

I. Background

The tropical diseases are a group of infectious diseases which primarily affect the poorest sectors of a society in tropical and subtropical areas especially the populations living in remotes and disadvantage regions in the developing countries. More than one billion people in the world suffer from neglected tropical diseases (NTDs), but these diseases are characterized by little attention from policy-maker, lack of priority within health strategy, inadequate research, limited resources allocation and few interventions, in which cestode zoonoses are just the examples. In comparison with other NTDs such as schistosomiasis and malaria, cestode zoonoses are emerging, re-emerging or spreading but still far neglected infectious diseases and do cause serious public health problems in the Asia and the Pacific region. It is urgent to apply modern tools to obtain scientific evidence on the parasite species, strains or isolates as well as confirmation of the diseases themselves, to further understand epidemiology and transmission, and to consider optimal opportunities and strategy for control. International collaborations are increasingly required to study those features and to improve diagnosis, treatment and control. This symposium, joint-proposed and co-organized by the National Institute of Parasitic Diseases, China CDC, PR China and Asahikawa Medical University, Japan, bring together scientists in research, public health and health policy to explore a new collaborative mechanism for effective control of tropical diseases with focus on cestode zoonoses. Historically, this symposium is the third one held in China. The first one was held in Chengdu in 2000 when the late Dr. C. Urbani from WHO (WPRO) joined us (Ito et al. *Acta Tropica* 2003, 86, 3-17) and the second one was in 2006 in Chengdu (Craig et al. *Emerg Infect Dis* 2008, 14,1674-1675).

II. General Objectives

The purpose of this symposium is to share and exchange latest knowledge and experience on control, prevention of cestode zoonoses as well as basic research in cestode biology, and to discuss potential approaches towards forming an international collaborative network for control and study that will make great contribution to disease elimination eventually. Basic research is still very important for all of us to improve our skills and knowledge towards control of cestode zoonoses. Therefore, we have many basic scientific approaches such as molecular taxonomy or phylogeny on zoonotic cestodes in this symposium.

III. Specific objectives

- To overview the current epidemic situation of cestode zoonoses, the current national and international control strategy for these diseases including opportunity, challenge, feasibility, sustainability and technique demand.
- To assess prevailing strategies and novel approaches required to achieve good control from comprehensive view.
- To discuss how to conduct more effective international cooperation on cestode zoonoses control and research.
- To share the basic science and technology in cestode biology, immunology, molecular taxonomy and phylogeny which may give us new tools for better resolution for transmission ecology, epidemiology and control of cestode zoonoses.

IV. Expected outcome

- To make a critical assessment on the potential for cestode zoonoses control focusing on the regions where the populations are at risk for getting infections.
- To establish research and validation agenda on novel tools for study and control of the diseases.
- To develop a work-plan of action targeting interventions.

V. Organization Committee

Chairman:

Dr. Yang Wei-zhong, Deputy Director General, China CDC.

Vice Chairmen:

Dr. Zhou Xiao-nong, Director, National Institute of Parasitic Diseases, China CDC.
Dr. Akira Ito, Emeritus Professor, Visiting Professor, Asahikawa Medical University, Japan.

Members :

Dr Cao Jian-ping, Deputy Director, National Institute of Parasitic Diseases, China CDC.
Dr. Xiao Ning, Deputy Director, National Institute of Parasitic Diseases, China CDC.
Dr. Qiu Dong-chuan, Director, Institute of Parasitic Diseases, Sichuan CDC.

VI. Scientific Committee

Dr. Yang Wei-zhong, Deputy Director General, China CDC.
Dr. Akira Ito, Emeritus Professor, Visiting Professor, Asahikawa Medical University, Japan.
Dr. Zhou Xiao-nong, Director, National Institute of Parasitic Diseases, China CDC.
Dr. Philip S Craig, Professor, University of Salford, UK.
Dr. Patrick Giraudoux, Professor, University of Franche-Comté, France.
Dr. Qiu Dong-chuan, Director, Institute of Parasitic Diseases, Sichuan CDC.
Dr. Cao Jian-ping, Deputy Director, National Institute of Parasitic Diseases, China CDC.
Dr. Tang Lin-hua, Professor, National Institute of Parasitic Diseases, China CDC.
Dr. Hu Wei, Professor, Fudan University, Shanghai, China.
Dr. Xiao Ning, Deputy Director, Director, the National Institute of Parasitic Diseases, China CDC.
Dr. Munehiro Okamoto, Professor, Kyoto University, Inuyama, Japan.

Provisional Agenda

International Symposium on Cestode Zoonoses Control

Paradise Hotel, Shanghai, Oct. 29-30, 2012

28 October Activities

10:00-20:00 Arrival and Registration

Venue: Hotel Lobby

29 October Activities

08:30-09:00 Opening Ceremony

Venue: Reporting Hall

Welcome Remarks-Chairman: Dr. Zhou Xiaonong

Dr. Padmasiri Eswara Aratchige (WHO/WPRO)

Dr. Akira Ito (Asahikawa Medical University)

Dr Wang Liying (Ministry of Health, P.R. China)

9:00-10:30 Keynote Speeches: Current Regional Situation

Venue: Reporting Hall

Chairperson: Dr. Philip Craig and Dr. Xiao Ning

Investigation on the alveolar echinococcus species and their developments in Hulunbeier steppe pasture, Northeastern Inner Mongolia, China (Prof. Tang Chongti) **p12**

Research priority setting in WPRO Region – Neglected Tropical Diseases (Dr. Padmasiri Eswara Aratchige) **p13**

Prioritizing Research for one-health one-world with focus on cestode zoonoses (Dr. Zhou Xiaonong) **p15**

10:30-11:00 Group photo and Coffee Break

11:00-12:30 Plenary Session 1: Current Status of Cestode Zoonoses in Asia

Venue: Reporting Hall

Chairperson: Dr. Wen Hao and Dr. Akira Ito

International collaboration and cooperation towards control of cestode zoonoses in Asia (Dr. Akira Ito) **p18**

Echinococcosis in Asia - with focus on role of dogs(Dr. Philip Craig) **p19**

Echinococcosis management, networks and improvement in China(Dr. Wen Hao) **p20**

Genetic diversity of Echinococcus spp. in Russia (Dr. Sergey Konyaev) **p21**

12:30-13:30 Lunch Venue: Sunshine Western Restaurant (1F)

13:30-15:45 Plenary Session 2: Molecular taxonomy

Venue: Paradise Hall (2F)

Chairs: Dr. Zhu Huaimin and Dr. Don McManus

Current status of the genetics/molecular taxonomy of Echinococcus species(Dr. Don McManus) **p23**

