) than in the larger mesh bags, but not different from each other.

Decomposition rates in large mesh bags at an unsprayed site were greater than at sprayed sites. Surface-tethered litter bags showed no significant difference in litter decomposition either between mesh sizes or between treated and untreated areas and showed lower decomposition rates than buried bags. Mesofauna extracted from buried litter bags were dominated numerically by the Acari, with relatively few nematodes and Collembola. A significant difference in relative abundance of certain detritivorous cryptostigmatic mites between buried bags in sprayed and unsprayed areas had no detectable effect on degradation of leaf litter in the 600 μm bags. The contribution of biotic factors to decomposition is discussed in relation to the finding that litter degraded more slowly in areas with low-level DDT contamination of the woodland floor.

9425 **Vreysen, M.J.B., Vloedt, A.M.V. van der and Barnor, H., 1996.**

Comparative γ -radiation sensitivity of *Glossina tachinoides* Westw., *Glossina fuscipes fuscipes* Newst. and *Glossina brevipalpis* Newst. (Diptera, Glossinidae). *International Journal of Radiation Biology*, **69** (1): 67-74.

Vreysen: IAEA Project URT/5/016, c/o Ministry of Agriculture, P.O. Box 159, Zanzibar, Tanzania.

The effect of γ -radiation doses ranging between 10 and 180 Gy on 4-6-day-old adult males of *G. tachinoides*, *G. f. fuscipes* and *G. brevipalpis* was studied. Fecundity of their mates was reduced by 95% following exposure to 120, 80-100 and 50 Gy of adult male *G. tachinoides*, *G. f. fuscipes* and *G. brevipalpis* respectively. Insemination ability of the males and sperm motility were not adversely affected by the radiation treatment. The higher proportion of dominant lethals in the sperm of the three species with increasing radiation doses was reflected in the reproductive status of the female mates, i.e. an increasing percentage of females showing imbalances between intra-uterine content and ovarian development (females with an empty uterus due to expulsion of a dead embryo after embryonic arrest or a degenerating egg *in utero*) and an acceleration in follicle development associated with successive unsuccessful cycles. In the F₁ progeny of all treated groups, no significant bias of the sex ratio was found. The average life span of *G. tachinoides* and *G. f. fuscipes* males treated with doses of \geq 80 Gy and of *G. brevipalpis* males treated with doses of $>$ 140 Gy was significantly reduced as compared with untreated controls. Male *G. brevipalpis* treated with doses ranging between 10 and 40 Gy, however, showed a significant radiation-induced increase in average life span.

4. epidemiology: vector-host and vector-parasite interactions

(See also **19**: nos. 9405, 9411, 9413, 9415, 9416.]
9426 **Gibson, W., 1994.** Identification of trypanosomes in animals, humans and *Glossina*. *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 315-318.

Department of Pathology and Microbiology, University of Bristol Veterinary School, Langford, Bristol BS18 7DU, UK.

A number of biochemical methods are now available for the identification of African trypanosomes. The method of choice depends on the number of trypanosomes present in the sample and the taxonomic level required. DNA probes based on repetitive DNA elements allow identification to subgeneric (e.g. *Trypanozoon*), species (e.g. *Trypanosoma congolense*, *T. simiae*) or subspecific (e.g. *T. congolense* savanna) levels. These probes are particularly useful for identification of trypanosomes in the fly midgut, where sufficient numbers are present to allow simple dot blot hybridisation to be used ($>$ 100). Greater sensitivity has been achieved by

amplification of these repetitive DNA sequences by PCR (polymerase chain reaction), so enabling the small numbers of trypanosomes found in the fly mouthparts to be identified (> 1). At the subspecific level, isoenzyme analysis and latterly RFLP (restriction fragment length polymorphism) analysis have been widely used to characterise isolates within the *T. brucei* species. Two other techniques, karyotype analysis and RAPD analysis, are also useful for fingerprinting isolates. Molecular karyotypes are produced by size fractionation of chromosomal DNAs by PFGE (pulsed field gel electrophoresis). RAPD (random amplified polymorphic DNA) is a PCR-based technique, using arbitrary primers to generate a fingerprint consisting of 20 or so bands.

9427 **Mihok, S., Moloo, S.K., Oden'y, J.O., Brett, R.A., Rakwar, J.G., Munyoki, E., Kiilu, J. and Kyorku, C.A., 1996.** Attractiveness of black rhinoceros (*Diceros bicornis*) to tsetse flies (*Glossina* spp.) (Diptera: Glossinidae) and other biting flies. *Bulletin of Entomological Research*, **86** (1): 33-41.

Mihok: ICIPE, P.O. Box 30772, Nairobi, Kenya.

During translocations of black rhinoceros in Kenya, we studied the relationships between the rhinoceros and biting flies. In trapping experiments, rhinoceros waste products (urine or dung) were substituted for known attractants such as cow urine, 1-octen-3-ol or acetone. Catches of *Glossina pallidipes*, *G. longipennis*, *Stomoxys* spp. and *Haematopota* spp. were not affected by these substitutions. NG2G and Vavoua traps sited near captive animals caught similar numbers and kinds of flies as traps set without animals. Any minor attractive properties of rhinoceros odours were probably due to the presence of known attractants such as 4-cresol and 3-n-propylphenol, which were confirmed to be present through gas chromatography-mass spectroscopy. In feeding trials with laboratory-reared tsetse, *G. brevipalpis* and *G. morsitans centralis* fed well on immobilised animals, whereas *G. longipennis* fed reluctantly. Catches of *G. brevipalpis* were doubled in one trapping experiment when rhinoceros urine was used as odour bait. *Philoliche* spp., *Haematopota* spp. and other Tabanidae fed on captive rhinoceroses. Many species of Stomoxyinae were associated with rhinoceroses. Of these, the most frequent association was with *Rhinomusca dutoiti*, a species found previously only in South Africa. *R. dutoiti* was found in two highland rhinoceros sanctuaries, Nairobi National Park and Solio Ranch Game Reserve.

- 9428 **Moloo, S.K. and Okumu, I.O., 1995.** A comparison of the susceptibility to stocks of *Trypanosoma brucei brucei* of *Glossina pallidipes* originating from allopatric populations in Kenya. *Medical and Veterinary Entomology*, **9** (4): 438-440. Moloo: ILRI, P.O. Box 30709, Nairobi, Kenya. Infection rates of male and female *G. pallidipes* from laboratory colonies originating from Nguruman and Shimba Hills, Kenya, were compared using *T. b. brucei* stocks IL 3965 (from Lambwe Valley, Kenya) and IL 3294 (from Serengeti, Tanzania). Tsetse were infected by feeding on an infected goat, thereafter maintained on clean goats, and dissected and examined on day 30 after the infected bloodmeal. Survival and growth of both stocks of *T. b. brucei* in the midgut were found to be better in female than in male tsetse from both Nguruman and Shimba Hills, whilst the maturation rate, as shown by salivary gland infection, was higher in males than in females. *G. pallidipes* from Nguruman were significantly more susceptible than those from Shimba Hills to both stocks of *T. b. brucei*. These differences in susceptibility may reflect differences in epidemiology between these two areas of Kenya.
- 9429 **Woolhouse, M.E.J., McNamara, J.J., Hargrove, J.W. and Bealby, K.A., 1996.** Distribution and abundance of trypanosome (subgenus *Nannomonas*) infections of the tsetse fly *Glossina pallidipes* in southern Africa. *Molecular Ecology*, **5** (1): 11-18. Woolhouse: Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK. Over 10,000 *G. pallidipes* were collected during two field studies in the Zambezi Valley, Zimbabwe, and one in the Luangwa Valley, Zambia. These were screened for mature trypanosome infections and 234 dot-blot preparations were made of infected midguts, which were screened using DNA probes or PCR with primers specific to different species or types of the trypanosome subgenus *Nannomonas*. Over 70% of midgut infections were successfully identified as either *Trypanosoma godfreyi*, *T. simiae* or three types of *T. congolense*, savanna, riverine-forest and Kilifi. The relative abundance of species and types did not vary significantly between study locations, habitat, season or tsetse age or sex, although there were differences between DNA probe and PCR results. Mixed species and/or mixed type infections were common and were more often detected using PCR. The distribution of infections among flies was highly aggregated, but there was no tendency for multiple infections to accumulate in older flies,

implying that sequential superinfection may be uncommon. Possible explanations for these patterns are discussed.

5. human trypanosomiasis

(a) SURVEILLANCE

[See also **19**: nos. 9398, 9426, 9437.]

