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ADVANCES IN THE CONTROL OF THEILERIOSIS

Proceedings of an International Conference held at the International Laboratory for Research on Animal Diseases in Nairobi, 9-13th February, 1981

Edited by

A.D. Irvin

International Laboratory for Research on Animal Diseases
P.O. Box 30709, Nairobi, Kenya

M.P. Cunningham

International Centre for Insect Physiology and Ecology
P.O. Box 30772, Nairobi, Kenya

A.S. Young
Veterinary Research Department, Kenya Agricultural Research Institute,
P.O. Box 32, Kikuyu, Kenya

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PREFACE

Approximately five years have elapsed since the Conference on "Tick-borne Diseases and their Vectors" (Wilde, 1978, University of Edinburgh) was held at the Centre for Tropical Veterinary Medicine in Edinburgh. Theileriosis was one of the main topics at that Conference and some 20 scientific presentations were given. Also in the same year a Workshop on "Theileriosis" was held at the Kenyatta Conference Centre in Nairobi (Henson & Campbell, 1977, IDRC, Ottawa). Both of these meetings provided a valuable up-dating of theilerial diseases,and the Proceedings have been a constant source of reference for scientists in the ensuing years. The meetings played a significant role in setting the scene for a number of important advances which have been made since then.

In February of this year, attention was focused on these advances when nearly 200 scientists from over 30 countries were assembled at the International Laboratory for Research on Animal Diseases in Nairobi for the international conference on "Advances in the Control of Theileriosis". The interest and concern shown in this subject has now grown to the extent that more than 70 scientific presentations were given over the course of a very busy week. An important facet of the Conference was the attention given to the control of Theileriosis, since this must be the ultimate aim of all those involved with the disease. Control will be difficult. The Conference made it clear that an understanding of the epidemiology, the ability to manipulate the organisms *in vitro*, and elucidation of the mechanisms of immunity, may be prerequisites to developing rational chemotherapy and immunization programmes. Effective control will be achieved only by establishing a balance between livestock management, tick control, chemotherapy and immunization. The relative emphasis given

to each factor will vary under different conditions and in differen situations. Having weighed up all the options, consideration must then be given to the cost of proposed programmes and the benefits likely to accrue.

We are pleased to present these Proceedings with the knowledge that they cover all the many aspects discussed above. We trust, therefore, that this volume will find a place on the bookshelf of the immunologist and the donor agencies; the entomologist and the administrator; and the veterinarian and the farmer.

June 1981

A.D. Irvin
M.P. Cunningham
A.S. Young

ORGANISING COMMITTEE

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Thanks are also due to all those who attended the Conference and to those who presented papers. The typing of these papers was carried out by Mrs. J.A. Stevenson and we are pleased to express our gratitude for the efficiency and accuracy with which this work was conducted. We also thank Dr. P.G.W. Stevenson for help in editing the Proceedings. The Organising Committee is also pleased to acknowledge the help and support supplied by I.L.R.A.D. and its staff, in particular Mrs. R. Ndumbu who bore the load of the secretarial work.

A final word of thanks is due to the Publishers, Martinus Nijhoff, for their cooperation and help in bringing the Conference to a successful conclusion with the publication of these Proceedings.

OPENING ADDRESS

by

THE HON. J.C.N. OSOGO, M.P., E.G.H.,
MINISTER OF LIVESTOCK DEVELOPMENT, KENYA

I would like to thank the Organising Committee for inviting me to open this international Conference on Advances in the Control of Theileriosis. The Government of Kenya is very pleased that the Organising Committee should have chosen this country as the venue for the Conference. Under the leadership of our President, His Excellency the Honourable Daniel Arap Moi, we firmly believe in a policy of international cooperation and collaboration, and actively encourage harmony and goodwill between peoples of all races and creeds. One way that we can demonstrate our nation's philosophy is by hosting international conferences such as the current one starting at I.L.R.A.D. today. The Kenya Government welcomes the presence of such international organisations since they provide further demonstration of the part Kenya is playing in promoting active cooperation between nations.