Mitochondrial phylogeny of the genus Echinococcus (Cestoda: Taeniidae) with emphasis on relationships among Echinococcus canadensis genotypes(Dr. Minoru Nakao) **p24**

Immunoproteomic analysis of Echinococcus granulosus in screening and identification of antigenic proteins for serodiagnosis(Dr. Zhang Ting) **p25**

Molecular phylogeography of zoonotic Taeniid tapeworms(Dr. Tetsuya Yanagida) **p26**

What is Taenia asiatica?(Dr. Munehiro Okamoto) **p27**

15:45-16:00 Coffee Break

16:00-18:00 Plenary Session 3: Transmission and control

Venue: Paradise Hall (2F)

Panelist: Dr. Cao Jianping and Dr. Patrick Giraudoux

Assessment of novel health educational materials on raising compliance of Tibetan population against echinococcosis (Dr. Xiao Ning) **p29**

Spatial approach of Echinococcus multilocularis transmission ecology in continental Asia(Dr. Patrick Giraudoux) **p30**

The emergence of echinococcosis in central Asia (Dr. Paul R.Torgerson) **p31**

The role of national registries for human alveolar echinococcosis and long term surveillance of foxes: is early warning possible?(Dr. Zeinaba Said Ali) **p32**

Taeniasis/cysticercosis in farmer communities of Western Sichuan, China: a spatial study(Dr.

Francis Raoul) **p33**

Control of *Taenia solium* cysticercosis: past efforts and new prospects(Dr. Marshall Lightowlers) **p34**

19:00-21:00 Reception dinner Venue: Paradise Hall (2F)

30 October Activities

08:00-10:30 Parallel session 1: Current regional situation in echinococcosis

Venue: Paradise Hall (2F)

Panelist: Dr. Wu Weiping and Dr. MW Lightowlers

Echinococcosis in wildlife species on the Eastern Tibetan plateau, a study on the infection rates in Tibetan fox and its prey small mammal species(Dr. Wang Zhenghuan) **p38**

Echinococcosis training in Tibet (Dr. Bill Warnock) **p39**

Development of EgAgB8/3 targeted copro-antigen test for dogs infected with *Echinococcus* spp(Dr. Wulamu Mamuti) **p40**

Proteomic analysis of *Echinococcus granulosus* adult worms(Dr. Wang Ying) **p41**

A survey of *Echinococcus* spp. in wild small animals in Sichuan plateau, China (Dr. Zhu Huaimin and Dr. Zhou Zhengbin) **p42**

Screening of Echinococcosis by serological methods and ultrasonography (Dr. Hiroshi Ohmae) **p43**

Parallel Session 2: Taeniasis and cysticercosis Epidemiology and Control strategy

Venue: Huanghe Hall (3F)

Panelist: Dr. Li Tiaoying and Dr. Munehiro Okamoto

Recent advances in immunodiagnosis of cysticercosis(Dr. Yasuhito Sako) **p45**

Current status of taeniasis/cysticercosis in Tibetan populations of Sichuan province, China(Dr. Li Tiaoying) **p46**

Overview of the present situation of taeniasis/cysticercosis in Indonesia(Dr. Toni Wandra) **p47**

Taeniasis/cysticercosis In Karangasem, Bali, Indonesia(Dr. Kadek Swastika) **p48**

Pig cysticercosis in Karangasem, Bali, Indonesia(Dr. Nyoman Sadra Dharmawan) **p49**

Taeniasis and cysticercosis on the Thai-Myanmar border: an update(Dr. Paron Dekumyoy) **p50**

Taeniasis in Mongolia, 2002-2011(Dr. Anu Davaasuren) **p51**

Transmission of Taeniasis and cysticercosis in Southeast Asia (Dr. Ai Lin) **p52**

10:30-10:50 Coffee break

10:50-12:30 Parallel Session 3: Current research and Control strategy in echinococcosis

Venue: Paradise Hall (2F)

Panelist: Dr. Zhang Wenbao and Dr. P. R. Torgerson

Recent advances in serodiagnosis of both alveolar and cystic echinococcoses and monitoring of progression of AE(Dr. Akira Ito) **p54**

Transmission Factors of Echinococcus in Qinghai Tibetan Region, China(Dr. Wu Weiping)

Seasonal infection pattern of Echinococcus spp. in dogs in Tibetan communities in Sichuan Province(Dr. Wang Qian) **p55**

Study on the distribution characteristics of intermediate host of Echinococcus multilocularis(Dr. Wang Liying) **p56**

A study on dynamic changes of Cytokines in BALB/c mice infected with Echinococcus granulosus(Dr. Tian Liguang) **p57**

Parallel Session 4: Clinical treatment and case study

Venue: Huanghe Hall (3F)

Panelist: Dr. Wu Weiping and Dr. Hiroshi Yamasaki

Usefulness of pumpkin seeds combined with areca nut extract in community-based treatment of human taeniasis in northwest Sichuan Province, China(Dr. Li Tiaoying) **p59**

Vaccine development against alveolar echinococcosis using tetraspanin(Dr. Dang Zhisheng) **p60**

Echinococcus granulosus- a treatment report: Combination use of praziquantel and albendazole in a patient with multi-infected organs(Dr. Huang Yan) **p61**

Outbreak of Taenia asiatica infection in Japan(Dr. Hiroshi Yamasaki) **p62**

Enhancement Effect of Oily Dispersion Phases on Benzimidazoles' Bioavailability and Cysticidal Efficacy (Dr. Zhang Haobing) **p63**

12:30-14:00 Lunch Venue: Sunshine Western Restaurant

14:00-16:00 Round-table Discussion:

Venue: Paradise Hall (2F)

Panelist: Dr. Zhou Xiaonong, Dr. Akira Ito, Dr. Philip Craig, Dr. Patrick Giraudoux

Round-table Discussion:

A. Reports of Parallel sessions:

1. Dr. Wu Weiping
2. Dr. Li Tiaoying
3. Dr. P. R. Torgerson
4. Dr. Hiroshi Yamasaki

B. Experience & knowledge sharing and surveillance system exploring

16:00-16:30 Coffee break

16:30-17:30 Closing Session

Venue: Paradise Hall (2F)

Chair person: Dr. Zhou Xianong & Dr. Akira Ito

Closing Session -Summary report

ABSTRACTS

29th OCT 2012 Day 1

Keynote Speeches

Current Regional Situation

Investigation on the alveolar echinococcus species and their developments in Hulunbeier steppe pasture , Northeastern Inner Mongolia, China