9430 **Meirvenne, N. van, 1994.** Diagnostic sérologique de la trypanosomose humaine africaine. [Serodiagnosis of human African trypanosomiasis.] (Abstract only.) *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 311. Institut de Médecine Tropicale, Nationalestraat 155, B-2000 Antwerp, Belgium.

Detection of a trypanosome remains the only certain criterion for diagnosis of human African trypanosomiasis. Parasitological examination, however, is so time-consuming and poorly sensitive that it should be preceded or accompanied by serological screening tests. Bloodstream form trypanosomes contain a multitude of invariable antigens. Moreover, they are coated with a variable surface glycoprotein (VSG) which determines the variable antigen type (VAT) of individual organisms and frequently changes in the course of infection. The serum of the host thus contains a complex spectrum of antibodies to variable and invariable antigens. None of the existing antibody detection tests is fully reliable. Rigorous standardisation of the antigen preparation is a prerequisite for obtaining reproducible results. Immune lysis and direct agglutination tests with living trypanosomes are strictly VAT specific. Using a set of selected predominant VATs, such tests can be successfully applied to spot infections with *Trypanosoma brucei gambiense*, which displays much less diversity in VAT repertoires than *T. b. rhodesiense*. Test systems using fixed trypanosomes (immunofluorescence, CATT) or crude extracts (ELISA, indirect haemagglutination, etc.) usually detect an undefined cocktail of antibodies to variable and invariable antigens. Here again, in the case of *T. b. gambiense*, it would be desirable to incorporate selected VATs or purified VSGs. Surprisingly little research has been done on the serodiagnostic use of defined invariable antigens. Direct agglutination tests with uncoated procyclic trypanosomes (PAT) are an attractive possibility. A

breakthrough might be expected from the introduction of recombinant or synthetic antigens. Unlike antibodies, the presence of specific trypanosomal antigens is a certain indication of ongoing or recently cured infection. A first generation of antigen detection tests already exists and awaits critical evaluation. Another research priority is the development of tests allowing more precise determination of the stage of the disease and follow-up after drug treatment.

9431 **Otte, J.A., Nouwen, J.L., Wismans, P.J., Beukers, R., Vroon, H.J. and Stuiver, P.C., 1995.** Afrikaanse slaapziekte in Nederland. [African sleeping sickness in the Netherlands.] *Nederlands Tijdschrift voor Geneeskunde*, **139** (41): 2100-2104. Havenziekenhuis, afd. Tropische Geneeskunde en Neurologie, Haringvliet 2, 3011 TD Rotterdam, Netherlands.

Two cases of human African trypanosomiasis are reported from the Netherlands: a Cameroonian woman resident in the Netherlands for 2 years with West African-type sleeping sickness (*Trypanosoma brucei gambiense*), and a Dutch tourist who acquired East African-type sleeping sickness (*T. b. rhodesiense*) while travelling through Zimbabwe. Differential diagnosis is difficult. The former is rarely observed in Europeans and the disease runs a chronic course. The latter runs an acute course in Europeans and rapid diagnosis is essential as it can be fatal within days. Both patients recovered after specific therapy.

(b) PATHOLOGY AND IMMUNOLOGY

[See also **19**: no. 9456.]

9432 **Brandenberger, G., Buguet, A., Spiegel, K., Stanghellini, A., Mouanga, G., Bogui, P., Montmayeur, A. and Dumas, M., 1994.**

Maintien des relations entre la sécrétion pulsatile des hormones et la structure interne du sommeil dans la trypanosomiase humaine africaine. [Persistence of the relationship between hormone pulses and internal sleep structure in human African trypanosomiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 383-389.

Brandenberger: Laboratoire de Physiologie et de Psychologie Environnementales, Strasbourg, France.

The 24 h profiles of cortisol, prolactin and plasma renin activity were analysed in six sleeping sickness patients in Brazzaville and in five healthy African controls in Abidjan. Polysomnographic recordings were done continuously and blood was taken every 10 min throughout the 24 h period. The circadian rhythm of cortisol was attenuated in patients but, as in normal

subjects, slow wave sleep remained associated with the declining phases of secretory episodes. Prolactin profiles, which are strongly influenced by the sleep-wake cycle, did not show the increase normally associated with long sleep periods and reflected the spreading of sleep and wakefulness throughout the 24 h period. However, rapid-eye movement (REM) sleep began in sleeping sickness patients, as in normal subjects, during the descending phases of prolactin pulses. In both groups, plasma renin activity reflected the sleep stage distribution, with non rapid-eye movement (NREM) sleep occurring during the ascending phases and REM sleep during the descending phases of the oscillations. However, in sleeping sickness patients, the marked sleep fragmentation often did not allow sufficient time for plasma renin activity to increase significantly. These results demonstrate that, despite disruption of the sleep-wake cycle, the relationship between hormone pulses and specific sleep stages persists, which suggests a strong coupling between hormone release and the internal sleep structure.

9433 **Buguet, A., Bert, J., Tapie, P., Bogui, P., Doua, F., Mouanga, G., Stanghellini, A., Sarda, J., Tabaraud, F., Gati, R., Montmayer, A., Chauffard, F., Lonsdorfer, J. and Dumas, M., 1994.** Distribution du sommeil et de la veille dans la trypanosomose humaine africaine. [Distribution of sleeping and waking in human African trypano-somiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 362-367.

Buguet: Unité de Physiologie de la Vigilance, Centre de Recherches du Service de Santé des Armées, B.P. 87, 38702 La Tronche Cedex, France.

Last century, patients with human African trypanosomiasis were described as sleepy by day and restless by night. However, it was only in 1989 that the first 24 h recording was performed by our team in Niamey (Niger) in a patient with sleeping sickness who had contracted the disease in Côte d'Ivoire.

Polysomnographic recordings (electroencephalogram, EEG, electrooculogram, electromyogram, electrocardiogram, buccal and nasal airflow, and chest respiratory movements) showed a disappearance of the circadian distribution of sleep and wakefulness, which tended to occur evenly throughout the day and night, with a sleep-wake alternation of approximately 80 min. Two investigations were conducted thereafter, the first at Daloa (Côte d'Ivoire) in eight patients who were recorded during two 24 h periods, with and without hourly blood samples, the second at Brazzaville (Congo)

in 10 patients recorded for 24 h before and after treatment with melarsoprol. All patients were at the stage of early meningoencephalitis. At Daloa, the EEG trace of the most severely sick patient was invaded with slow waves, and stages 1 and 2 and stages 3 and 4 could not be distinguished from one another. In the other patients, all sleep stages were easily scored. No difference was seen between recordings, regarding blood collection. All patients presented a marked disturbance in the circadian organisation of their sleep-wake cycle, this alteration being proportional to the severity of the clinical symptoms. These results were confirmed in the 10 Brazzaville patients, the major circadian disturbance in the sleep-wake cycle being observed in the most severely sick patients. The alteration of the circadian rhythmicity of sleep and wakefulness was not found in six healthy volunteers from Abidjan recorded in the same experimental conditions. Human African trypanosomiasis thus represents a dysregulation of the circadian rhythms due no doubt to a disruption of the internal circadian body clock.

9434 **Claustrat, B., Buguet, A., Geoffriau, M., Montmayer, A., Bogui, P., Mouanga, G., Stanghellini, A. and Dumas, M., 1994.** Le rythme nyctéméral de la mélatonine (MLT) est conservé dans la trypano-somose humaine africaine. [The circadian rhythm of melatonin is preserved in human African trypanosomiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 380-382.

Claustrat: Centre de Médecine Nucléaire, Service de Radio-pharmacie et Radioanalyse, Hôpital Neuro-cardiologique, B.P. Lyon, Montchat, 69394 Lyon Cedex 03, France.

Plasma melatonin profiles were studied by radioimmunoassay in nine patients suffering from human African trypanosomiasis and six healthy controls matched according to age and photoperiodic conditions. The circadian periodicity of the sleep-wake cycle was disturbed in proportion to the degree of severity of the disease. On the contrary, the melatonin profile of patients was qualitatively and quantitatively identical to that of controls and showed no change after melarsoprol treatment. These results suggest that, besides a master internal clock generating the main circadian rhythms, an additional regulatory system for the melatonin rhythm could be involved.

9435 **Hamon, J.F., Mendoza, J.L.J. de and Camara, P.A., 1995.**

Trypano-somiose: détermination de groupes de patients à

partir de données cliniques et électroencéphalographiques. [Trypanosomiasis: determination of subgroups of patients from clinical and electroencephalographic data.] *Neurophysiologie clinique*, **25** (4): 196-202.