A further reason for welcoming the holding of this Conference in Kenya is that theileriosis still remains one of the major constraints to the development of the livestock industry in this country. My Ministry is only too aware of the enormity of the problem, and it is our hope that, following your deliberations and discussions this week, we may be in a better position to understand the complexities of the problem and ways of combating the disease.

Theileriosis is an enormous problem in many developing countries of the world particularly in Africa, Asia and the Middle East. In the case of East Coast fever, it has been estimated that one animal dies of the disease every minute. This means that during the course of this Conference approximately seven thousand cattle will have died of East Coast fever.

In addition there are the other losses which are more

difficult to assess: such as loss of productivity and expenses incurred in controlling ticks. Such losses obviously place enormous strains on the economy of the developing countries, many of which derive a substantial part of their national income from the cattle industry.

While it may seem trite to quote figures such as those just given, they serve to remind us of the impact of the disease; that theileriosis is a disease that kills and debilitates cattle, and that this in turn affects the quality of life of millions of people in developing countries.

In the brochure describing the theme of the Conference, I was pleased to see that the emphasis will be on practical aspects of theileriosis: recent development, problems, and possible solutions. I welcome this approach since I feel that in this way we can most profitably develop our strategies for combating the disease. However, let us not imagine that the solutions will be easy to find; many gifted scientists have worked for many years and still the disease has the upper hand. The problems are very complex and as advanced scientific technology is applied to tackling them, the complexities seem to grow rather than recede.

I believe however that we are now at an exciting stage in understanding theileriosis: on one hand we have the tremendous wealth of practical experience of understanding theileriosis and on the other hand we are gaining an understanding of the nature of the bovine immune system thanks to sophisticated technology recently developed and now being applied to theileriosis. It is important that we now integrate these two approaches into solving the problems.

A valuable component of this Conference has been the bringing together of the practical scientist and the fundamental scientist; it is now vital that they interact and appreciate and understand each other's viewpoints and methods of approach. It is my earnest hope that the Conference will achieve this interaction.

In many countries of the world, financial and technical aid play important roles in development of resources, expertise and welfare, but as we all know there are increasing restrictions or

aid. Many of the participants have been assisted in attending this Conference as a result of financial aid and many are dependent on aid for their scientific work. In these days of financial restraint it is incumbent on all of us to utilize these dwindling resources efficiently and wisely. For this reason, international scientific collaboration and cooperation, such as this Conference seeks to promote, is to be greatly encouraged. In this way we can foster good relations with the donor agencies and demonstrate that we can utilize their funds in a responsible and effective way.

At this Conference we have participants from all the continents of the world and it is now my very pleasant duty to welcome you to this country of ours. You have come at the best time of year and I hope that many of you will take the opportunity, when your scientific programme is over, to visit the countryside, to enjoy the hospitality of the people and to see the wildlife. Having done that perhaps you will be able to return again with your families.

I would like again to thank the Organising Committee for inviting me to open this Conference. I wish you well in your scientific deliberations and now have pleasure in declaring the Conference open.

THEILERIAL SPECIES OF DOMESTIC LIVESTOCK

G. UILENBERG

The taxonomy of parasites of the genus Theileria of domestic animals appeared straightforward to most specialists in the western world about 20 years ago. Apart from the six species shown in Table 1, there were two doubtful ones in camels and reindeer, T. camelensis and T. tarandirangiferis. Species were differentiated by the host in which they were found, their pathogenicity and epidemiology, absence or presence of the carrier state after recovery and the influence of splenectomy, numbers of piroplasms and schizonts, size and percentages of different morphological types of piroplasms and size of the macroschizont. Immunological strain differences had been reported for T. annulata by Adler & Ellenbogen (1935) and subsequent authors, but it was generally believed that there was only one antigenic type of T. parva, even though Jezierski et al (1959) had demonstrated an antigenic difference between strains from Zaire and South Africa.