Tang Chong Ti

School of Life Sciences, Xiamen University

Echinococcus multilocularis Leuckart, 1863, E. sibiricensis Rausch et Schiller, 1954 and E. russicensis Tang et al., 2007 were found from same endemic area and same final host, sand foxes (*Vulpes corsac*) in Hulunbeier pasture of Inner Mongolia. (Infection rates respectively: 6.21% (9/145) ; 7.58% (11/145)); 7.58% (11/145)); Juvenilia 3.97% (6/151)). In the same intermediate host, voles (*Microtus brandti*) (Infection rates respectively: 0.15%(1/674)-0.36%(9/2483); 7.57%(51/674)-3.92% (97/2483); 0.74%(5/674)- 1.07%(25/2483). Their adults provided different structure of uterus. E. multilocularis with vasselike uterus, E. sibiricensis with pyriform uterus, and E. russicensis with spherical uterus at

segment top. Their metacestode development in rodents also different. In E. multilocularis, many germinal cells grew on the inner surface of mother cyst, most of which into host tissue to form brood vesicles with protoscoleces in center, and they also grew from the inner surface of the vesicle and meshes; and had an appearance of proliferating alveolar buds from alveolar tissue outward to form new alveolar foci. In E. sibiricensis the formation of alveolar vesicle was due to the metastasizing of germinal tissue into host tissue, protoscoleces grew in the center of alveolar vesicles. In E. russicensis, the formation of the alveolar vesicle was by multiplication of germinal cell layers on the inner surface of alveolar cysts, protoscoleces grew from inner surface of mesh in the vesicle.

Research priority setting in WPRO Region – Neglected Tropical Diseases

Padmasiri Eswara Aratchige

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A substantial programmatic and research gaps exist in control and prevention of infectious diseases of poverty. These neglected tropical diseases (NTDs) continue to cause significant burden of health and most of this burden is felt in developing countries and in the most vulnerable population groups. While many programmes to control and eliminate these diseases have met with considerable success, there is a vital need to consolidate these successes and further reduce the burden of disease. Research questions exist which prevent them functioning in the most effective and efficient way.

Key challenges facing operational research in infectious diseases of poverty include: capacity building; governance and quality control of research; identifying knowledge gaps including estimation of burden of diseases, development of socioeconomic indicators; resource mobilization; need of development of inter-programmatic, inter-sectoral prevention and control strategies; and linking research, program and policy for evidence-based decision making. To tackle these challenges, it requires the adoption of a regional approach through sustained collaboration between countries, research institutions, and internal organizations in order to implement evidence-based interventions and use the identified best practices.

In the Western Pacific Region, WHO has been developing a series of disease-specific as well as comprehensive regional strategies and frameworks to accelerate the effort of disease control and elimination of infectious diseases of poverty. Regional Action Plans on Dengue, Malaria and Neglected Tropical Diseases in the Western Pacific (2012-2016) have been endorsed by countries. In addition, WHO WPR is developing a Regional Research Framework to Strengthen Communicable Diseases Control and Elimination in the Western Pacific

Among those strategies and frameworks, the WHO Regional Action Plan for NTDs in the Western Pacific (2012-2106) will be the Region's NTD roadmap for the next five years. Cestodiasis and echinococcosis are among the NTDs targeted under this plan. The purpose

of the Regional Action Plan is to link the global NTD roadmap with national plans of action, to monitor national NTD programmes, and to mobilize internal and external resources. The regional goal is to reduce the health and socio-economic impact due to NTDs, especially among vulnerable groups, and eliminate specific NTDs where feasible.

The purpose of the Regional Research Framework is to support research aimed at strengthening key communicable disease programmes. Given the limited resources available for communicable disease research, the framework aims to improve effective use of these resources through detailing of WHO's collaboration with Member States and areas through liaising with stakeholders, use of its convening role in harmonizing intersectoral partners, and setting and fulfilling priority research goals.

Prioritizing Research for one-health one-world with focus on cestode zoonoses

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The tropical diseases are a group of infectious diseases which primarily affect the poorest sectors of a society in tropical and subtropical areas especially the populations living in remotes and disadvantage regions in the developing countries. More than one billion people in the world suffer from neglected tropical diseases (NTDs), but these diseases are characterized by little attention from policy-maker, lack of priority within health strategy, inadequate research, limited resources allocation and few interventions, in which cestode zoonoses are just the examples. Climate change, globalization, urbanization, deforestation, and intensification of agriculture are all major drivers of environmental changes.

They affect human health and create or widen gaps with regard to the socio-economic status between rich and poor in this world. Indeed, the poor may not benefit from the ongoing economic development as much as others do. One of the most important consequences of this is the continued vulnerability of marginalized people to infectious diseases, which is fueled by factors such as poverty, low social status, environmental degradation and changing ecosystems. For example, new evidence shows that the highest burden of zoonotic infectious diseases worldwide is mainly found in the poverty-stricken areas of the LDCs as well as low and low-middle income countries. The numbers of infected humans and animals cause huge economic losses through the establishment of vicious circles of disease, reduced work ability and poverty.

Recent data showed that cestode zoonoses are emerging, re-emerging or spreading but still far neglected infectious diseases and do cause serious public health problems in the Asia and the Pacific region. China is one of countries with the highest disease burden of cestode zoonoses in the world, for example, human alveolar echinococcosis (AE) is known to be common in certain rural communities in China. About 91% new cases of AE per annum

globally occurring in China, with about 380 endemic counties and about 86 million people at risk in whole China, particularly in the Tibetan plateau. A total of three catalogues of endemic areas could be classified, including (1) the high endemic provinces/autonomous regions, consisting of Tibet, Qinghai, Sichuan, Gansu, Ningxia, Xinjiang and Inner Mongolia; (2) the low endemic provinces including Jilin, Heilongjiang, Shanxi, Shaanxi, Yunnan, Hebei and Henan; (3) none endemic areas with imported cases, all other provinces could be imported areas. Cystic echinococcosis (CE) was mainly endemic in Tibet, Sichuan, Qinghai, Gansu, Xinjiang, Ningxia and Inner Mongolia; alveolar echinococcosis (AE) was found in Tibet, Sichuan, Qinghai, Gansu, Xinjiang, Ningxia and Inner Mongolia. In recent years, the disease was spread to none endemic areas, the exported cases increased.

