



REPORT OF WHO WORKING GROUP MEETING ON ECHINOCOCCOSIS  
 RESEARCH AND CONTROL

Beijing, China, 12 October 1993

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## INTRODUCTION

Dr T. Fujikura, Veterinary Public Health, World Health Organization, welcomed the participants (Annex I) and thanked the organizing committee of the 16th International Congress of Hydatidology and the Ministry of Public Health, Beijing, for the excellent arrangements made for the WHO working group meeting. He opened the meeting on behalf of the Director-General of WHO and explained its purpose and scope:

- to review working group activities with special reference to medical aspects and chemotherapy of echinococcosis;
- to discuss surveillance, epidemiology and control of echinococcosis worldwide and promotion of international cooperation;
- to review recent developments in research on immunization against E. granulosus in sheep; and
- to make work plans for 1994-1995.

After addressing the participants as Chairman of the Coordinating Group of the WHO echinococcosis working groups, Professor Eckert was elected Chairman, Professor Z.S. Pawlowski Vice-Chairman, and Professor P.S. Craig served as Rapporteur.

## 1. MEDICAL ASPECTS AND CHEMOTHERAPY IN ECHINOCOCCOSIS TREATMENT

The length and persistence of clinical manifestations, including suffering in many echinococcosis patients require that earlier diagnostic tools, better chemotherapy, safer surgery for re-section of liver cysts and more effective rehabilitation techniques be developed. Social and economic assurance of patients under medical care and welfare also need further development in affected countries.

Views on early diagnosis were expressed by the medical workers and scientists at the meeting based on serological reactions, clinical symptoms, community surveillance and diagnosis in endemic areas, initial optimum timing for starting chemotherapy, surgery as well as their effectiveness and related economical aspects according to their own experience. Some constructive proposals were made by Chinese physicians based on experience in endemic areas of Western China. Medical ethics were also discussed, since present diagnostic methods, including application of sonographic analysis and locally-developed serological diagnosis are not as yet fully defined for accuracy and specificity, especially when one or several such methods were used in populations at risk. Many opinions were expressed, including on the adverse effects of a certain chemotherapeutic agent inducing immunosuppression in treated patients. The discussions were, however, inconclusive and the group will continue research in this area taking into account experience gained on a wide scale in endemic countries such as China, in line with the content of the report made in Besançon, October 1992 (document WHO/CDS/VPH/93.118). Initiatives by WHO would be vital in promoting medical and chemotherapeutic aspects of echinococcosis.

## 2. SURVEILLANCE AND MONITORING FOR ECHINOCOCCOSIS CONTROL

With regard to echinococcosis surveillance and epidemiology, the group urged establishment of human and animal case definition, including serological diagnosis, clinical manifestations, sonographic examination, slaughterhouse observation, dog faecal samples and some others, since the

basis of surveillance data is not always clear (e.g. size of sample, differentiation between E. granulosus and E. multilocularis). These efforts may improve analysis of epidemiological data obtained from different endemic areas on a common basis.

A participant from China reported significant progress in echinococcosis control in his country since creation of the National Hydatid Disease Control Centre (NHDCC) at Urumqi, Xinjiang Province in 1988. The Centre recorded 26 065 cases of human echinococcosis with surgery only in the last four decades in six highly endemic provinces. Major control measures since 1988 have been (1) improved slaughterhouse inspection and waste management, including proper disposal of condemned organs to break down the transmission cycle to dogs; and (2) systematic de-worming of infected dogs by arecoline. It is thought that these two simple measures have reduced dog infection ratios from 30% before 1988 to 10.4% in 1989 and 0.7% in 1991, thus also reducing the potential sources of infection in humans. Locally-based government public education campaigns have increased people's awareness of the risks to 95-98% of persons interviewed.

The above achievements in China illustrate that control of echinococcosis is attainable through campaigns based on local as well as central government using the NHDCC's research results on serological diagnosis, epidemiology, clinical medicine and training of professionals engaged in the campaigns. Following the campaign in China it is, however, too early to observe a significant reduction in human cases. The government is continuing and extending the control programme and appreciates the cooperation with scientists from other countries, for example, the USA and the UK, as well as with international organizations such as WHO. The government greatly hopes that this cooperation can be strengthened even further.

### 3. RECENT PROGRESS IN RESEARCH ON IMMUNIZATION AGAINST E. granulosus INFECTION IN SHEEP

The report from the working group on immunology centred on the recently reported joint Australian/New Zealand team development of a candidate recombinant vaccine (oncosphere antigen) against E. granulosus infection in sheep, which in two independent experiments protected about 97% of sheep against cyst formation after challenge infection (Table 1). Studies by the group will continue to define optimal conditions of vaccine production, application and field trials.