Hamon: Laboratoire de Psychologie Expérimentale et Comparée, Université de Nice-Sophia-Antipolis, 98 boulevard E. Herriot, B.P. 209, 06204 Nice Cedex 3, France.

Data constituted from clinical and waking electroencephalographic signs in 104 patients at the meningoencephalitic stage of trypanosomiasis were subjected to correspondence analysis in order to determine clinical profiles. Three profiles were identified. The first, encountered in patients with minor clinical disturbances and slightly modified waking electroencephalographic patterns, is suggestive of the stage of onset of cerebral involvement. The second, observed in patients with vigilance disturbances, behavioural and motor impairment, and highly abnormal EEG traces, is indicative of a more severe stage of encephalitis. The third, found in patients with EEG sharp waves organised in a more or less recurring fashion and accompanied by epileptic seizures, is consistent with an acute cerebromeningitis.

9436 **Jauberteau, M.O., Bisser, S., Ayed, Z., Brindel, I., Bouteille, B., Stanghellini, A., Gampo, S., Doua, F., Breton, J.C. and Dumas, M., 1994.**

Détection d'autoanticorps anti-galactocérébrosides au cours de la trypanosomose humaine africaine.

[Detection of anti-galacto-cerebroside autoantibodies in human African trypanosomiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 333-336.

Jauberteau: Laboratoire d'Immunologie, Faculté de Médecine de Limoges, 2 rue du Docteur-Marcland, 87025 Limoges Cedex, France.

The pathogenesis of neurological involvement in human African trypanosomiasis is not currently understood but could involve an autoimmune mechanism as in Chagas' disease. We have therefore searched for autoantibodies directed against CNS glycosphingolipids, initially in the sera of an experimental sheep model infected with *Trypanosoma brucei brucei* and then in sera of trypanosomiasis patients from Côte d'Ivoire and Congo. In all cases, the major reactivity was observed with two components (types I and II) of galacto-cerebroside (GalC), the major glycolipid of myelin. These autoantibodies were detected in 25% of patients from Congo and in 42.8% of

patients from Côte d'Ivoire, contrasting with the low proportion of controls found positive. The proportion of anti-GalC antibodies increased in patients with neuropsychiatric symptoms (72% in patients from Côte d'Ivoire). Anti-GalC antibodies were also detected in the CSF of 24.4% of patients from Congo. The pathogenic significance of these anti-GalC antibodies remains to be determined. They may constitute a predictive marker of neurological involvement.

9437 **McGovern, T.W., Williams, W., Fitzpatrick, J.E., Cetron, M.S., Hepburn, B.C. and Gentry, R.H., 1995.** Cutaneous manifestations of African trypanosomiasis. *Archives of Dermatology*, **131** (10): 1178-1182.

McGovern: Dermatology Service, Fitzsimons Army Medical Center, Aurora, CO 80045, USA.

The cutaneous manifestations of African trypanosomiasis are described in a white American man who travelled to Tanzania. Whilst on safari, he was frequently bitten by tsetse flies. A tender, purple-black lesion developed on his left calf and 2 weeks later, fever, rigors, fatigue and myalgias developed during his flight home to the USA. Four weeks after the onset of symptoms, a pruritic rash developed on his trunk; 2 weeks after this he sought medical attention. Upon examination he had a temperature of 38.4°C and several blotchy, erythematous, annular macules on his chest, abdomen and legs, some of which had evolved into targetoid and purpuric lesions. Trypanosomes were identified in a peripheral blood smear and in a touch preparation of a punch biopsy specimen of the targetoid lesion on the lower abdomen. CSF protein and IgM levels were also elevated. *Trypanosoma brucei rhodesiense* trypanosomiasis was diagnosed and the patient treated with suramin, melarsoprol and dimercaprol.

9438 **Montmayer, A., Brosset, C., Imbert, P. and Buguet, A., 1994.**

Cycle veille-sommeil au décours d'une trypanosomose humaine africaine à *Trypanosoma brucei rhodesiense* chez deux parachutistes français. [The sleep-wake cycle after *T. b. rhodesiense* human African trypanosomiasis in two French parachutists.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 368-371.

Montmayer: Unité de Physiologie de la Vigilance, Centre de Recherches du Service de Santé des Armées 'Emile-Parde', B.P. 87, 38702 La Tronche Cedex, France. The sleep-wake cycle of two French military personnel, who contracted human African trypanosomiasis in Rwanda, was examined by polysomnography 4, 6 and 11 months after infection. Patient A presented with *T. b. rhodesiense*

infection with CNS involvement. An acute encephalitic attack, with pyramidal and cerebellar symptoms which disappeared progressively by the 6th month, had complicated melarsoprol treatment. Patient B presented with *T. b. rhodesiense* at the lymphatic-blood stage with trypanosomes in the blood and the medulla, the CSF and serology remaining normal. Polysomnography recordings were made continuously over a 48 h period using a portable system. The different stages of vigilance were scored according to the classical Rechtschaffen and Kales criteria. In the 4th month, both patients showed several long sleep episodes during the day, which progressively disappeared. Many electroencephalographic abnormalities were seen in patient A, especially in the 11th month: these consisted of transitory arousal phases concomitant with myoclonic jerks of the lower limbs and phases of awakening with slow waves after stage 4 sleep.

9439 **Petzke, F., Heppner, C., Mbulamberi, D., Winkelmann, W., Chrousos, G.P., Allolio, B. and Reincke, M., 1996.** Hypogonadism in Rhodesian sleeping sickness: evidence for acute and chronic dysfunction of the hypothalamic-pituitary-gonadal axis. *Fertility and Sterility*, **65** (1): 68-75.

Reincke: Medizinische Universitätsklinik Würzburg, Joseph-Schneider-Strasse 2, 90780 Würzburg, Germany. An observational, cross-sectional study was carried out at primary health care centres under the care of the National Sleeping Sickness Control Programme in southeast Uganda to investigate acute and long-term effects of Rhodesian sleeping sickness on the function of the hypothalamic-pituitary-gonadal (HPG) axis in men. Fifty-two male patients with sleeping sickness at different stages of treatment and 11 clinically healthy male volunteers recruited from health care personnel were questioned about loss of libido and impotence. All received 100 µg GnRH i.v. Blood was drawn before and 30 min after GnRH administration. Loss of libido and/or impotence were present in 39% of men with active disease before therapy, whereas 84% were biochemically hypogonadal. After cure, 45% of men still were symptomatic and 45% were biochemically hypogonadal. Compared with controls (806 ± 59 pg/ml (mean ± SEM)), T concentrations were decreased substantially in patients before (249 ± 48 ng/dl), during treatment (429 ± 56 ng/dl), and after cure (431 ± 58 ng/dl). Corresponding baseline LH concentrations were inappropriately low and the relative LH response to GnRH was reduced both before and during treatment

(794% \square 131% versus 322% \square 68%). FSH concentrations increased gradually up to 8.0 \square 1.3 mIU/ml at the end of treatment, returning to 4.2 \square 0.6 mIU/ml after cure. It is concluded that Rhodesian sleeping sickness causes acute and chronic HPG axis dysfunction. The clinical and biochemical picture suggests a combined central and peripheral hypogonadism. This is only in part reversible after cure and most likely due to direct parasitic infiltration and/or secondary inflammation causing necrosis and/or fibrosis at the pituitary and gonadal levels.

9440 **Radomski, M.W., Buguet, A., Bogui, P., Doua, F., Lonsdorfer, A., Tapie, P. and Dumas, M., 1994.** Disruptions in the secretion of cortisol, prolactin, and certain cytokines in human African trypano-somiasis patients. *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 376-379.

Radomski: Defence and Civil Institute of Environmental Medicine, 1133 Sheppard Avenue West, P.O. Box 2000, Toronto, Ontario M3M 3B9, Canada.

It has been shown previously that sleeping sickness at the stage of meningoencephalitis manifests itself as a significant disturbance in the circadian rhythm of sleep-wakefulness. The objective of the current study was to examine the extent of circadian disruption in infected patients by measuring 24 h patterns of plasma cortisol, an example of a classical circadian rhythm relatively independent of sleep, and prolactin, a primarily sleep-related rhythm. Plasma levels of certain cytokines were also measured to examine the immuno-pathogenesis of human African trypanosomiasis. An attempt was made to relate any circadian disruptions to the severity of the disease. The three most advanced patients demonstrated circadian disruptions in cortisol, prolactin and sleep-wake rhythms. The prime cytokine factor that correlated with the progression of the disease in humans was interferon-gamma, levels being 7- to 12-fold higher in the patients without any circadian rhythms. Our findings support the hypothesis that human African trypanosomiasis induces selective changes in the suprachiasmatic nucleus, important as a pacemaker for biological rhythms, resulting in disruptions of circadian rhythmicity in advanced stages of the disease.