Therefore, it is recommended to explore new avenues in research to better understand the relationship between infectious diseases and poverty, and to contribute to priority settings for plans to control those diseases by introduction of the “One health - One world” concept with trans-disciplinary approaches with following focuses, including (1) applying modern tools to obtain scientific evidence on the parasite species, strains or isolates as well as confirmation of the diseases themselves, (2) further understanding epidemiology and transmission, (3) promoting optimal opportunities and strategy for control, and (4) international collaborations with emphasis on those features and improving diagnosis, treatment and control.

Plenary Session 1

Current Status of Cestode Zoonoses in Asia

International collaboration and cooperation towards control of cestode zoonoses in Asia

Akira Ito

Akira Ito and the working groups joining in Asia (Japan, China, Thailand, Indonesia, France, UK and USA)*

**Asahikawa Medical University, Asahikawa, Japan*

From 1994 onwards, my international joint projects towards control of cestode zoonosis mainly in Asia have continuously been supported by the Ministry of Education, Japan. The main target cestodes are *Taenia solium* and *Echinococcus multilocularis*. The first step was to establish highly reliable serodiagnosis for both cysticercosis in humans and pigs and even dogs, and for alveolar echinococcosis in humans. Highly reliable serology for these diseases has well been established, but it provides indirect evidence. Therefore, we simultaneously challenged to establish molecular tools for semi-direct identification of the pathogenic cestodes. It served not only for identification of pathogens but also for re-evaluation of

the cestode phylogeny. We worked in several Asian countries for evaluation of the usefulness and reliability of our original tools and reached the conclusion of the importance of the real-time detection of carriers, patients and animals for taeniasis/cysticercosis. However, these tools are not sufficient for us to grasp the transmission dynamics of these cestode zoonoses between humans and animals, another tool of GIS has been introduced. Recent advances using these tools are briefly overviewed. The main purpose of this talk is to stress the importance of international joint collaboration and cooperation towards control of cestode zoonosis.

Echinococcosis in Asia - with focus on role of dogs

Philip Craig¹, Jasmin Moss¹, Wang Qian², Iskender Ziadinov³, Paul Torgerson³

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WHO has recently listed echinococcosis as both a neglected zoonotic disease (NZD, 2006) and a neglected tropical disease (NTD, 2010) to prioritise attention for control strategies leading up to 2018. Asia currently has the greatest burden of the cystic (and alveolar) echinococcosis in humans with > 75% of global lost DALYs, primarily occurring in China (west and north) and the Central Asian Republics (especially Kazakhstan, Kyrgyzstan, Uzbekistan). Dogs are the main definitive host of *E.granulosus* (G1 sensu strictu) in those areas, and an important domestic host of *E.multilocularis* , also with

evidence in some regions for low prevalence infection with *E.canadensis* (G6), *E.equinus* (G4), or *E.shiquicus* (restricted to Tibetan Plateau), as well as a few mixed *Echinococcus* spp infections in dogs. Dog centred hydatid control interventions in rural pastoral communities will be more difficult in CE /AE co-endemic regions. Dog data remains to be fully acquired in such areas and is needed to answer key epidemiological questions ie. What is the natural reinfection rate in dogs for *E.granulosus* and *E.multilocularis*? Can dogs maintain fox-independent transmission of *E.multilocularis*?

Echinococcosis Management, Networks and Improvement in China

Hao Wen

*First Teaching Hospital of Xinjiang Medical
University*

The medical level development status in echinococcosis highly endemic area is imbalanced and limited for those patients who live in relatively remote and underdeveloped area. However, tertiary hospital can greatly increase echinococcosis medical burden both by relatively high direct and indirect medical cost. Meanwhile, due to the high credibility to experts at tertiary hospital in public mind patients are hopeful to be transferred to the tertiary

hospital even for the minor problem can be solved by territorial hospital. This increases the difficulty and costs to see a doctor. In order to satisfy the reasonable need of the people from different ethnic groups, tele-consultation served as a new medical service pattern in the aspect of remote consultation, multi-disciplinary discussion, surgery demonstration and theoretical training of echinococcosis. With the simplicity, operability, low cost and expert's resource sharing, tele-consultation developed rapidly and displayed its unique role in diagnosis and control of echinococcosis. Tele-consultation center was developed in our hospital since April 2008 and now cooperation has been established with more than 130 city and county hospital. To date, more than 15,000 a variety of consultations have been finished with transfer rate of 8.26%. Technical instruction and support to different levels of hospital is provided in a total number of 1312 patient in different level hospital, including 529 echinococcosis consultations. The application of tele-consultation and implementation of local treatment, correct referral and less transfer concept may let patients with echinococcosis in remote area get benefit and provide them high quality, inexpensive and convenient medical service.

Genetic diversity of Echinococcus spp. in Russia

Sergey Konyaev^{1) 2)}, Tetsuya Yanagida²⁾, Minoru Nakao²⁾, Yasuhito Sako²⁾,
Valeriy Odnokurtcev³⁾, Galina Ingovatova⁴⁾, Oleg Andreyanov⁵⁾, Akira Ito²⁾

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In Russia, both alveolar and cystic echinococcoses are endemic in humans and domestic/wild animals. The present study aimed to identify the etiological agents of the diseases and to investigate the distribution and host range of each parasite species in Russia. A total of 61 Echinococcus specimens were collected from 14 host species including humans. Based on the mitochondrial gene sequences, they were identified as Echinococcus granulosus, E. multilocularis and E. canadensis. E. granulosus was found in humans, sheep and a cat. Three genotypes of E. multilocularis

were confirmed; the Mongolian genotype from voles in Baikal lake island and Altai Republic, the Asian genotype from humans, voles, wolves and red foxes in the areas close to Asian countries and also from red foxes in the European part, and the North-American genotype from arctic foxes in Yakutia, Far East Siberia. The three genotypes of E. canadensis were detected in Yakutia; G6 from domestic reindeer, G8 from moose and G10 from moose and wolves. G6 was also found from humans and wolves in Altai region. The rich genetic diversity of Echinococcus spp. demonstrates the importance of Russia in investigating the evolutionary history of the genus.

