



REPORT OF THE WHO WORKING GROUP MEETING ON ECHINOCOCCOSIS RESEARCH

Zurich, 18 August 1990

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INTRODUCTION

Dr T. Fujikura, Veterinary Public Health, Division of Communicable Diseases, welcomed the participants (Annex I) and opened the meeting on behalf of Dr H. Nakajima, Director-General of the World Health Organization. He recalled the background and aims of the meeting as reflected by the Agenda (Annex II). Dr Fujikura briefly spoke about the value of the WHO Guidelines on Surveillance, Prevention and Control of Echinococcosis (VPH/81.28, Rev.1). They have been translated into several languages and many requests for the Guidelines have been received by WHO. Dr Fujikura considered there was a need to revise and update the Guidelines.

Dr P. Schantz was elected Chairman, Professor J. Eckert, Vice Chairman and Professor R. C. A. Thompson, Rapporteur.

1. REPORT ON WORKING GROUP ACTIVITIES IN 1989-1990

The activities of the various Working Groups were summarized by the respective Chairmen (see list in Annex III). See also Annex IV.

The following specific points and recommendations arose from discussions of the Working Group activities.

1.1 It was proposed that each Working Group should develop its rules for co-authorship of collaborative research. The participants agreed that any potential problems should be identified and solutions be found when a collaborative project is started.

1.2 Professor Pawlowski suggested that Professor Thompson, as Chairman of the Working Group on Biology and Strain Variation, should develop a protocol for the identification of strains of Echinococcus from human infections to ensure uniform examinations. The protocol should include the size and nature of sample, subsequent processing and transportation. Initially, WHO would select endemic areas in 5-7 countries for this work.

1.3 Participants emphasized the need for more international cooperation, particularly on research projects associated with control programmes in South America. WHO was asked to follow up contacts and obtain more information. Cooperation of the zoonoses centres in the Mediterranean and South American areas should be encouraged.

1.4 The need for financial support from WHO for echinococcosis research was discussed. In order to improve this situation, it was decided that Dr Gemmell should draft a document to provide some background data on the status and importance of echinococcosis to be sent to all countries where echinococcosis

was perceived to present a problem including China, Germany, France, Switzerland, Japan, USSR, Uruguay, Kenya and Tunisia. By raising awareness in this way, endemic countries will be in a better position to decide on funding priorities at the World Health Assembly. A second letter, also to be drafted by Dr Gemmell, would be sent to countries without an echinococcosis problem, to solicit their support for research on the disease in the endemic areas.

1.5 In relation to 1.4, the meeting supported the suggestion that an expert in the field of echinococcosis be specifically employed to lobby the appropriate personnel in endemic countries. In such a way, a better awareness of the echinococcosis problem would be created. The Chairman, Dr Schantz, agreed to investigate this proposal initially, and how it could be funded.

1.6 Participants at the meeting were pleased to learn of the initiative of the group at the University of Cambridge (Drs Gemmell and Soulsby) who were planning a course in mathematical modelling.

1.7 As an example of the effectiveness of international working groups, Dr Schantz reported on the rapid progress being made on the development of coproantigens for immunodiagnosis.

1.8 A major task of the immunology working group is research on vaccines against taeniid parasites in the intermediate host. Although a vaccine against Taenia ovis has been developed by the research group at Melbourne University, with support from a commercial company, Professor Rickard had been unable to attract commercial support for the development of an echinococcosis vaccine. Participants agreed that the highly successful research on cestode vaccines by the Melbourne group should continue and that the Chairman, Dr Schantz, should write a letter to the Australian Government body, ACIAR, stressing the value of such research to controlling echinococcosis in countries where there is a major problem, e.g. China.

1.9 The chemotherapy working group has asked WHO, in a letter addressed to Dr Torrigiani, Director, Division of Communicable Diseases, to establish a new "Steering Committee" with the main aim to develop new drugs against human echinococcosis.

2. REVISION OF WHO GUIDELINES ON SURVEILLANCE, PREVENTION AND CONTROL OF ECHINOCOCCOSIS (VPH/81.28, REV.1)

2.1 Participants agreed that the Guidelines had proved useful and that their revision was justified.

2.2 It was decided that revision would necessitate complete re-writing of the Guidelines.

2.3 The meeting agreed on the basic format and content of the new Guidelines (Annex V).

2.4 Before proceeding any further with the new Guidelines, however, a formal response was requested from WHO concerning its level of interest and support. In light of this response, consideration would be given as to how the new Guidelines would be prepared.

3. PROPOSALS FOR ELABORATION OF NEW MANUALS OF PROTOCOLS FOR TREATMENT AND CARE OF ECHINOCOCCOSIS PATIENTS

3.1 Participants supported the need for new protocols and agreed that priority should be given to: (i) early diagnosis and treatment, and (ii) strain identification of Echinococcus from human patients.

3.2 It was noted that any future protocols for safety procedures should include reference to the new rodent model for adult Echinococcus developed by Professor Kamiya's group in Hokkaido.