9441 **Zola, J.M., Wassoumbou-Loubienga, S., Goma, G.C. and Mouanga-Yidika, G., 1994.** Méningo-encéphalite aiguë à *Trypanosoma brucei gambiense* révélée par un oedème papillaire. [Acute meningo-encephalitis due to *T. b. gambiense* revealed by papillo-oedema.] *Bulletin de la Société de Pathologie exotique*, **87**

(5/5 bis): 312-314.

Mouanga-Yidika: Service de Neurologie, Centre Hospitalier Universitaire de Brazzaville, B.P. 32, Brazzaville, Congo.

A 26-year-old woman, living in Brazzaville, was referred by her ophthalmologist about papillo-oedema. Neurological examination showed frontal syndrome and papillo-oedema with no other sign of intracranial hypertension. An electroencephalogram revealed bilateral delta waves and bifrontal points. Significant inflammatory syndrome was noted. Examination of cerebrospinal fluid showed trypanosomes and elevated levels of protein and cells. The patient was successfully treated with tetracosactide (anti-oedema) and eflornithine. The disconcerting feature of this clinical picture and the rarity of pseudotumoural forms of trypanosomiasis are stressed. The problems posed by urban forms of the disease and their control are also considered.

(c) TREATMENT

9442 **Ancelle, T., Barret, B., Flachet, L. and Moren, A., 1994.** Etude de deux épidémies d'encéphalopathies arsenicales dans le traitement de la trypanosomiase, Ouganda, 1992-1993. [Study of two outbreaks of arsenical reactive encephalopathy in the treatment of trypanosomiasis, Uganda, 1992-1993.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 341-346.

Ancelle: Epicentre, 8 rue Saint-Sabin, 75011 Paris, France.

Since 1988, a control programme run by Médecins Sans Frontières has diagnosed and treated human African trypanosomiasis in more than 7000 people in the Moyo district of northern Uganda. A strong seasonal variation in the incidence of arsenical reactive encephalopathy following melarsoprol treatment was noted, with an increase in the second half of the year. In August 1992 and September 1993 the incidence suddenly exceeded 10%. Two retrospective studies were conducted on 75 cases in 1992 and on 51 cases in 1993. The onset of 80% of these 'epidemic' cases occurred between the 5th and the 11th day of treatment. Of the risk factors studied, age, the prescription of thiabendazole to treat strongyloidiasis during melarsoprol treatment and poor general clinical condition of the patients appeared to increase the risk of arsenical reactive encephalopathy. Alcohol consumption during treatment may also be implicated. A

prospective study has been set up in order to identify more precisely the role of these exogenous factors and to control them.

9443 **Doua, F. and Boa Yapo, F., 1994.** Actualités thérapeutiques de la trypanosomiase. [Current chemotherapy for trypanosomiasis.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 337-340.

Doua: Projet de Recherches Cliniques sur la Trypanosomiase, B.P. 1425, Daloa, Côte d'Ivoire. The available drugs used to treat human African trypanosomiasis (pentamidine, suramin, melarsoprol and the new compound DFMO) are reviewed. The administration of pentamidine at the beginning of the nervous stage, when the number of cells in the CSF does not exceed $20/\text{mm}^3$, is a new therapeutic approach. At this stage of the disease, patients are generally healthy and pentamidine therapy avoids the use of the toxic melarsoprol (Arsobal). An alternative protocol for melarsoprol therapy (2.16 mg/kg/day for 10 consecutive days) is proposed from pharmacokinetic data to decrease the rate of relapses and the duration of hospital care. Efficacy and tolerance of this new protocol must be evaluated by randomised clinical trials. Preliminary results of clinical trials using short-term DFMO therapy are encouraging, giving hope of reducing the cost of using this drug which, from its efficacy and tolerance, is the drug of choice for treatment of human trypanosomiasis, especially for patients resistant to the usual trypanocides. Both MLD 73811 and IMOL 881 are new trypanocidal compounds, effective against *Trypanosoma brucei rhodesiense* and *T. b. gambiense*. In addition, IMOL 881 is effective against the animal trypanosomes, *T. evansi* and *T. equiperdum*.

9444 **Gustafsson, L.L., Bronner, U., Rombo, L., Doua, F., Ericsson, O. and Miézan, T., 1995.** Multiple-dose pharmacokinetics and adverse reactions of pentamidine in patients with African sleeping sickness. (Meeting abstract no. 474.) *Thérapie*, **1995** (Suppl., pp. 1-192): [unnumbered].

Unit of Tropical Pharmacology, Division of Clinical Pharmacology, Huddinge Hospital at Karolinska Institute, S-14186 Huddinge, Sweden.

The pharmacokinetics and adverse reactions of the traditional pentamidine dose regimen for *Trypanosoma brucei gambiense* infection were assessed. A total of 10 i.v. infusions of pentamidine were administered every second day to 12 patients. Plasma drug concentrations were determined (HPLC) before every infusion, repeatedly during the last infusion and for a median of 6 months

afterwards. Drug concentrations were also assessed in urine and in CSF samples. Adverse reactions were registered by enquiry, blood pressure monitoring and blood and urine tests. The trough plasma drug concentrations increased gradually indicating drug accumulation. The median plasma half-lives associated with the first, second and last phases in a three-compartment model were 4 min, 6.5 h and 307 h, respectively. The median plasma pentamidine clearance, V and MRT were 513 ml/min, 8500 L and 315 h, respectively. Pentamidine renal clearance accounted for a median of 12% of total plasma clearance. Nephrotoxicity was observed in all subjects, although generally mild. There was a significant negative correlation between trough plasma concentrations before the 10th infusion and renal clearance 0-24 h after this dose. Other adverse reactions were benign and unrelated to trough plasma concentrations. Pentamidine was detected in CSF for up to 30 days after the last dose. The plasma concentrations achieved suggest that treatment with a reduced number of doses should be evaluated in clinical trials.

9445 **Mallia, C.C. and Wood, M.J., 1994.** Central nervous system parasitoses. *Current Opinion in Infectious Diseases*, **7** (6): 692-695.

Department of Infection and Tropical Medicine, Birmingham Heartlands Hospital, Birmingham B9 5ST, UK. Parasitic infections of the central nervous system remain a considerable health burden in many areas of the world. There have been no dramatic developments in their management within the past year. In trypanosomiasis, further evidence has been obtained that the encephalopathy following melarsoprol therapy is a response to viable organisms persisting within the central nervous system. A study has suggested that the dose of eflornithine used in children with West African trypanosomiasis needs to be comparatively higher than that used in adults.

9446 **Onyeyili, P.A. and Egwu, G.O., 1995.** Chemotherapy of African trypanosomiasis: a historical perspective. *Protozoological Abstracts*, **19** (5): 229-241.

Faculty of Veterinary Medicine, University of Maiduguri, Maiduguri, Nigeria.

This review examines the chemotherapy of trypanosomiasis in man and animals, the development of new trypanocidal drugs (particularly eflornithine), trypanocidal drug combinations, and chemotherapeutic successes and limitations. It is concluded that

combination chemotherapy offers promise for the effective treatment of early and late stage African trypanosomiasis.

9447 **Pépin, J. and Milord, F., 1994.** The treatment of human African trypanosomiasis. *Advances in Parasitology*, **33**: 1-47. Pépin: Service des Maladies Infectieuses, Centre Hospitalier Universitaire, 3001 12ème Avenue Nord, Sherbrooke, Quebec J1H 5N4, Canada.

Methods which can be used by the clinician seeking to find out whether a patient is infected with trypanosomes, which subspecies is involved, whether it is early or late stage disease, and also whether treatment has been effective, are outlined. The chemistry and mode of action, pharmacokinetics, efficacy, toxicity, and availability and cost of pentamidine, diminazene, suramin, melarsoprol, eflornithine and nifurtimox, and the treatment of early-stage, late-stage and relapses of *Trypanosoma brucei gambiense* and *T. b. rhodesiense* are discussed. New drugs and better use of currently available drugs, as well as combinations of drugs, are also reviewed.

6. animal trypanosomiasis

(a) SURVEY AND DISTRIBUTION

[See also **19**: no. 9426.]