Plenary Session 2

Molecular taxonomy

Current status of the genetics/molecular taxonomy of *Echinococcus* species

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The taxonomy of *Echinococcus* has long been controversial. Based mainly on differences in morphology and host-parasite specificity characteristics, 16 species and 13 subspecies were originally described. Subsequently, most of these taxa were regarded as synonyms for *E. granulosus* and only 4 valid species were recognised: *E. granulosus*; *E. multilocularis*; *E. oligarthrus* and *E. vogeli*. Recent laboratory and field observations have revealed considerable phenotypic variability between isolates of *Echinococcus*, particularly those of *E. granulosus*, which include differences in: morphology in the larvae and adults, in vitro/ in vivo development, host infectivity

and specificity, chemical composition, metabolism, pathogenicity and antigenicity. Molecular analysis has revealed differences in nucleic acid sequences that reflect this phenotypic variation. That some of these variants or strains are poorly or not infective to humans has resulted in a reappraisal of the public health significance of *Echinococcus* in areas where such variants occur. A revised taxonomy for species in the *Echinococcus* genus has been proposed and generally accepted, and is based on the new molecular data and the biological and epidemiological characteristics of host-adapted species and strains. This paper will provide an overview of the history of the taxonomy of *Echinococcus*, how the concept of a “strain” was developed, demonstrated by fundamental differences in the developmental biology of *E. granulosus* of horse and sheep origin, and how molecular data reinforced the necessity to revise the taxonomic status so that up to 9 species are now recognised.

Mitochondrial phylogeny of the genus *Echinococcus* (Cestoda: Taeniidae) with emphasis on relationships among *Echinococcus canadensis* genotypes

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²*Siberian Branch Russian Academy of Sciences, Russia,* ³*Haartman Institute, University of Helsinki, Finland.*

The mitochondrial genomes of the genus *Echinococcus* have already been sequenced in most species and genotypes to reconstruct their phylogeny. However, the two important taxa, *Echinococcus felidis* and *Echinococcus canadensis* G10 genotype (cervid strain), were lacking in the published phylogeny. In this study, the genome-based phylogeny was revised by adding these taxa. The new phylogenetic tree highly supported the old one, with topological data showing further sister relationships between *E. felidis* and *Echinococcus granulosus sensu stricto* and between *E. canadensis* G10 and *E. canadensis* G6/G7 (closely related genotypes referred to as camel and pig

strains, respectively). The latter relationship has a crucial implication for the species status of *E. canadensis*. The cervid strain is composed of two genotypes (G8 and G10), but the new phylogeny clearly showed that they are a paraphyletic group. The paraphyly was also demonstrated in another mitochondrial tree inferred from the complete sequences of cytochrome c oxidase subunit 1 (cox1) of *E. canadensis* genotypes in various localities. Domestic and sylvatic life cycles based on the host specificity of *E. canadensis* strains have been important for epidemiological considerations. However, the taxonomic treatment of the strains as separate species or subspecies is invalid in view of molecular cladistics.

Immunoproteomic analysis of *Echinococcus granulosus* in screening and identification of antigenic proteins for serodiagnosis

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Cystic echinococcosis (CE) caused by *Echinococcus granulosus* (Eg), is highly prevalent in west China, and the disease burden appears the highest in the world. To meet the challenge, there is a pressing need for research and development of rapid, sensitive and specific sero-diagnostics. It requires finding highly specific and sensitive antigens. Therefore, the specific aim of the present study is to screen and identify new antigens by immunoproteomic analysis to improve the efficiency of the existing diagnostics for CE.

Through the immunoproteomics study, a total of 21 antigenic proteins were identified from Eg cyst fluid and Eg protoscolex, among them, 12 new antigens had not been reported. They were actin-binding and severin family group-like protein, annexin, serine protease inhibitor, ribosomal proteinL18, 40S ribosomal protein RPS15, protein containing coiled-coil domain, adapter molecular crk, beclin, pyruvate dehydrogenase, nuclear pore complex protein and two proteins (p26,p111) with unknown function. The new antigens were cloned, from which 7 antigens were successfully expressed by *E. coli* system. The recombinant nuclear pore complex protein and recombinant 40S ribosomal protein RPS15 were confirmed antigenic by western bolt. The new antigens identified in this study may provide clues for further development of CE immune- diagnostic method.

Keywords: cystic echinococcus; immunoproteomics; antigen; serodiagnosis

Molecular phylogeography of zoonotic Taeniid tapeworms

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Molecular phylogeography has shed light on the evolution and dispersal history of zoonotic Taeniid cestodes. Based on the phylogeographic analyses using mitochondrial gene markers, differences in genetic population structure were identified among species. *Echinococcus multilocularis* has 4 genetic subgroups corresponding to European, Asian, North American and

Mongolian geographic isolates. It suggests that the distinct parasite populations derived from glacial refugia have been maintained by indigenous hosts. On the other hand, *Echinococcus granulosus* has a common haplotype throughout the world, suggesting the rapid dispersal by the anthropogenic movement of domestic animal hosts. Although *Taenia solium* also utilizes the domestic animal host, it has two genetically distinct geographic subgroups, Asian and Afro-American. Diversification between the two is inferred to have occurred in Pleistocene, much before the beginning of domestication. These two lineages only coexist in Madagascar, and population genetics using nuclear gene markers indicates the hybridization of the two lineages. It suggests that these two genetic groups encountered in the island after tens of thousands years of separation, resulting from the human immigration within this 2000 years. Molecular phylogeography may provide a good insight into the species status of closely related *Taenia saginata* and *Taenia asiatica*, and *Echinococcus canadensis* species complex.

What is *Taenia asiatica*?

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There has long been a debate as to the specific status of the cestode *Taenia asiatica*, with some people regarding it as a distinct species and some preferring to recognize it as a strain of *Taenia saginata*. We examined the nucleotide sequences of one mitochondrial gene (*cox1*) and of alleles at two nuclear loci (*ef1* and *elp*) from taeniid worms, which had been tentatively identified as *T. saginata* or *T. asiatica* using multiplex PCR. All phylogenetic trees from three genes showed that all samples were divided into clear two clades. These facts indicate that *T. saginata* and *T. asiatica* were

separated into two independent groups once. On the other hand, phylogenetic analyses also revealed that some worms showed nuclear-mitochondrial discordance, suggesting that they originated from hybridization between *T. saginata* and *T. asiatica*. The fact that some nuclear loci in such worms were still heterozygous means that hybridization might have occurred recently. Hybridization between *T. asiatica* and *T. saginata* is probably an ongoing event in many areas in which they are sympatrically endemic.

Plenary Session 3

Transmission and control

Assessment of Novel Health Educational Materials on Raising Compliance of Tibetan Population against Echinococcosis

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Echinococcosis is known as a severe chronic zoonosis. According to the survey data available, the eastern part of Tibetan plateau region is the highest endemic area of echinococcosis in the world. Because the Tibetan population has his special life style and production model, some control measures are difficult to be implemented effectively. To raise compliance of Tibetan population in controlling echinococcosis, health education is regarded as one of good approaches. So we developed a series of

target-specific health educational materials and applied them for community-based health education. Assessment of the effectiveness on using these materials was conducted based on improvement of knowledge and behavior. The results show that the novel materials for health education are acceptable by most populations. The effects are distinct on improving knowledge and behaviors among different groups, especially in students and herdsmen with a significant increase. Use of these materials has demonstrated to be practical in health education and promotion and very useful in carrying out control program of echinococcosis in the Tibetan communities.

