Pan American Health Organization

ADVISORY COMMITTEE ON MEDICAL RESEARCH

Seventh Meeting

Washington, D.C., 24-28 June 1968

Item 23.1 of the Agenda

SCIENTIFIC GROUP ON COMPARATIVE STUDIES OF AMERICAN AND AFRICAN TRYPANOSOMIASES

Report of the First Meeting

Ref: RES 7/14

5 June 1968

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION

Washington, D.C.

SCIENTIFIC GROUP ON COMPARATIVE STUDIES ON AMERICAN AND AFRICAN TRYPANOSOMIASES*

Report of the First Meeting

Under the auspices of the World Health Organization, the First Scientific Group on Comparative Studies of American and African Trypanosomiasis met in Washington from the 11th to the 15th of December, 1967.

Dr. Charles L. Williams, Jr., Deputy Director of the PAHO opened the meeting on behalf of the Director-General, WHO, and outlined the importance of the trypanosomiasis as diseases of developing countries in both hemispheres noting the problems of control and the role of research in the elucidation and solution of these problems.

It was the task of the Scientific group to review the advances in the respective disciplines with particular emphasis on the aspects of research which were common to the two diseases and which would lend themselves to comparative study.

The group was composed of 28 individuals, 16 of whom might be designated members; 6 of whom were considered advisors, and 6 of whom were staff members of the WHO. The personnel involved are listed in appendix A. Dr. F. C. Goble was elected Chairman, Dr. R. Zeledon, Vice-Chairman and Dr. M. P. Hutchinson, Rapporteur.

A proposed agenda (appendix B) was accepted in principle at the first plenary session and it was agreed that the material could probably best be presented, digested and assimilated if the group could be divided into sub-groups which could meet separately to consider the details in

---

Prepared for the Seventh Meeting of the PAHO Advisory Committee on Medical Research, 24-28 June 1968, by Dr. F. C. Goble, CIBA Research Department, Summit, New Jersey.

their specialties and formulate reports and recommendations which could subsequently be presented to the whole group. Four subgroups were organized, each of which selected its own chairman and spokesman and the subgroups met each afternoon.

When documents representative of the consensus of the members of these subgroups had been prepared they were presented for consideration to the plenary sessions held each morning. The subgroups were designated as follows:

I. General Biology, Physiology and Chemotherapy
II. Epidemiology
III. Pathology
IV. Immunology

The subgroups were all approximately of the same size but certain individuals who had interest or information in more than one area were free to migrate from group to group.

Prior to the meeting a number of members of the group had been asked to prepare working papers on the various subjects included in the agenda. Fifteen of the group had submitted such documents by the beginning of the meeting, certain individuals having prepared as many as 5 to 7 and the total number of working papers available for review and discussion was about 40. This assemblage of predigested information was invaluable to the deliberation of the subgroups and group.

The details concerning the differences and similarities in the various aspects of American and African trypanosomiasis will be enumerated in the report of the group which is still in preparation. It should be pointed out here, however, that there was almost complete agreement between the members of the group that there were many facets of research in American and African trypanosomiasis in which either similar phenomena were observed

in both diseases or in which similar methods might be used to elucidate the phenomena. It was the feeling of the group that such meetings of experts from different regions were valuable and that the interchange of information and ideas between the individuals of this specific group had been very useful and convening of similar meetings in the future would be desirable.

Each of the four subgroups pointed out the research needs in their respective areas, and definite proposals and recommendations will form a part of the complete report. It should suffice here to enumerate some of the subjects which more urgently require investigation. These will be listed under the categories used in defining the subgroups.

I. General, Physiology, Chemotherapy

1. The establishment of at least two separate banks for the maintenance of both African and American trypanosomes in the frozen state so that a collection of stable isolates, strains, or stabilates from many areas and hosts would be available for comparative studies.

2. The establishment of standard procedures for isolation, maintenance, and cultivation.

3. The synthesis of isotopically labelled trypanocidal drugs for studies in the absorbtion, metabolisms and mode of action of these agents.

II. Epidemiology

1. The extension of physiological studies on insect vectors in relation to the factors affecting their infectability and their efficacy as transmittors.