9448 **Abdurahman, O.S. and Bornstein, S., 1991.** Diseases of camels (*Camelus dromedarius*) in Somalia and prospects for better health. *Nomadic Peoples*, no. 29: 104-112.

Swedish University of Agricultural Sciences.

The diseases frequently diagnosed in Somalian camels, including trypanosomiasis, are listed. The difficulties in interpreting the results of seroepidemiological studies of camels using methods originally designed for cattle are discussed.

9449 **Ahmed, M.I., Osiyemi, T.I.O. and Ardo, M.B., 1994.** Prevalence of bovine trypanosome infections in Damboa local government area Borno State. *Nigerian Journal of Animal Production*, **21** (1/2): 186-187.

Department of Veterinary Microbiology and Parasitology, Faculty of Veterinary Medicine, University of Maiduguri, Maiduguri, Nigeria.

The prevalence of bovine trypanosomiasis in the area of Damboa, Borno State, Nigeria, was investigated. A total of 151 blood samples (each c. 3 ml) was collected from 11 sedentary herds of cattle between February and April 1992. The overall prevalence of trypanosome infection was 7.3% (males 7.7%, females 7.0%), with 11 animals (5 males and 6 females) infected. The 151 cattle comprised four breeds (74 Wadara, 18 White

Fulani, 27 Mbala and 12 Kuri) together with 20 crossbreed animals. The prevalence of trypanosome infections in each of the breeds was: Wadara 9.5% (7 animals), White Fulani 0%, Mbala 7.4% (2 animals), Kuri 0%, crossbreeds 10% (2 animals). *Trypanosoma vivax* was recorded in 9 of the infected animals and *T. congolense* in 2.

9450 **Anene, B.M. and Ezekwe, A.G., 1995.** Trypanosomosis in intensively reared Muturu calves in Nigeria. *Tropical Animal Health and Production*, **27** (4): 229-230.

Anene: Department of Veterinary Medicine, University of Nigeria, Nsukka, Nigeria.

Four batches of trypanotolerant Muturu calves (total number 37) were purchased from neighbouring villages between January 1989 and August 1990 for experimental studies under intensive management at the university farm, Nsukka. More than half succumbed to trypanosomiasis (*Trypanosoma vivax*, *T. congolense*) shortly after arrival. A survey of 53 healthy Muturu cattle from the same source as the calves revealed 3 of 43 adults infected with trypanosomes (*T. vivax*, *T. congolense*, *T. brucei*) but none of the 10 calves. Also, a 2 year survey (1989-1991) of trypanosomiasis prevalence in the resident university herds showed 5.4% of 53 N'Dama and 0.0% of 11 Muturu animals infected. It is thus possible that the university farm was the source of infection to the calves. However, the stress of translocation (possible premature weaning, change to different husbandry and environment) could have resulted in a breakdown of trypanotolerance, and is considered a more likely explanation of their sickness.

9451 **Egbe-Nwiyi, T.N. and Antia, R.E., 1995.** Use of monoclonal antibodies for detecting *T. brucei brucei* infection in splenectomised dogs. *Journal of Small Animal Practice*, **36** (5): 229-232.

Egbe-Nwiyi: Department of Veterinary Pathology, University of Maiduguri, P.M.B. 1069, Maiduguri, Borno State, Nigeria.

A monoclonal antibody against a plasma membrane antigen of *Trypanosoma brucei rhodesiense* was used for the detection of *T. brucei* group-specific circulating antigen in 24 adult local dogs experimentally infected with *T. b. brucei* strain 8/18. Ten of the dogs were splenectomised and the remainder non-splenectomised (intact). Five dogs each from the splenectomised and intact groups were inoculated i.v. with trypanosomes. The infected dogs developed trypanosomiasis between days 4 and 8 p.i. The circulating antigens were detected as early as 6

days p.i. and remained high until 2 weeks after treatment, when the circulating antigen declined. The detection of the antigens showed the existence of infection, unlike the antibody test. The treatment of the infected dogs with diminazene aceturate (Berenil) at a dose of 7.0 mg/kg on day 21 p.i. cleared all the parasites but elevated the circulating antigen levels. The antigen capture ELISA is thus a useful diagnostic tool for complementing parasitological diagnosis, for detecting infection in the field and for ascertaining the efficacy of trypanocidal drugs.

9452 **Kalejaiye, J.O., Ayanwale, F.O., Ocholi, R.A. and Daniel, A.D., 1995.** The prevalence of trypanosome in sheep and goats at slaughter. *Israel Journal of Veterinary Medicine*, **50** (2): 57-59. Veterinary and Livestock Studies Division, NITR, Vom, Nigeria.

The prevalence of trypanosome infections in sheep and goats was investigated in slaughtered animals at Bodija Municipal Abattoir, Ibadan, Nigeria. Wet film and stained thin film examinations as well as the haematocrit centri-fugation technique were used to detect trypanosomes in the jugular blood of the animals. The PCV was also determined. A total of 482 goats and 163 sheep were examined between April and September 1990 and the prevalence rates in goats and sheep were found to be 2.28% and 4.20%, respectively. The average PCV of infected goats was 13.6% and of uninfected goats, 23.5%. The average PCV of infected sheep was 7.8% and of uninfected sheep, 22.0%.

Trypanosoma vivax accounted for 1.65%, *T. brucei* spp. 0.4% and *T. congolense* 0.2% of the infections in goats. The infection rates in sheep were 3.68% for *T. vivax*, 0.61% for *T. brucei* and 0% for *T. congolense*. Sex did not significantly ($P > 0.05$) affect infection rates.

Although the prevalence of trypanosomiasis in sheep and goats appeared low, natural trypanosomiasis could be of great economic importance in these species at slaughter.

9453 **Monzón, C.M., Jara, G.A. and Hoyos, C.B., 1995.**

Determinación de la supervivencia de *Trypanosoma evansi* en sangre de equinos, empleando el método del microhematocrito. [Determination of *T. evansi* survival in equine blood, using the microhaematocrit technique.] *Revue scientifique et technique de l'Office International des Epizooties*, **14** (3): 753-759.

Hoyos: Centro de Diagnóstico e Investigaciones Veterinarias Formosa, Casilla de Correo 292, 3600 Formosa, Argentina.

Using a microhaematocrit technique, the survival of *T. evansi* was studied in blood from two herds of naturally infected horses. Samples were treated with ethylenediaminetetraacetic acid and sodium citrate, either alone or with 1% glucose, and sent to the laboratory packed in ice. In general, the number of samples yielding positive results showed the least variation during the first 24-36 h post-collection. Survival varied with the anticoagulant used but declined rapidly from 48 h post-collection. However, live parasites were still observed in up to 10% of samples until day 7 post-collection. The use of sodium citrate is recommended for treating equine blood samples prior to testing for *T. evansi*.

9454 **Olaho-Mukani, W., Nyang'ao, J.M.N. and Ouma, J.O., 1996.** Use of Suratex for field diagnosis of patent and non-patent *Trypanosoma evansi* infections in camels. *British Veterinary Journal*, **152** (1): 109-111.

Olaho-Mukani: KETRI, P.O. Box 362, Kikuyu, Kenya. The Suratex card latex agglutination antigen detection test was compared with other methods for the diagnosis of *T. evansi* infection in nine herds comprising 549 camels in Eastern Province and Rift Valley Province, Kenya. Of the 549 camels, 50 (9.1%), 127 (23.1%) and 254 (46.3%) were positive by the microhaematocrit centrifugation technique (MHCT), mouse sub-inoculation test (MI) and Suratex, respectively. Trypanosomal antigens were detected in 46 (92%) out of the 50 MHCT-positive camels and in 106 (88%) out of 121 MI-positive camels. Suratex was also used to evaluate the chemotherapeutic response in six camels experimentally infected with *T. evansi* and treated with Cymelarsan or Trypan. All camels were MHCT-positive by the 2nd week p.i. Antigens were detected in three camels 2 weeks p.i. and in the other three 3 weeks p.i. Parasites disappeared 24 h after Cymelarsan treatment while antigens persisted for 3-4 weeks. Trypan failed to cure the infection. These results confirm that trypanosomal antigens may not be detected during the early stage of the disease. Also, under field conditions, persistence of antigens after treatment could be misinterpreted as current infection in camels whose history of treatment is not known. Where possible, therefore, antigen detection assays should be used together with MHCT. For non-patent infections, Suratex, although less sensitive than MI, offers potential for rapid field diagnosis.

(b) PATHOLOGY AND IMMUNOLOGY

[See also **19**: no. 9470.]