Spatial approach of *Echinococcus multilocularis* transmission ecology in continental Asia

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From continental to regional scales, human alveolar echinococcosis spatial distribution is aggregated and forms discrete patches of endemicity within which hotspots of much larger prevalence may occur. Since the late 80s, a number of hotspots have been identified in continental Asia, mostly in China, wherein the ecology of intermediate host communities has been described. This is the case in South Gansu, at the eastern border of the Tibetan plateau, in south Ningxia and in the western Tian Shan of Xinjiang. More recently a new hotspot has been disclosed in the Alay valley of south Kirghizstan, and its ecology is under study. Here we present the natural history of those hotspots comparatively. Based on regional spatial models, we show how interactions

between the biodiversity of intermediate host communities, landscape and climate help to explain why transmission is more intense in distinct systems with various intermediate host communities. On this basis, regional types of transmission and their ecological characteristics may be proposed in a general framework and may help to understand the location of other Asian foci that have been reported in literature (e.g. Siberian foci of Russian Altai, Mongolia and Inner Mongolia, north-east China, etc.).

The emergence of echinococcosis in central Asia

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Following the dissolution of the Soviet Union in 1991 there emerged 5 new independent republics in central Asia. There were major changes in farming systems with the replacement of large collectivized farms with small livestock units. Veterinary public health services were poorly funded and large abattoirs with veterinary inspection were abandoned. Dog populations increased due to an increased need associated with animal husbandry changes, increased

numbers of pets and for personal security. These changes permitted a major increase in the transmission of cystic echinococcosis (CE) between dogs and livestock. In the late 1990s a large increase in the numbers of human cases of CE were reported throughout the region with at least a 4 fold increase compared to the numbers seen previously. The numbers of human cases of CE is approaching 1000 per year in Kazakhstan and Kyrgyzstan and possibly as high as 4000 per year in Uzbekistan. There is now a high prevalence of *Echinococcus granulosus* in sheep and dog populations throughout the region. More recently there is evidence that human alveolar echinococcosis (AE) is also emerging. In Kyrgyzstan there are now over 60 cases of AE reported per year compared to none reported previously. There is also a high prevalence of *E. multilocularis* infection in dogs in Kyrgyzstan and this may have resulted in onward transmission to humans. It is hypothesized that *E. multilocularis* has colonized the dog population because of the high population of dogs compared to previously and because of rural poverty which encourages dogs to scavenge for rodents. This presentation will review the evidence of the emergence of both CE and AE which appears to be both linked to the socio economic changes following the dissolution of the Soviet Union.

The role of national registries for human alveolar echinococcosis and long term surveillance of foxes: is early warning possible?

Zeinaba Said Ali

University of Franche-Comté

In France, the monitoring of human alveolar echinococcosis (AE) is organized by the FrancEchino network, and fox infection surveillance mostly by the Entente de Lutte Interdépartementale contre les Zoonoses (ELIZ). A retrospective analysis of the patient data (1982-2011) indicates that the disease occurs in nested spatial clusters geographical position of which varies over time. Furthermore a large scale survey of fox infection, based on necropsy, carried out from 2005 to 2010 in 42 French départements, indicates an extension of the distribution range of the parasite towards

West with a prevalence increase in most areas. Often, detection of human AE is the only way to detect new risk areas. However due to the long asymptomatic development of the parasite in human (10-15 years), monitoring fox (and/or dog) populations should be a better way to anticipate risks for human exposure. However fox sampling is logistically difficult at the relevant scales and time frequency and seldom an option for a rare disease in Europe. A new quantitative PCR that could be used to detect more efficiently *E. multilocularis* in carnivore faeces may overcome this problem and be used for large scale as well as fine spatial resolution studies.

Taeniasis/cysticercosis in farmer communities of Western Sichuan, China: a spatial study

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The analysis of spatial patterns of human and animal cases distribution can provide information on transmission processes of infectious diseases and thus might help to design evidence based monitoring and control programs. Between 2009 and 2012 we screened a Tibetan farmer community in five villages of Malangcuo township, Yajiang county (Western Sichuan) for the detection of both human taeniasis/cysticercosis and pig cysticercosis. Here we present the analysis of data on two nested spatial scales: (i) whole study area: spatial distribution of

human cases and prevalence among villages, (ii) Marihe village: spatial distribution of both pig and human cases and prevalence, and preliminary data on the spatial ecology of pigs, ie their activity range within the village. We failed to detect differences in *Taenia solium* and *Cysticercosis* prevalence among villages and a spatial structure in pig infection within Marihe village (however analysis of human data is still in progress). In Marihe, we also showed that most pigs (14/21) roamed outside owner's house at maximum distances ranging from 65 to 475 meters during the study time span, thereby being potentially contaminated at any place in the village.

Control of *Taenia solium* cysticercosis: past efforts and new prospects

Marshall Lightowlers

The University of Melbourne

Infection with the metacestode life cycle stage of *Taenia solium* in humans may cause neurocysticercosis and serious medical consequences. For this reason, there is an ambition to control transmission of the parasite. An understanding of the life cycle of *Taenia solium* and some basic parameters about the transmission dynamics of the infection, suggest a number of obvious options for control of the disease. Improved sanitary practices, control of the disposal of human faeces and controls on the management of pigs are all practices that could be predicted to affect *T. solium* transmission. Indeed, changes in these areas in parts of the first world

have led to the disappearance of the full transmission cycle in many parts of the developed world. Economic development in developing countries is also likely to lead to a decline in *T. solium* transmission in the future, however many areas currently have high levels of parasite transmission and a high incidence of human infection. There is a need to reduce the incidence of human disease in the short term. Theoretically at least, the disease is capable of being eradicated entirely, due to the obligatory nature of the role of humans as definitive hosts, the availability of efficient and inexpensive drugs for treatment of taeniasis, and the absence significant of animal reservoirs other than domestic pigs.