Table 1. Results of experiments with recombinant oncosphere antigen to vaccinate sheep against infection with E. granulosus eggs

	Number of Sheep	Number of cysts		Protection
		Mean	Range	
<u>TRIAL 1</u>				
Vaccinates	10	5.4	0 - 16	96%
Controls	8	156.6	70 - 270	
<u>TRIAL 2</u>				
Vaccinates	5	8.4	0 - 22	97%
Controls	5	256	32 - 445	

#### 4. CONCLUSIONS AND WORK PLANS FOR 1994-1995

The meeting agreed on the urgent need to improve medical care and chemotherapy for echinococcosis patients under the conditions prevailing in most endemic countries, particularly in the developing world.

As highest priority the group would like to further strengthen international cooperation in research, exchange of information and the necessary systematic ground work. In this context, WHO is requested to further assist the working group to promote collaborative research on methods for effective and efficient medical and chemotherapeutic treatment of echinococcosis as well as applicability of these regimens under different socioeconomic conditions.

#### 5. RECOMMENDATIONS

1. The group confirmed that significant progress has been made in echinococcosis research but that collaborative research should be continued and further developed on the following topics:

##### Clinical medicine and chemotherapy

- (1) The use of albendazole and praziquantel in combination as well as the combined application of albendazole and cimetidine.
- (2) Assessment of a liposome formulation of these drugs.
- (3) Delineation of the patient's immune status prior to chemotherapy, and in relation to follow-up and subsequent evaluation.
- (4) Development of guidelines on ethical considerations for the use of anti-echinococcus drugs as well as availability in endemic areas.
- (5) Definition of roles and application of pre-surgical chemotherapy.
- (6) Identification of problems in liver transplantation for alveolar echinococcosis treatment.

##### Surveillance and epidemiology

- (1) Consideration of human populations at risk.
- (2) Use of ultrasound and its application to screening patients in human populations at risk.
- (3) Assessment of serological tests in conjunction with ultrasound examination.
- (4) Assessment of the efficacy of available techniques for diagnosing echinococcus patients including ultrasound, X-ray and serological tests.
- (5) Proper characterization of age and origin of major livestock animal hosts at slaughter.
- (6) Improvement of immunodiagnostic techniques such as coproantigen detection techniques available for canine echinococcosis.

### Biology and immunology

(1) Improvement of strain identification and characterization by morphological and molecular techniques applicable in control programmes.

(2) Promotion of further research on immunoprophylaxis with special reference to oncosphere recombinant antigen for immunization of the intermediate host including, eventually, man.

(3) Establishment of international centres for provision of reference materials including monoclonal antibodies, DNA probe and other materials.

2. Further research in clinical medicine and chemotherapy is urged for the treatment of echinococcosis patients by collecting recent information from endemic countries. The group agreed to undertake such data collection. WHO was asked to convene working group meetings to discuss and elaborate protocols for the treatment of echinococcosis patients throughout all the phases of infection and possible effective combination with other regimens and treatment. In this context, WHO was asked to prepare an international meeting.

3. The Guidelines for Surveillance, Control and Diagnosis of Echinococcosis now in preparation should cover the major points which the group thinks necessary to update and recommend the application of efficient/effective methods of treatment and chemotherapy for echinococcosis patients.

4. The group recommended further close collaboration between international organizations involved in controlling echinococcosis. WHO, FAO, UNEP, OIE and any other bodies including the International Association of Hydatidology should cooperate and promote echinococcosis control worldwide.

### ACKNOWLEDGEMENTS

The group wishes to thank most sincerely Dr Feng Cheng, Institute of Parasitic Diseases, Wuhan, Hubei, People's Republic of China, as well as staff of the Ministry of Public Health, Beijing, for their excellent audiovisual facilities throughout the meeting.

ANNEX I

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## ANNEX II

### REVIEW OF WHO ACTIVITIES IN ECHINOCOCCOSIS RESEARCH AND CONTROL

The Veterinary Public Health unit in WHO has been developing activities in close collaboration with leading experts in this field all over the world for many years. In the last decade, a series of meetings and missions for technical cooperation to endemic countries have been implemented. Three WHO Collaborating Centres for Research, Control and Training (in Cambridge, UK; Zurich, Switzerland; and Murdoch, Western Australia) have been established and also play a vital role in provision of reference materials, epidemiological information support, training and education of scientists and consultative assistance to endemic countries.

The unit published in 1981 the "WHO/FAO/UNEP Guidelines on Surveillance, Prevention and Control of Echinococcosis/Hydatidosis". A revised version was also issued in 1983 and distributed worldwide to facilitate surveillance, diagnosis and control of the diseases as well as training and education in endemic countries.