2. A pilot project for a long term study on Chagas disease taking anthropological and social factors into consideration.

3. A pilot project on the effect of environmental temperature on T. cruzi in both intermediate and definitive hosts.

4. The development of standardized and genetically defined insect vectors.

III. Pathology

1. Standardized procedures and criteria in the study of the chronic stages in both African and American Trypanosomiasis.

2. Attention to the possible role of antigen-antibody reaction in pathogenesis.

3. Further studies on the pathogenesis of cardiac lesions in both diseases.

4. Further studies of the extra-cardiac manifestation.

5. Wider attention to the congenital disease.

IV. Immunology

1. Refined definition of antigenic types and production of homologous antisera.

2. Further investigation of antigenic variation.

3. Search for trypanosomal antigens and antigen antibody complexes in the mammalian host.

4. Isolation of different antigensand their correlation with immunoglobulin classes.

5. Studies on IgM levels and mechanisms of synthesis.

6. Standardization of serological tests and extension of their use.

7. Establishment of banks for the preservation of stabilates to be used as antigens, and antisera for reference.

The manner in which the WHO and/or PAHO may assist in the pursuit of these desired programs will be more specifically spelled out in the report of the group. It was the feeling of the group that another such meeting would be desirable and might profitably be held after an interval of about 3 years.

APPENDIX A

SCIENTIFIC GROUP ON COMPARATIVE STUDIES OF AMERICAN AND AFRICAN TRYPANOSOMIASIS

Washington 11-15 December 1967

MEMBERS

Professor E. Bertrand, Professeur Agrege a la Faculte de Medecine d' Abidjan, Service de Pathologie medicale, Abidjan, Cote d' Ivoire

Mr M.P. Cunningham, Project Manager, UNDP/SF Tick-Borne Diseases Project, East African Veterinary Research Organization, Kabete, Kenya

Professor R. Geigy, Director, Swiss Tropical Institute, Basle, Switzerland

Dr. P.C. Goble, Director of Chemotherapy, CIBA Pharmaceutical Co., Summit, New Jersey, United States of America (Chairman)

Dr. C. Greenblatt, Acting Chief, Section on Cell Biology, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, United States of America

Dr. M.P. Hutchinson, Senior Assistant, Wellcome Museum of Medical Science, London, United Kingdom (Rapporteur)

Professor W.E. Kershaw, Department of Biology, University of Salford, Salford, Lancashire, and Chairman, Trypanosomiasis Advisory Panel, Ministry of Overseas Development, London, United Kingdom

Dr. F. Koberle, Head, Department of Pathology, Faculdade de Medicina, Universidade de Sao Paulo, Ribeirao Preto, Brazil

Dr. W.H.R. Lumsden, Head, Protozoology Research Unit, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, United Kingdom

Dr. G.A. Maekelt, Institute of Tropical Medicine, Central University of Venezuela, Caracas, Venezuela

Dr. A.S. Parodi, Professor of Microbiology and Parasitology, Faculty of Medicine, Buenos Aires, Argentina

Dr. J.J. Puigbo, Department of Clinical Cardiology, University of Caracas, Caracas, Venezuela

Mr. M. Steinert, Chef de Travaux, Faculte des Sciences, Universite de Bruxelles, Bruxelles, Belgique

Dr. A. Trejos, Chief, Laboratory Department, Pan American Zoonoses Center, Buenos Aires, Argentina

Dr. M.A. Vaucel, Directeur general honoraire des Instituts Pasteur Outre-Mer, Paris, France

Dr. R. Zeledon, Professor, Department of Parasitology, University of Costa Rica, San Jose, Costa Rica (Vice-Chairman)

ADVISORS

Dr. Z. Brener, Laboratory of Chagas Disease, Instituto Nacional de Endemias Rurais, Belo Horizonte, Brazil

Dr. J.H. Edgcomb, Pathologist, Gorgas Memorial Laboratory, Balboa Heights, Panama

Dr. C.M. Johnson, Chief, Clinical Investigation and Experimental Pathology, Gorgas Memorial Laboratory, Balboa Heights, Panama

Dr. H. Muhlpfordt, Department of Protozoology, Tropical Institute, Hamburg, Germany