4. WORK PLANS

4.1 The meeting agreed that future activities should proceed as outlined in the working group reports (Annex IV), but were aware that some activities may not be possible without additional funding.

5. CONCLUSIONS AND RECOMMENDATIONS

In considering progress and future research, participants supported the overview presented in document VPH/ECH.RES/WP/90.10 "Present situation and recommendations for future WHO activities for echinococcosis research", prepared by the Chairman of the Coordinating Group, Professor Eckert. The Chairman, Dr Schantz, said he was impressed and pleased that so much progress had been made in spite of the constant lack of financial support. The participants agreed that many benefits had accrued from the activities of the working groups, but expressed concern about the future of such activities. In closing, Dr Fujikura said he hoped that the collaboration would continue in spite of financial difficulties, and thanked all concerned.

Dr Schantz thanked Professor Eckert for hosting the meeting and for his hospitality.

ANNEX I

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ANNEX II

AGENDA

1. Report on working group activities in 1989
 - 1.1 Recent progress in research on echinococcosis
 - 1.2 Recent epidemiology
 - 1.3 International cooperation
 - 1.4 Proposed activities

2. Revision of WHO Guidelines on Surveillance, Prevention and Control of Echinococcosis (VPH/81.28, Rev.1)
 - 2.1 Proposed sections, chapters and annexes for revision
 - 2.2 Proposed authors for the revisions
 - 2.3 Administrative arrangements and implementation of the revisions
 - 2.4 Financial matters

3. Proposals for elaboration of new manuals of protocols for treatment and care of echinococcosis patients
 - 3.1 Lay-out of Manual
 - 3.2 Proposed authors
 - 3.3 Administrative arrangements
 - 3.4 Time schedule
 - 3.5 Financial matters

4. Work plans
 - 4.1 Working group activities
 - 4.2 Meetings and training courses
 - 4.3 International cooperation

5. Conclusions and recommendations

ANNEX III

LIST OF WORKING DOCUMENTS

- VPH/ECH.RES/WP/90.0 Purpose and Scope
- VPH/ECH.RES/WP/90.1 Proposed Agenda
- VPH/ECH.RES/WP/90.2 List of Participants
- VPH/ECH.RES/WP/90.3 Proposed revision of FAO/UNEP/WHO Guidelines for surveillance, prevention and control of echinococcosis/hydatidosis (VPH/81.28, 1981) by Dr M.A. Gemmell, Cambridge, UK
- VPH/ECH.RES/WP/90.4 Proposed contents and authors of a new edition of FAO/UNDP/WHO Guidelines for surveillance, prevention and control of echinococcosis/hydatidosis (VPH/81.28, 1981) by Professor J. Eckert, Zurich, Switzerland
- VPH/ECH.RES/WP/90.5 Comments on revision of the FAO/UNEP/WHO Guidelines for surveillance, prevention and control of echinococcosis/hydatidosis (VPH/81.28, 1981) by Professor Z.S. Pawlowski, Poznan, Poland
- VPH/ECH.RES/WP/90.6 Report on Activities of Working Group on Echinococcosis: biology and strain variation by Dr R.C.A. Thompson, Murdoch, Western Australia (Chairman)
- VPH/ECH.RES/WP/90.7 Report on Activities of Working Group on Epidemiology and Control in Echinococcosis Research by Dr M.A. Gemmell, Cambridge, UK (Chairman)

- VPH/ECH.RES/WP/90.8 Report on Activities of Working Group on Immunology in Echinococcosis research, and Proposals for New Vaccine development by Professor M.D. Rickard, Parkville, Australia (Chairman)
- VPH/ECH.RES/WP/90.9 Report on Activities of Working Group on Medical Aspects in Echinococcosis Research, and Planned Activities by Professor Z.S. Pawlowski, Poznan, Poland (Chairman)
- VPH/ECH.RES/WP/90.10 Present situation and recommendations for future WHO activities for echinococcosis research by Professor J. Eckert, Zurich, Switzerland
- VPH/ECH.RES/WP/90.11 Report on WHO Working Groups on Echinococcosis (Activities 1988-1990 and Plan of Work 1990-1992) by Professor J. Eckert, Institute of Parasitology, University of Zurich, Zurich, Switzerland
- VPH/ECH.RES/WP/90.12 Report on Activities of Working Group on Echinococcosis: Immunodiagnosis by Dr B. Gottstein, Zurich, Switzerland (Chairman)

ANNEX IV

SUMMARY OF MAJOR WORKING GROUP ACTIVITIES (1989-1990)

Diagnostic antigens and vaccine development

1. The Em2-ELISA has been established as a WHO reference technique for immunodiagnosis of alveolar echinococcosis (AE) (Echinococcus multilocularis infections). Three positive reference standard sera (A, B, and C) have been created in collaborative work between multiple institutes. They are presently available on request for performing standardized Em2-ELISA within the scope of sero-epidemiological studies.

A new recombinant E. multilocularis antigen (antigen II/3-10) has preliminarily proved its suitability in detecting active cases of AE, thus providing potentially additional information to the Em2-antigen on the biology of the parasite lesions.