9455 **Dam, J.T.P. van, Hofs, P., Ogwu, D., Verstegen, M.W.A. and Zwart, D., 1995.** Increased energy requirements during trypanosomiasis infection in goats. *Proceedings of the Nutrition Society*, **54** (1): 75A.

Dam: Section of Animal Production Systems, Agricultural University, P.O. Box 338, 6700 AH Wageningen, Netherlands.

A trial was carried out to study the energy metabolism of West African Dwarf goats infected with *Trypanosoma vivax*, whose feed intake patterns had been evaluated during a previous infection. A total of 24 adult castrated bucks, receiving a diet of pelleted lucerne,

was used. Of 16 animals infected with *T. vivax*, 12 were fed *ad libitum* while 4 were given a restricted diet. Of 8 control animals, 4 were fed *ad libitum* and 4 restricted. The animals were housed in individual respiration chambers in weeks 2, 4 and 6 p.i. to measure energy balance. The feed intake of *ad libitum* fed animals was low. *Ad libitum* gross energy intake was reduced in infected goats below the restricted rations. Metabolisability was not affected by infection. Heat production was increased in both infected groups, resulting in a more negative energy balance. Body temperature was increased in infected animals. It is concluded that infection reduced energy balance at a given level of metabolisable energy intake. Consequently maintenance needs are increased during trypanosomiasis infection.

9456 **Igbokwe, I.O., 1995.** Nutrition in the pathogenesis of African trypano-somiasis. *Protozoological Abstracts*, **19** (12): 797-807.

Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Maiduguri, P.M.B. 1069, Maiduguri, Nigeria.

The role of nutrition in the pathogenesis of African trypanosomiasis is reviewed with special emphasis on energy nutrition. Nutritional disorders may aggravate trypanosomiasis and the disease itself may influence the nutritional status of the host. Low energy nutrition predisposes to more severe disease and it is hypothesised that this may be mediated through free radical mechanisms due to ascorbic acid depletion, since endogenous ascorbic acid biosynthesis from glucose in animals not dependent on a dietary ascorbic acid supply may be inadequate. Protein or amino acid and vitamin B and C deficiencies due to poor diet or the disease itself may influence immune and erythropoietic responses. Low lipid nutrition may not affect the disease but high lipid nutrition may terminate parasitaemia. It is suggested that nutritional management of trypanosomiasis patients may be beneficial in the treatment of the disease, especially during the chronic phase.

9457 **Katunguka-Rwakishaya, E., 1996.** Effect of nutritional level on bodyweight, degree of anaemia and carcass composition of sheep infected with *Trypanosoma congolense*. *Research in Veterinary Science*, **60** (1): 29-32.

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

The influence of nutritional level on the bodyweight,

degree of anaemia and carcass composition of 24 sheep infected experimentally with *T. congolense* was investigated. The infection caused a marked retardation of growth in the animals fed a low protein ration whereas the infected and control animals fed a high protein ration grew at similar rates. Both groups of infected animals developed similar degrees of anaemia but the infected group fed the high protein diet tended to sustain a higher intensity of parasitaemia than the group fed the low protein diet. The infection was also associated with low killing out percentages and a general reduction of total carcass protein, energy and fat. The decline in these carcass components was greater in the animals fed the low protein diet than in those receiving the high protein diet.

9458 **Lutje, V. and Taylor, K.A., 1995.** T-cell and B-cell responses in resistant and susceptible cattle during primary infection with *Trypanosoma congolense*. (Meeting abstract no. C1-321.) *Journal of Cellular Biochemistry*, **1995** (Suppl. 21A): 28.

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

T-cell and B-cell responses during primary infection with *T. congolense* were analysed in an attempt to elucidate differences in immune functions between resistant and susceptible cattle. Proliferative responses, IL-2 and gamma-IFN production were measured in lymph node cells draining the site of infection in a group of six susceptible Boran cattle and six resistant N'Damas. Antigen- and isotype-specific antibody responses were measured in spleen cells by an ELISPOT assay. Surface phenotype of lymph node cells was analysed by cytofluorimetry. Proliferation to trypanosome antigens was detected in lymph node cells of cattle from both breeds; responses were higher 11 days p.i. and greatly reduced by 35 days p.i. This was paralleled by a reduction in responses to Con A. B-cells from lymph nodes had surface activation markers such as IL-2 receptor and transferrin receptor, and antibody responses to VSG were detected in spleen cells, confirming a differential isotypic response between breeds. It is not yet known which subsets of T-cells are proliferating and how this short-lived response in the lymph node affects B-cell responses. However, no major quantitative differences in T-cell responses between the two cattle breeds were detected.

9459 **Lutje, V., Taylor, K.A., Boulangé, A. and Authié, E., 1995.** *Trypanosoma congolense*: tissue distribution of long-term T-

and B-cell responses in cattle. *Immunology Letters*, **48** (1): 29-34.

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

Memory T- and B-cell responses to trypanosome antigens were measured in peripheral blood mononuclear cells, spleen and lymph node cells obtained from four trypanotolerant N'Dama cattle which had been exposed to six experimental infections with *T. congolense*. These cattle were treated with trypanocidal drugs following each infection and had remained aparasitaemic for 3 years prior to this study. The antigens used were whole trypanosome lysate, variable surface glycoprotein, a 33-kDa cysteine protease (congopain) and a 70-kDa heat-shock protein. As parameters of T-cell-mediated immunity, we measured T-cell proliferation and IFN- γ production. Lymph node cells, spleen cells and peripheral blood mononuclear cells all proliferated to a mitogenic stimulus (concanavalin A) but only lymph node cells responded to trypanosome antigens. Similarly, IFN- γ was produced by both lymph node and spleen cells stimulated with concanavalin A but only by lymph node cells stimulated with variable surface glycoprotein and whole trypanosome lysate. *T. congolense*-specific antibodies were detected in sera and in supernatants of cultured lymph node and spleen cells after *in vitro* stimulation with lipopolysaccharide and recombinant bovine interleukin-2. In conclusion, we have demonstrated that memory T- and B-cell responses are detectable in various lymphoid organs in cattle 3 years following infection with *T. congolense* and treatment.

9460 **Mwangi, D.M., Hopkins, J. and Luckins, A.G., 1996.** *Trypanosoma congolense* infection in sheep: cellular phenotypes in lymph and lymph nodes associated with skin reactions. *Journal of Comparative Pathology*, **114** (1): 51-61.

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

Intradermal inoculation of sheep with culture-derived metacyclic forms of *T. congolense* resulted in the development of localised skin reactions (chancres) and enlargement of the draining lymph nodes 7 days p.i. Changes in the expression of surface antigens of lymphocytes in lymph leaving the affected skin reactions and in the associated lymph nodes were monitored by cannulating the afferent and efferent lymphatic ducts. Trypanosomes appeared in afferent and efferent lymph 3-5 days p.i. and persisted even as the chancres regressed. The cellular output in both afferent and efferent lymph increased markedly after

the onset of parasitosis. Sequential analysis of the phenotypes of lymphocytes by immunofluorescent staining and flow cytometry revealed that in afferent lymph draining the chancre there was an early response which was due to an increase in T cells, particularly CD4⁺ and CD8⁺ cells; however, as the chancres regressed there was an increase in lymphoblasts and surface immunoglobulin-bearing cells. In contrast, in the efferent lymph, the increase in lymphocytes was due predominantly to a higher number of cells bearing surface immunoglobulins.

9461 **Okech, G., Luckins, A.G., Watson, E.D. and Makawiti, D.W., 1996.**

Suspected *in utero* infection in a Boran heifer experimentally infected with *Trypanosoma vivax*. *British Veterinary Journal*, **152** (1): 105-107.

Okech: KETRI, P.O. Box 362, Kikuyu, Kenya.

In an experiment to determine the effects of infection with *T. vivax* on the later stages of pregnancy, three Orma Boran and three Galana Boran cattle aged 2.5-3.5 years were infected during the third trimester with *T. vivax* KETRI 2501 using *Glossina morsitans morsitans* and kept in fly-proof accommodation. Six similar uninfected control animals all produced live calves at term which remained negative for trypanosomes during the 9 week study period. Three of the six calves of infected dams were premature, births occurring 245, 254 and 258 days post-insemination, i.e. 54, 35 and 60 days p.i. respectively, and all died within 24 h. Two calves were born at term, 56 and 79 days p.i., but died within 24 h. No trypanosomes were found in any of these five calves. The remaining calf was born 282 days post-insemination, 83 days p.i., and was weak and emaciated with low birth weight and PCV. Trypanosomes appeared in its blood 57 days later. Since the calf was not diagnosed as infected at birth, it is suggested that infection could have occurred during the birth process rather than *in utero*.