Several programs have been evaluated that have been directed specifically towards control of *T. solium*. None of those for which an evaluation has been published has clearly led to a sustainable reduction in disease transmission. More recently, there have been two significant developments that have potential to revolutionise the effectiveness of active programs for *T. solium* control. Firstly, treatment of pigs with oxfendazole can eliminate all viable parasites in the muscle tissues. The value of this as a stand-alone method for control is beginning to be evaluated. This method requires the implementation of a withholding period of at least 17 days before meat from treated animals is acceptable for human consumption. Also, cysticerci killed by the drug transform into caseous lesions present in the meat for as

long as 6 months after treatment. Meat containing significant numbers of caseous lesions would be unacceptable for human consumption. While this might seem good from a disease transmission point of view, it risks farmers reject this control procedure if they were to find that some of their treated animals subsequently had zero commercial value. The second development in *T. solium* control has been the development of an extremely effective vaccine for pigs that has been shown to be efficient in preventing porcine cysticercosis in the field. Indeed a field trial of the vaccine in Cameroon led to the complete elimination of disease transmission by the vaccinated pigs.

While many practical issues remain as challenges to the implementation of *T. solium* control using oxfendazole and/or vaccination, the prospects have never been better for implementation of sustainable and effective control measures leading to a substantial reduction in the global burden of neurocysticercosis.

30th Oct 2012 Day 2

Parallel session 1

Current regional situation in echinococcosis

Echinococcosis in wildlife species on the Eastern Tibetan plateau, a study on the infection rates in Tibetan fox and its prey small mammal species

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The vast pasturing area on eastern Tibetan plateau, China, is one of the most important endemic areas of echinococcosis in the world. In contrast with mainly focusing on human and domestic animals, studies on the epidemiology of the tapeworm within wildlife reservoir are lack of concern in China. The food chain of Tibetan foxes (*Vulpes ferrilata*) comprises a typical wildlife transmission cycle of *Echinococcus* in this area. We thus evaluated the prevalence

of *Echinococcus* in a Tibetan fox population and two main prey species, the plateau pika (*Ochotona curzoniae*) and the plateau vole (*Lasiopodomys fuscus*) using PCR analyses based on copro-DNA from foxes and tissue DNA from prey species. All the samples were collected in Shiqu county, Sichuan Province, between July and August, 2011 and 2012. The total prevalence of *Echinococcus* of the Tibetan fox population was 64.5% (20 / 31), 48.4% for *E. multilocularis* (Em) (15 / 31), 29.0% for *E. shiquicus* (Es) (9 / 31), and 12.9% mixed infection of the two species (4 / 31). In contrast, both of the prevalence of Em in pikas and plateau voles were less than 1% (3 / 314 in pikas and 3 / 304 in plateau voles). No plateau voles were found infected with Es, and only two pikas were found mixed infected with both Em and Es. We also modeled the habitat use patterns of the fox and the prey. Spatial use patterns and their influence on the transmission of *Echinococcus* were then discussed.

Echinococcosis Training in Tibet

Bill Warnock

Boulder-Lhasa Sister City Project, USA

During 2010 September 20-26, five experts from Japan and Sichuan, China, provided training on diagnosis and treatment of cystic and alveolar echinococcosis for more than fifty Lhasa Prefecture medical personnel. Lectures were given on introductory topics, histopathological diagnosis and X-ray

diagnosis, histopathology practice, ultrasound diagnosis, serodiagnosis, chemotherapy, and surgery. Two surgeries for hepatic cystic echinococcosis were demonstrated on a young man and a young woman from rural Lhasa Prefecture. Demonstration of screening for echinococcosis using abdominal B-ultrasound and a rapid serological kit was performed in a rural village. A total of 53 adults, including men and women of all ages, were screened. Ultrasound detected two cases of hepatic cystic echinococcosis, one active and one inactive. The active cyst was a 10-cm lesion in a young woman who was apparently unaware of her infection, which was confirmed with the rapid serological kit. She was informed regarding how humans are infected and then given a regimen of albendazole. We greatly increased the expertise of Lhasa Municipal Health Bureau, Lhasa Municipal Hospital, Lhasa Center for Disease Control, and seven county hospitals in rural Lhasa Prefecture on all of the echinococcosis training topics.

Development of EgAgB8/3 targeted copro-antigen test for dogs infected Echinococcus spp

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E.granulosus and E.multilocularis are main causative agents of human echinococcosis. In China, the dogs are main transmission source of the both types of human Echinococcus. Therefore, the definitive diagnosis of infected dogs is important for epidemiological study and control of human echinococcosis. The 8-kDa subunit 3 (AgB8/3) of Antigen B is an Echinococcus genus specific excretory-secretory protein

and over expressed at adult stage of Echinococcus. Therefore, it could be pass through infected dog feces and supposed to be a specific hallmark for coprodiagnosis of infected dogs. In this study, the target gene fragment EgAgB8/3 was cloned and expressed in a bacterial expression system. The polyclonal antibody against recombinant EgAgB8/3 (rEgAgB8/3) was produced in rabbits. The Sandwich ELISA copro-antigen testing method has been successfully established, and its sensitivity and specificity were preliminary evaluated using fecal samples from 90 dogs, including 16 dogs infected with Echinococcus granulosus, 34 dogs mix infected with Toxocaracanis and Taenia hydatigena, 4 dogs mix infected with Echinococcus granulosus oxocaracanis+Taenia hydatigena and, 36 none infected healthy dogs. Statistical analysis revealed that the Sandwich ELISA copro-antigen testing method has revealed 85% sensitivity and 95.7% specificity to detect Echinococcus granulosus infected dog feces. However, the stability and practical applicability of this method should be further confirmed using epidemiological mass data.

Proteomic analysis of Echinococcus granulosus adult worms

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Cystic echinococcosis (CE), caused by infection with *Echinococcus granulosus*, is one of the most widespread zoonotic helminth diseases and affects humans and livestock. The *E. granulosus* has a complex life cycle involving two hosts. The definitive hosts are primarily dogs, which harbor adult worms in their small intestines. Humans and herbivore, particularly sheep and cattle, are intermediate hosts of this parasite.

Intermediate hosts become infected by ingesting the eggs released in the feces of definitive hosts or consuming food contaminated with eggs. Dogs, as definitive hosts, are pivotal in the transmission of CE. However, dog and adult worm have received relatively little attention. Proteomic analyses of *E. granulosus* have been restricted to pre-adult stage, the proteomic profile of *E. granulosus* adult worm remains obscure. In this work, we performed a proteomic analysis of the adult stage of *E. granulosus* during infection of a dog definitive host. A series of protein associated to survival, development, movement and modulation of parasite were identified by MALDI-TOF MS. More than 200 protein spots were presented on the gels, most of these spots distributed in pI 4.5-9, 192 spots were excised for mass spectrometry. 61 spots were identified, corresponding to 32 different proteins. To identify antigenic proteins, we performed 2-DE immunoblots using serum from *E. granulosus* infected dog. 36 antigenic protein spots were revealed by immunoblotting, 21 spots of antigenic protein were identified, corresponding to 13 different proteins, 7 of these were described here for the first time. According KOG functional classification, most of the identified proteins are related to Z (cytoskeleton), O (post-translational modification, protein turnover, and chaperones) and G (Carbohydrate transport and metabolism). Overall, our results are expected to improve the repertoire of candidate protein molecules for vaccination, immunodiagnosis and drug development.