In recent years more criteria for distinguishing species and strains have become available and the situation has become far more complex. Moreover, it has become apparent since the work of the FAO team at Muguga that immunological diversity in T. parva is real. Several criteria are used to identify species:

1. Morphology of the piroplasms. The size and percentages of elongate, rod- and comma-shaped, oval and round forms may sometimes be of help, but as they are to some extent variable during the course of the infection this criterion cannot be considered as reliable. Its injudicious use has, for instance, led to fallacious reports on the occurrence of T. annulata and T. hirci in Nigeria and T. parva in Pakistan and Syria. Good criteria are the presence or absence of a bar-like structure and/or an oval or rectangular veil-like body in the cytoplasm of infected red cells. The

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bar structure was first found by Tsunoda et al (1961) and was shown by Young et al (1978b) to be connected with the parasite, as well as with the outside of the red cell. The parasitic origin of the bar is also indicated by the fact that it fluoresces at the same rate as the piroplasm in the indirect fluorescent antibody test (IFAT) (unpublished results). In T. separata of sheep, the bar appears to be reduced to a dot. The oval or rectangular bodies ("veils"), first detected by Uilenberg (1964b), consist of a crystalloid haemoglobin-derived substance (van Vorstenbosch et al, 1978; Young et al, 1978b).

2. Morphology of the schizont. So far, only the large macroschizonts of T. mutans, with their big nuclei, are sufficiently distinctive to be useful in species differentiation (Schreuder et al, 1977; Young et al, 1977a; Young et al, 1978c). Schizonts of some species have not yet been described.

3. Serological characterization. This is one of the most conclusive criteria. The IFAT, first employed for Theileria by Schindler & Wokatsch (1965), is most commonly used. Sera containing antibodies to the unidentified species are tested against a range of antigens of different species, and antigen of the unidentified parasite is tested against positive antisera to different species.

4. Cross-immunity tests in animals have been used for species differentiation. They are conclusive if solid cross-immunity is demonstrated and probably also if there is a complete absence of cross-immunity, but the question is complicated by the occurrence of important intraspecific immunological differences, at least in T. parva.

5. Host specificity, for the tick vector as well as for the mammalian host, may also be of help. However, host specificity is not always absolute. For instance, T. parva can be transmitted experimentally by several species of Rhipicephalus and Hyalomma, although in nature R. appendiculatus is the usual vector, and a bovine Theileria sp. from Australia may give rise to a patent parasitaemia in sheep (Hoyte, 1971).

6. Pathogenic and epidemiological characteristics may give some indication, but we now know for instance that there are more

species of low pathogenicity in cattle than T. mutans, more in sheep than T. ovis, and that T. mutans is occasionally fatal. We also know that parasites with such biologically and epidemiologically different properties as those causing East Coast fever (E.C.F.), Corridor disease and Rhodesian theileriosis belong to one species.

7. Biological differences have hardly been looked at, but it has been shown that at least glucose phosphate isomerase (GPI) isoenzyme patterns may differ between species (Melrose & Brown, 1979; Melrose et al, 1980; Musisi, 1979; van der Meer et al, in press)

A combination of criteria should be used to reach definite conclusions.

In the following review of species and strains (see also Tables 2 and 3), the changes brought about since 1960 will be stressed. Some of the definitions of species are deliberately provocative and will be commented upon. In this review only the genus Theileria is recognized, with Gonderia, Cytauxzoon, and Haematoxenus as synonyms.

1. T. parva (Theiler, 1904)

Synonyms: T. kochi (Stephens & Christophers, 1903), a name which has in fact priority over T. parva.

T. lawrencei (Neitz, 1955)

T. bovis (Neitz, 1957)

Definition: T. parva is a parasite of wild African buffalo (Syncerus caffer), also infective to cattle and domestic buffalo. The main vector is Rhipicephalus appendiculatus, but other Rhipicephalus spp. as well as some Hyalomma spp. are experimental vectors. T. parva occurs in eastern, central and southern Africa. It is highly pathogenic to cattle and domestic buffalo causing Corridor disease, E.C.F. and Rhodesian malignant theileriosis. Piroplasms are predominantly rod-shaped and small. In cattle they are not associated with intra-erythrocytic bars or veils, but in S. caffer a veil may occur in infected red cells (Uilenberg & Schreuder, in van Vorstenbosch et al, 1978). Macroschizonts of T. parva are small, but may increase in size in the course of infection.