A monoclonal antibody (G11) has been raised against the Em2-antigen, resulting (a) in an easy producibility of large quantities of Em2-antigen, and (b) in the immunochemical characterization of the antigen. The G11 MAb was employed to establish a sandwich-ELISA for the easy diagnostic determination of E. multilocularis larval material.

An E. multilocularis DNA-probe has been further developed for the diagnostic identification and characterization of Echinococcus and Taenia spp. by the polymerase chain reaction (PCR).

2. A recombinant E. granulosus antigen has been tested in ELISA for diagnosis of E. granulosus in dogs. The antigen is specific for E. granulosus; however, its sensitivity for detecting specific antibody in infected dogs (20%) is not high enough for practical application. Several cDNA clones expressing E. granulosus antigens in E. coli have been selected and tested for diagnosis of human cystic hydatidosis. The clones show high sensitivity for diagnosis of E. granulosus infection; however, they are not species-specific and cross react with antibodies in the sera of patients with alveolar hydatidosis and cysticercosis.

The E. granulosus cDNA library will be screened for clones expressing oncosphere antigens and the recombinant proteins tested in vaccination trials in sheep against infection with E. granulosus. Additional antigens for diagnosis of E. granulosus in dogs will be sought from the protoscolex cDNA library. They will be tested in ELISA in combination with the antigen mentioned above, in an attempt to improve the sensitivity of the assay for diagnosis of E. granulosus in naturally infected dogs. Cloned antigens expressing E. granulosus species-specific epitopes will be sought from the protoscolex cDNA library in order to develop a specific test for serological diagnosis of cystic hydatidosis.

Animal model

The complete life cycle of E. multilocularis has been established in cricetid rodents alone. Alternative definitive hosts of E. multilocularis have also been tried in heteromid rodents (obtained from New Mexico). Severe combined immunodeficient (SCID) mice are being tried out as alternative hosts for E. granulosus, Taenia saginata, etc., by transplantation of lymphocytes from homologous definitive hosts. Experiments are in progress to study the immuno-explulsion of E. multilocularis after challenge infection in inbred golden hamsters.

Assessment was made of the use of the adjuvant muramyl dipeptide in a vaccination trial against E. multilocularis in experimental models and in natural definitive hosts (e.g. dogs and cats) after clarification of the role of those in the transmission of E. multilocularis in the endemic area of eastern Hokkaido, Japan.

ANNEX V

PROPOSED CONTENTS AND AUTHORS OF A NEW EDITION OF
ECHINOCOCCOSIS GUIDELINES

1. Preface
 - 1.1 General background
 - 1.2 Objectives of the guidelines
 - 1.3 Definitions and glossary

2. Parasites and life cycles (Thompson)
 - 2.1 General morphology
 - 2.2 General life cycle
 - 2.3 Species of the genus Echinococcus species

3. Geographical distribution of species and strains and prevalence in man and animals
 - 3.1 North, Central and South America (Schantz)
 - 3.2 Europe (except European USSR) (Eckert)
 - 3.3 USSR (Podoprigora)
 - 3.4 Asia
 - 3.4.1 Near East/Eastern Mediterranean
 - 3.4.2 Indian Subcontinent (Pathak)
 - 3.4.3 China (Umel)
 - 3.4.4 Japan and other Asian countries (Takahishi)
 - 3.5 Australia and New Zealand (Gemmell)

- 3.6 Pacific Region
- 3.7 Africa
 - 3.7.1 North Africa (Dakkak)
 - 3.7.2 Central and South Africa (Macpherson)

- 4. General Epidemiology
 - 4.1 E. granulosis (Gemmell)
 - 4.1.1 Sources of infection
 - 4.1.2 Resistance, dispersal and transmission of eggs
 - 4.1.3 The larval parasites within the hosts
 - 4.1.4 Parasite stability and its impact for control
 - 4.2 E. multilocularis, E. vogeli and E. oligarthrus (Rausch)
 - 4.2.1 Etc. See 4.1

- 5. Surveys and Surveillance (including seroepidemiology)
 - 5.1 Human populations (Pawlowski, Schantz, Gottstein)
 - 5.2 Animal populations (Soulsby, Gemmell)

- 6. Control and Prevention
 - 6.1 Established control strategies (Gemmell)
 - 6.2 Developing technologies (Rickard)
 - 6.3 Prevention
 - 6.4 Safety precautions (several authors)

7. Clinical Aspects, Diagnosis and Treatment
 - 7.1 Animals (Jenkins)
 - 7.2 Humans (Pawlowski)
 - 7.3 Immunodiagnosis (Gottstein and Schantz)
 - 7.4 Parasitological and clinical diagnosis in man (Vuitton, Ammann)
 - 7.5 Parasitological and clinical diagnosis in animals (Eckert, Gemmell)

8. Economic Implications and Cost Benefits of Control

ANNEX VI

LIST OF WHO WORKING GROUPS ON ECHINOCOCCOSIS RESEARCH

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