9462 **Taylor, K.A., Gichuki, B., Lutje, V., Naessens, J. and Williams, D.J.L., 1994.**

In vitro activation and detection of antibody-secreting cells from *Trypanosoma congolense*-infected cattle. *Immunology Letters*, **43** (3): 183-187.

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

B cells from the peripheral blood and spleen of *T. congolense*-infected cattle and from the peripheral blood of an uninfected cohort were analysed for ability to secrete antibody and for expression of surface antigens before and after *in vitro* culture with interleukin 2, lipopolysaccharide and pokeweed mitogen. Antibody-

secreting cells (ASC) were only detected in lymphocytes from peripheral blood after *in vitro* stimulation. The frequency of ASC was greater in cultures of lymphocytes from infected cattle than from the uninfected cohort. The frequency of ASC was positively correlated with the number of B cells expressing the transferrin receptor but not with the expression of the CD5 antigen.

(c) TRYPANOTOLERANCE

[See also 19: nos. 9450, 9458.]

9463 **Dossa, S.C., Kaaya, G.P., Essuman, S., Odulaja, A. and Assoku, R.G.K., 1996.** Acquisition of resistance to the tick *Amblyomma variegatum* in Boran cattle, *Bos indicus* and the effects of *Trypanosoma congolense* and *Babesia bigemina* on host resistance. *Veterinary Parasitology*, **62** (3-4): 317-330.

Kaaya: ICIPE, P.O. Box 30772, Nairobi, Kenya.

Boran cattle when repeatedly infested with adults and nymphs of *A. variegatum* were found to acquire resistance starting with the second or third infestation. This acquired immunity, however, tended to break down at the fourth or fifth infestation. Infection of tick-resistant cattle with *T. congolense* or *B. bigemina* does not suppress the acquired resistance against *A. variegatum* but instead tends to enhance it.

9464 **Little, D.A., Wassink, G.-J., Riley, J.A., Agyemang, K., Badjie, B. and Dwinger, R.H., 1994.** Feed supplementation of village-based N'Dama calves. *Tropical Agriculture*, **71** (3): 219-222.

ITC, P.M.B. 14, Banjul, Gambia.

Four experiments were conducted in four villages as part of a project designed to establish practical and economical nutrition interventions to improve productivity of N'Dama cattle under traditional village husbandry and varying degrees of tsetse challenge in a sub-humid environment in West Africa. Supplements of locally available proteinaceous by-products were given to young, mainly pre-weaned calves which ranged in initial weight from 30 to 90 kg. The supplements included groundnut cake, sesame cake and cotton seed, supplied during both the dry and wet seasons. While significant increases in growth rate were obtained to both dry and wet season supplementation, the responses were both inconsistent and much smaller than those obtained in other studies with older weaned N'Dama cattle. It is concluded the feed supplementation of young cattle should probably be restricted to animals whose liveweight exceeds 100 kg.

9465 **Mattioli, R.C., Cassama, M. and Kora, S., 1992.** A comparative study of gastrointestinal nematode egg output in

N'Dama, Zebu and N'Dama \times Zebu crossbred cattle.

Parassitologia, **34** (1-2-3): 109-113.

ITC, P.M.B. 14, Banjul, Gambia.

N'Dama cattle on a field station near Banjul showed a significantly lower prevalence of strongyle infection, as measured by faecal egg output, than Zebu and crossbred cattle. In strongyle-infected animals, mean egg output was also significantly lower in N'Damas than in Zebras. A previous trypanosomiasis infection did not affect the results. The presence of a natural resistance trait to strongyle infection in N'Dama cattle is postulated.

9466 **Mattioli, R.C. and Dempfle, L., 1995.** Recent acquisitions on tick and tick-borne disease resistance in N'Dama (*Bos taurus*) and Gobra Zebu (*Bos indicus*) cattle.

Parassitologia, **37** (1): 63-67.

ITC, P.M.B. 14, Banjul, Gambia.

Studies carried out in The Gambia show a higher resistance to ticks and tick-borne diseases in N'Dama than in Gobra cattle. Tick resistance in N'Dama appears to be effective against those species with a long hypostome, such as *Amblyomma variegatum* and *Hyalomma* spp. The possible mechanisms involved are discussed.

(d) TREATMENT

[See also **19**: nos. 9446, 9451.]

9467 **Camus, E., 1995.** Evaluation of trypanosomiasis and brucellosis control in cattle herds of Ivory Coast.

Agriculture and Human Values, **12** (2): 90-94.

CIRAD, B.P. 2386, Jarry Cedex 97002, Guadeloupe.

A project to control bovine trypanosomiasis and brucellosis in Côte d'Ivoire is described. A single trypanocidal treatment of young calves dramatically reduced their mortality rate. Treatment was carried out initially (1975-1980) in a limited area by the government agency SODEPRA, followed by demonstrations on nearly all the farms (1980-1985), the costs being covered by SODEPRA. Over a period of time the farmers took charge of the treatments, both financially and physically. In 1992, the trypanocidal treatments were still being widely used. The reasons for this success are considered to be the dramatic efficacy of the treatment, the simple technology employed, the low cost that was progressively charged to the farmers, and the fact that this was a long-term extension project with continuous farmer training.

9468 **Gummow, B., Preez, J.L. du and Swan, G.E., 1995.** Paired-ion extraction and high-performance liquid chromatographic

determination of diminazene in cattle plasma: a modified method. *Onderstepoort Journal of Veterinary Research*, **62** (1): 1-4.

Gummow: Faculty of Veterinary Science, Private Bag X4, Onderstepoort 0110, South Africa.

The high performance liquid chromatographic method was modified in order to improve peak separation in the determination of plasma diminazene concentrations in cattle. Solid-phase extraction with acetonitrile/0.025 M Na-octane sulphonate and 2% acetic acid as eluent, followed by sample concentration, gave recoveries of > 90% for diminazene and the internal standard. A mobile phase of acetonitrile/0.005 M Na-octane sulphonate, 0.1% triethyl-amine, pH 3.2 with acetic acid on a Nova Pak C18 column was used for the analysis. Wavelength switching was used to determine the internal standard (Imidocarb) and diminazene at their respective wavelengths of maximum absorbance, resulting in a fivefold increase in the limit of detection for diminazene. The modified method attained a detection limit of 2 ng/ml (peak 4 \exists baseline noise), limit of quantitation of 10 ng/ml (coefficient of variation < 15%) and an accuracy of > 96% over the range from 10 to 5000 ng/ml.

9469 **Nyang'ao, J.M., Olaho-Mukani, W., Maribei, J.M. and Omuse, J.K., 1995.**

Evaluation of the efficacy of melarsenoxyde cysteamine (Cymelarsan[®]) in treatment of camels experimentally infected with *Trypanosoma evansi* using antigen trapping enzyme-linked immuno-sorbent assay. *Journal of Veterinary Pharmacology and Therapeutics*, **18** (6): 468-470.

Nyang'ao: KETRI, P.O. Box 362, Kikuyu, Kenya.

Various diagnostic techniques (Ag-ELISA, Ab-ELISA, MHCT and mouse sub-inoculation) were assessed for the evaluation of the efficacy of Cymelarsan treatment of *T. evansi*-infected camels. Eleven dromedary camels were divided into three groups: Group A (4 camels) and group B (5 camels) were inoculated i.v. with *T. evansi* KETRI 2468. Group A were allowed to develop the clinical disease over the entire study period (16 weeks) while group B were treated with Cymelarsan (0.25 mg/kg) at the onset of clinical disease. Group C (2 camels) were kept as uninfected controls. The pre-patent period of the infected camels was 6 or 7 days determined by MHCT. Two group A camels died of acute disease 11 and 12 days p.i. and a third died on day 110. The camels in group B achieved clinically apparent cure as indicated by improved health status and disappearance of parasites from the peripheral circulation within 24 h after

treatment. Mice inoculated with blood from untreated camels at the end of the study period became infected while those inoculated with blood from treated camels were not infected. Circulating trypanosomal antigens were detected in three infected camels in the first week, in another three during week 2 and in two during weeks 3 and 4. Antigenaemia was not demonstrated in the camel that died on day 11. Antigen concentrations in the group A camels showed a progressive increase and remained detectable throughout the study period. In group B camels, there was a sharp rise in antigen concentration up to week 4, followed by a gradual fall, to below the limit of detection by week 10 (in one camel by week 3). Trypanosomal antibodies in both infected groups were first detected during week 1 p.i., with levels increasing steadily until week 4, followed by minimal fluctuations in untreated camels, and a slight decline towards the end of the experiment in treated camels. Cymelarsan at the recommended dose was thus shown to be effective. Ag-ELISA proved superior to Ab-ELISA and MHCT in assessing cure.