Dr. B.C. Newton, Sub-Department of Chemical Microbiology, Department of Biochemistry, University of Cambridge, Cambridge, United Kingdom

Dr. E.H. Sadun, Assistant Director, Walter Reed Army Institute of Research, and Chief, Department of Medical Zoology, Washington, D.C., United States of America

WHO PERSONNEL

Dr. N. Ansari, Chief, Parasitic Diseases, Division of Communicable Diseases, World Health Organization, Geneva, Switzerland (Co-Secretary)

Dr. Z. Fejfar, Chief, Cardiovascular Diseases, WHO

Dr. L.J. Olivier, Parasitic Diseases Adviser, Pan American Health Organization, Washington, D.C., United States of America (Co-Secretary)

Dr. D.S. Rowe, Director, WHO Immunoglobulins Reference Laboratory, Lausanne, Switzerland

Dr. F. Tross, Regional Adviser on Communicable Diseases, WHO Regional Office for Africa, Brazzaville, Republic of the Congo

Dr. K.C. Willett, Project Manager, WHO/UNDP Trypanosomiasis Project, Kabete, Kenya

APPENDIX B

SCIENTIFIC GROUP ON COMPARATIVE STUDIES OF AMERICAN AND AFRICAN TRYPANOSOMIASIS

Washington, 11-15 December 1967

DRAFT AGENDA

1. PARASITES

1.1 The nature of morphologic and biologic variations between "species" and "strains" of pathogenic trypanosomes (e.g. between different strains of Trypanosoma cruzi and "T. cruzi-like" organisms on the one hand and T. brucei, T. gambiense and T. rhodesiense on the other)

1.2 Patterns of parasitaemia and their relationship to other characteristics of strains, to antigenicity, to size of inoculum and to presence of humoral antibodies

1.3 The significance and possible cause of polymorphism in the two types of trypanosomes, and their metacyclic forms

1.4 Comparative studies of ultra structures

1.5 Comparative physiology, metabolism and biochemistry of the parasites

1.6 Variations in infectivity and pathogenicity in prolonged blood passage of trypanosomes

1.7 Penetrative power of trypanosomes and their metacyclic forms

2. PATHOLOGY

2.1 Distribution of organisms in the tissue of the host during the course of the infection (organotropism)

2.2 The causation and importance of cardiac lesions in both forms of trypanosomiasis in the acute and chronic stage of the infection

2.3 The causation and importance of nervous lesions in both forms of trypanosomiasis in the acute and chronic stage of the infection

2.4 The possible importance of antigen-antibody reactions as a pathogenic factor in trypanosomiasis

2.5 Relationship between "strains" or "Species" and clinical manifestations of the disease

2.6 How much is there in common between the "chagoma" and the "trypanosome" chancre?

2.7 Congenital trypanosomiasis (mechanisms of transmission and recognition)

3. EPIDEMIOLOGY

3.1 Reservoir hosts (sylvatic, peridomestic, domestic)

3.2 Effect of the man-vector contact (effect of super-infection)

3.3 Human habits and environmental factors

4. COMPARATIVE CHEMOTHERAPY

4.1 Drugs sensitivity and resistance of trypanosomes

4.2 Mechanism of action of chemotherapeutic drugs in trypanosomes

5. PROBLEMS IN PARASITOLOGICAL DIAGNOSIS

5.1 Recognition of low parasitaemia (concentration techniques for blood trypanosomes)

5.2 Trypanosome isolation techniques (culture, inoculation, xeno-diagnosis)

6. IMMUNOLOGY

6.1 Antigenic variation (so far not demonstrated in T. cruzi) - and its relation to polymorphism

6.2 Active immunization with dead and living vaccines

6.3 Serological diagnosis in the host; type and species differentiation and recognition of low antibody concentrations

6.4 Humoral manifestations (IgM, heterophile antibodies, etc.)

6.5 Chemical composition and antigenicity (sensitivity and specificity of antigens); purification and preparation of antigen

7. METHODS

7.1 Patterns for determination of virulence (penetrative power, infectivity)

7.2 Preservation and maintenance of trypanosomes (in vitro, in vivo maintenance, deep freezing, etc.)