T. parva has been extended to encompass T. lawrencei and

T. bovis. Neitz (1957) synonymized T. bovis with T. lawrencei and Barnett & Brocklesby (1966) first showed that the latter is not a separate species from T. parva. A trinomial nomenclature has been introduced (Lawrence, 1979; Uilenberg, 1976): T. parva parva for parasites causing classical E.C.F., T. parva lawrencei for buffalo strains causing Corridor or Buffalo disease, and T. parva bovis for strains with an intermediate character, producing Rhodesian malignant theileriosis. This nomenclature has been proposed solely for the sake of convenience and is probably not correct from a zoological point of view (cf. the trinomial names for nosodemes of Trypanosoma brucei). During a study of the behaviour of different strains, we have come to realize that it may be an over-simplification to divide T. parva into 3 biological subspecies. In reality there appears to be a gradual range of strains between 2 extremes: the lawrencei-type with few schizonts and none or very few piroplasms in cattle, and the parva-type with high parasitaemias and very numerous schizonts.

The name T. lawrencei has been tenacious. It was distinguished from T. parva as a parasite of wild African buffalo (Syncerus caffer), self-limiting in cattle where it produced no piroplasms and relatively few schizonts. T. bovis differed from T. lawrencei because piroplasms were produced in cattle, so that it could maintain itself in the cattle population without the presence of buffalo; it was considered to be different from T. parva because the carrier state ensued after recovery and the numbers of parasites in T. bovis infections were lower than in E.C.F. However, when Neitz (1957) discovered that T. lawrencei could produce piroplasms and the carrier state in cattle, T. bovis was made synonymous with T. lawrencei in a footnote to the paper in which it was described. Arguments for the synonymy of the 3 are at present manifold and conclusive. They cannot be distinguished in the IFAT, they are morphologically identical, they have the same main tick vector, the behaviour of T. lawrencei can be changed by tick-cattle passages in such a way that it first resembles T. bovis and later becomes indistinguishable from T. parva, and there are various degrees of cross-immunity between different strains of T. parva, T. bovis and T. lawrencei. Moreover, it is becoming apparent that

the carrier state after recovery from E.C.F. may occur and is possibly not even an exception; it is only after recovery from extreme parva-type strains that all parasites are usually eliminated from the host.

The cross-immunity is not linked to biological type or to geographical origin. In unpublished studies at Utrecht, so far using one animal for each test only, we have found for instance: a) Two parva-type strains of geographically widely separated areas, the well-known South African Schoonspruit and Kenyan Muguga strains, showed almost complete bilateral cross-immunity. b) A bovis-type strain from Rwanda (Nyakizu strain) caused severe reactions in animals immune to a bovis-type from Zimbabwe (Boleni strain), or to the Tanzanian Manyara lawrencei-type (Schreuder et al, 1977), or to the Muguga Schoonspruit or the Tanzanian Pugu 1 parva-type strains. c) The Nyakizu bovis-type and a Ugandan parva-type (Uganda) showed almost complete cross-immunity. d) The Uganda parva-type gave virtually complete protection against a cocktail of 8 different strains of parva-, bovis- and lawrencei-types (in addition to those mentioned above, the well-known Kiambu 5 and Serengeti "transformed" strains were included). e) The Uganda parva-type caused severe reactions in animals immune to the Muguga or the Kiambu 5 parva-types, or the Boleni bovis-type. Of course, the lack of reaction to heterologous challenge in a single animal is not a conclusive result.

The establishment of the cross-immunity pattern of strains is a lengthy procedure. Ticks have to be infected, stabilates to be prepared and each test requires infection and treatment, homologous challenge, followed by heterologous challenge. A laboratory in vitro test for identifying the immunological character of strains is urgently required. Monoclonal antibodies may constitute one promising approach (Pinder & Hewett, 1980), but isoenzyme patterns might prove to be another one. Melrose et al (1980), using the cell-cultured schizont stage, have shown differences between strains of T. annulata in the isoenzyme patterns of glucose phosphate isomerase (GPI).

We have also found strain differences of this isoenzyme in T. parva, both in the piroplasm stage (van der Meer et al, in press) and the schizont stage (Uilenberg, Spanjer, Jongejan & Perié