WHO-coordinated working groups cooperate actively with WHO in seven sub-groups: biology and strain variation, epidemiology and information support, immunodiagnosis, immunology, chemotherapy, medical aspects, and an overall coordinating group. Initiatives are taken by the respective group Chairmen, in collaboration with members of each group, and activities implemented in close cooperation with WHO. A series of meetings have been held in recent years, including:

- (1) Discussions on the ecology of Echinococcus multilocularis, Zurich, April 1987. This meeting was the first to assess the epidemiological situation with special attention to eco-epidemiology and recommended the formulation of projects on surveillance, prevention and control of alveolar echinococcosis, including population biology of the final host, development of new immunodiagnostic methods, and some others. It was also at this meeting that the present WHO-coordinated working groups were formulated.
- (2) WHO Consultation on research requirements for echinococcosis/hydatidosis, Montreal, August 1987. This meeting was held to discuss research requirements based on data collected through a questionnaire addressed to all working group members. Precise projects were discussed and recommended in priority order of research areas: parasite biology, host-parasite relationship, immunology, epidemiology, chemotherapy, control measures and some others. A number of the projects discussed in Montreal are still in progress now.
- (3) WHO Consultation on the ecology of Echinococcus multilocularis, Geneva, November 1987. The participants at this meeting went into deeper technical discussion of the epidemiology, surveillance, eco-epidemiological studies, disease transmission and assessment of E. multilocularis infection, with special emphasis on immunological techniques and serological survey/medical ethics in human populations.
- (4) WHO Consultation on E. multilocularis research, Zurich, June 1988. Discussions took place on the framework and responsibilities of the group's collaborative studies, and work plans. The group elaborated two working guidelines, namely: (1) guidelines for eco-epidemiological studies on

E. multilocularis infection, and (2) guidelines for Em2 enzyme immunosorbent assay (Em2-ELISA) for diagnosis of E. multilocularis infection. These guidelines facilitated further research and investigations of the group.

(5) WHO Meeting on working groups on echinococcosis research, Geneva, September 1988. The different groups exchanged research information and discussed possible mutual cooperation through their respective research areas. The report annexed each group's terms of reference and full addresses of all group members to facilitate further cooperation.

(6) WHO Consultation on alveolar echinococcosis, Hohenheim, Germany, August 1989. Working group members and other specially invited experts discussed the global situation in epidemiology, key factors of E. multilocularis transmission, diagnosis, pathogenesis, treatment (surgery/chemotherapy), methods of food decontamination of alveolar echinococcus. The participants elaborated (1) biosafety guidelines for laboratory and field examination of echinococcus infection, and (2) a specimen statement on alveolar echinococcosis addressed to health personnel and the general public in endemic countries.

(7) WHO working group meeting on echinococcosis research, Zurich, August 1990. The meeting proposed revision of the WHO/FAO/UNEP Guidelines on Surveillance, Prevention and Control of Echinococcosis (document VPH/81.28, Rev.1), with a new list of contents and authors. Proposals for the elaboration of new manuals/protocols for treatment and care of echinococcosis patients were also discussed, as well as work plans for elaboration of new Guidelines and the financial needs of working group activities.

(8) WHO editorial group on echinococcosis guidelines, Rome, November 1991. The group reviewed the draft guidelines prepared by the WHO secretariat based on the recommended contents and candidate contributors. The group urged further revisions and improvements to this draft, with a new revised list of contents and a number of additional contributors. WHO was asked to take prompt action in line with the new editorial policies; FAO and OIE representative expressed their interest in joining elaboration of the new guidelines. The participants also discussed the draft "Planning echinococcosis/hydatidosis control: methodological approach" prepared by the WHO/FAO Collaborating Centre for Research and Training in Veterinary Public Health, Rome, and recommended its publication.

As a result of the Rome meeting, the WHO secretariat produced a second draft version of the Guidelines and distributed it as a WHO document "Version 1992" to all the contributors and persons/offices concerned for further comments.

In March 1993, some editorial members met in Geneva and the WHO secretariat is now finalizing an updated and shortened version of the 1992 draft.

(9) WHO working group meeting on clinical medicine and chemotherapy of alveolar and cystic echinococcosis, Besançon, France, October 1992. The group discussed indications for chemotherapy, selection of drugs, dosage and duration of chemotherapy, monitoring patients and alternative treatment. Discussions also extended to the value of screening, and prevention of echinococcosis, but further collaboration would be necessary in this area and the next working group meeting in Beijing should focus on clinical medicine and chemotherapy.

(10) A VPH information circular, "Reports of Veterinary Public Health Working Groups" provides annual activity reports since 1990 from about 40 working groups in the various VPH fields of activity, including echinococcosis. The different sub-groups activities are highlighted in this circular.

The working groups have already developed Em2-ELISA as a routine method for immunodiagnosis in alveolar echinococcosis to detect infection at the earliest stage, before clinical symptoms emerge; have progressed in vaccine development with a molecular biology technology; have given new insight into epidemiology, with particular relation to eco-epidemiology of the intermediate and final hosts involved in the contamination of nature close to human populations; have progressed in chemotherapy and clinical medicine for treatment of patients; and contributed in many other surveillance and research areas for echinococcosis control. All these developments have been achieved in the spirit of international cooperation. However, further efforts and challenge must be made in order to control and even eradicate echinococcosis from many endemic countries and international cooperation has still to play an active responsible role to achieve this final goal. WHO calls on the groups to continue their valuable collaboratoin in this context.

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