7. experimental trypanosomiasis

(a) DIAGNOSTICS

[See **19**: no. 9430.]

(b) PATHOLOGY AND IMMUNOLOGY

[See also **19**: no. 9462.]

9470 **Antia, R., Nowak, M.A. and Anderson, R.M., 1996.** Antigenic variation and the within-host dynamics of parasites. *Proceedings of the National Academy of Sciences of the United States of America*, **93** (3): 985-989.

Antia: Department of Biology, Emory University, 1510 Clifton Road, Atlanta, GA 30322, USA.

Many parasites exhibit antigenic variation within their hosts. We use mathematical models to investigate the dynamical interaction between an antigenically varying parasite (*Trypanosoma vivax*) and the host's immune system. The models incorporate antigenic variation in the parasite population and the generation of immune responses directed against (i) antigens specific to individual parasite variants and (ii) antigens common to all the parasite variants. Analysis of the models allows us to evaluate the relative importance of variant-specific and cross-reactive immune responses in controlling the parasite. Early in the course of infection within the host, when parasite diversity is

below a defined threshold value (the value is determined by the biological properties of the parasite and of the host's immune response), the variant-specific immune responses are predominant. Later, when the parasite diversity is high, the cross-reactive immune response is largely responsible for controlling the parasitaemia. It is argued that increasing antigenic diversity leads to a switch from variant-specific to cross-reactive immune responses. These simple models mimic various features of observed infections recorded in the experimental literature, including an initial peak in parasitaemia, a long and variable duration of infection with fluctuating parasitaemia that ends with either the clearance of the parasite or persistent infection.

9471 **Bentivoglio, M., Grassi-Zucconi, G., Peng, Z.-C. and Kristensson, K., 1994.** Sleep and timekeeping changes, and dysregulation of the biological clock in experimental trypanosomiasis. [*T. b. brucei*; rats.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 372-375.

Bentivoglio: Institute of Anatomy and Histology, Medical Faculty, University of Verona, Strada le Grazie, 37134 Verona, Italy.

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Laboratoire de Parasitologie, Université de Bordeaux II, 146 rue Léo Saignat, 33076 Bordeaux Cedex, France.

9473 **Daulouède, S., Okomo-Assoumou, M.-C., Labassa, M., Fouquet, C. and Vincendeau, P., 1994.** Mécanismes de défense au cours des trypanosomoses. [Immune mechanisms in trypanosomiasis.] [*T. musculi*, *T. b. brucei*, *T. b. gambiense*; mice.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 330-332.

Laboratoire de Parasitologie, Université de Bordeaux II, 146 rue Léo Saignat, 33076 Bordeaux Cedex, France.

9474 **Kristensson, K., Eneroth, A., Olsson, T. and Wiesenfeld-Hallin, Z., 1994.** A new approach for the pathogenesis of human African trypanosomiasis. [*T. b. brucei*; rats.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 319-322.

Kristensson: Department of Neuroscience, Doktorsringen 17, Karolinska Institutet, S.171 77 Stockholm, Sweden.

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INSERM 42, 369 rue J. Guesde, 59650 Villeneuve d'Ascq, France.

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Pentreath: Department of Biological Sciences, University of Salford, Salford M5 4WT, UK.

(c) CHEMOTHERAPEUTICS

[See also **19**: nos. 9499, 9502, 9513, 9519.]

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Trypanocidal resistance in *Trypanosoma evansi in vitro*: effects of verapamil, cyproheptidine, desipramine and chlorpromazine alone and in combination with trypanocides. *Veterinary Parasitology*, **62** (1-2): 43-50.

Anene: Faculty of Veterinary Medicine, University of Nigeria, Nsukka, Nigeria.

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Antitrypanosomal activity of camptothecin analogs. Structure-activity correlations. [*T. brucei*.] *Biochemical Pharmacology*, **50** (7): 937-942.

Shapiro: Division of Clinical Pharmacology, Department of Medicine, Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, MD 21205-2185, USA.

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Dipartimento di Medicina e Oncologia Sperimentale, Sezione di Biochimica, Università di Torino, Torino 10126, Italy.

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Essais d'efficacité sur *Trypanosoma brucei brucei* de molécules franchissant la barrière hémato-méningée et du mégazol. [Efficacy trials against *T. b. brucei* of drugs passing through the blood-brain barrier and of megazol.] [*In vitro*, mice.] *Bulletin de la Société de Pathologie exotique*, **87** (5/5 bis): 347-352.

Marie-Daragon: Institut d'Epidémiologie

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Department of Veterinary Pathobiology, Division of Parasitology, University of Illinois, Urbana, IL 61801, USA.

9482 **Ndung'u, J.M., Ngure, R.M., Ngotho, J.M., Sayer, P.D. and Omuse, J.K., 1994.** Total protein and white cell changes in the cerebrospinal fluid of vervet monkeys infected with *Trypanosoma rhodesiense* and the post-treatment reaction. *Journal of Protozoology Research*, **4** (4): 124-135.

Ndung'u: KETRI, P.O. Box 362, Kikuyu, Kenya.

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Department of Veterinary Physiology and Pharmacology, University of Maiduguri, Maiduguri, Nigeria.

9484 **Othman, T., 1994.** The toxic effects of multiple doses of diminazene aceturate on the haematological values of rats. *Nigerian Journal of Animal Production*, **21** (1/2): 146-148.

Department of Veterinary Physiology and Pharmacology, Faculty of Veterinary Medicine, University of Maiduguri, Maiduguri, Borno State, Nigeria.

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

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Groupe de Chimie Organique Biologique, URA au CNRS 470, Université Paul-Sabatier, 118 route de Narbonne, 31062 Toulouse Cedex, France.

9487 **Rabo, J.S., Wakil, A.B. and Maduka, H.C.C., 1994.** Effects of Berenil on the pathogenesis of trypanosomiasis in

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Characterisation of cloned lines of *Trypanosoma brucei* expressing stable resistance to MelCy and suramin. *Acta Tropica*, **60** (4): 251-262.

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Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh 243 122, India.

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Yang: Laboratory of Pharmacology, Changchun Veterinary College, Changchun 130062, China.

8. trypanosome research

(a) CULTIVATION OF TRYPANOSOMES

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Military Medical Institute, Nanjing Military Area, Nanjing 210002, China.

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Military Medical Institute, Nanjing Military Area, Nanjing 210002, China.

(b) TAXONOMY, CHARACTERISATION OF ISOLATES

[See also **19**: no. 9426.]

9494 **Maslov, D.A., Lukes, J., Jirku, M. and Simpson, L., 1996.**

Phylogeny of trypanosomes as inferred from the small and large subunit rRNAs: implications for the evolution of parasitism in the trypanosomatid Protozoa. *Molecular and Biochemical Parasitology*, **75** (2): 197-205.

Simpson: Department of Biology, University of California, Los Angeles, CA 90095-1606, USA.

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

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Characterization of a transcription terminator of the procyclin PARP A unit of *Trypanosoma brucei*. *Molecular and Cellular Biology*, **16** (3): 914-924.

E. Pays: Department of Molecular Biology, University of Brussels, 67 rue des Chevaux, B-1640 Rhode St Genèse, Belgium.

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Clayton: Zentrum für Molekulare Biologie, Universität Heidelberg, Im Neuenheimer Feld 282, 69120 Heidelberg, Germany.

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Balber: Department of Immunology, P.O. Box 3010, Duke University Medical Center, Durham, NC 27710, USA.

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Englund: Department of Biological Chemistry, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.

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Herdewijn: Laboratory of Medicinal Chemistry (FFW), University of Ghent, Harelbekestraat 72, B-9000 Ghent, Belgium.

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Stuart: Seattle Biomedical Research Institute, 4 Nickerson Street, Seattle, WA 98109-1651, USA.
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Deshusses: Department of Biochemistry, University of Geneva, 30 Quai E. Ansermet, CH-1211 Geneva 4, Switzerland.
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Vasella: Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland.
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Department of Genetics, University of Leicester, University Road, Leicester LE1 7RH, UK.
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Phillips: Department of Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75235-9041, USA.
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Donelson: Department of Biochemistry, University of Iowa, Iowa City, IA 52242, USA.

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