A survey of Echinococcus spp. in wild small animals in Sichuan plateau, China

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Echinococcosis is a serious zoonotic disease affecting various species of herbivorous livestock and humans. A survey of echinococcosis in wild small mammals was conducted from September 2007 to October 2007 in an highly echinococcosis endemic region, Shiqu County, the Qinghai-Tibet plateau of western Sichuan, China. A total of 1006 small wild mammals were captured, 7.75%(78/1006) were found having hydatid cysts by naked eyes. Among them, the infection rate of *Ochotona curzoniae* and *Microtus fuscus* were 5.75%(5/87), and 7.95%(73/918), respectively. One of the

Myospalax sp. was not infected. Fifty one infected samples were detected by the hemi-nest PCR, 100% (3/3) *O. curzoniae*, 91.7%(44/48) were infected with *E. multiloculari*. One out of 48 (2.08 %) hydatid cysts from *M. fuscus* were identified as *E. granulosus*. Furthermore, 3 out of 48 (6.25%) of *M. fuscus* were infected with *Taenia taeniaeformis*. The investigation shows that the endemity of echinococcosis was widespread among *O. curzoniae* and *M. fuscus* in the region of Shiqu County.

Keywords: Alveolar echinococcosis, Cystic echinococcosis, *Taenia taeniaeformis*; wild rodents, PCR.

**Screening of echinococcosis by serological methods
and ultrasonography
-The comparison of screening approaches in echinococcosis
and schistosomiasis**

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The main aim of this paper is to introduce and discuss the present screening system of echinococcosis in Japan. The usefulness of screening methods using immunologic and ultrasonographic examinations is compared in echinococcosis and schistosomiasis.

Alveolar echinococcosis, caused by the larval stage of *Echinococcus multilocularis*, is an important zoonosis in Hokkaido, Japan. The first cases in main Hokkaido Island, were found in 1968. Since then human cases occur sporadically throughout Hokkaido.

E. multilocularis was eliminated on Rebun Island, however, the infectious rate among necropsied foxes in Hokkaido has increased 10% in 1985 to 42.8% in 2008.

About 10 persons each year are provisionally diagnosed as being infected by serologic and imaging examinations. Although the prevalence among inhabitants is very low, new infections are detected in urban area. As the first screening, serological screening using ELISA is performed for all the inhabitants living in Hokkaido every 5 years.

ELISA positive ones undergo ultrasonographic examination and serologic test using Western blotting. To compare the size of lesions in screened patients and non-screened patients diagnosed accidentally, small lesions were found more frequently in screened patients. The local government of Hokkaido launched a comprehensive control program including the deworming of foxes by the administration of praziquantel. In Hokkaido, the effectiveness of mass treatment with praziquantel was limited in the control program of echinococcosis.

Parallel Session 2

Taeniasis and cysticercosis

Epidemiology and Control strategy

Recent advances in immunodiagnosis of cysticercosis

Yasuhito Sako, Akira Ito

Asahikawa Medical University

Human cysticercosis caused by *Taenia solium* is one of the most serious zoonotic parasite infections worldwide and diagnosed primarily based on imaging techniques, including computed tomography and magnetic resonance imaging. These imaging techniques are sometimes limited by the small size of visualized lesions and atypical images, which are difficult to distinguish from abscesses or neoplasms. Therefore, efforts have been directed toward development of immunological tests to detect specific antibodies or antigens either in serum or in cerebrospinal fluid.

The glycoproteins of 10-26 kDa, consisting of a very closely related family of 7-kDa proteins, in cyst fluid of *T. solium* larvae are widely accepted antigens to detect specific antibodies in human and pig. And now recombinant antigens showing similar sensitivity and specificity to those of native antigen are available.

In this symposium, we will present a brief review of recent advances in immunodiagnosis of cysticercosis. In addition, we will introduce our recent works: 1) Development of an immunochromatographic test to detect specific antibodies with recombinant antigens for a simple and rapid examination of human cysticercosis and 2) Establishment of a simple and reliable purification method of glycoproteins and use of them as immunodiagnostic antigens for human and pig cysticercosis.

Current status of taeniasis/cysticercosis in Tibetan populations of Sichuan province, China

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Taeniasis and cysticercosis are known to be a serious parasitic zoonosis but under-recognized in minority communities of southwest China. Current village-based studies conducted during 2008 to 2012 indicate three human *Taenia* species are co-prevalent in Tibetan farming areas of Sichuan Province, where neurological morbidity due to infection of neurocysticercosis composes a major public health concern, with an overall infection rate of taeniasis ranging from 3%

to 20% and seroprevalence of human cysticercosis varying from 4% to 7%. Factors including the use of free-ranging pigs, a high proportion of consumption of undercooked beef/pork, a lack of latrine facilities, inadequate meat inspection and poor economy were considered to contribute to the high transmission of both *T. saginata* and *T. solium* in this area.

Overview of the present situation of taeniasis/cysticercosis in Indonesia

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Main aim was to overview the present situation of human taeniasis and cysticercosis in Indonesia. Through joint project from 1996, we have confirmed *Taenia saginata* (beef tapeworm) in Bali, *Taenia solium* (pork tapeworm) from Papua and Bali, and *Taenia asiatica* from Samosir island in Lake Toba, North Sumatra. These taeniasis cases were caused through eating uncooked pork and viscera of pigs for *T. solium* and *T. asiatica*, respectively, and beef for *T. saginata*. The distribution of these tapeworms in Indonesia is basically highly restricted by the traditional cultural and religious background in each island. *T. saginata* is rather common in Bali although people consume pork “lawar” much more

than beef “lawar”. *T. solium* is highly endemic in Papua (=Irian Jaya) and sporadic in Bali and some other islands where people eat uncooked/undercooked pork or imported cases. Among these species, *T. solium* is exceptional, since humans can be infected not only by larval stage (cysticerci) in pork but also by eggs released from tapeworm carriers, humans. Cysticercosis in humans, pigs and even dogs have been confirmed in Indonesia.

Taeniasis/Cysticercosis In Karangasem, Bali, Indonesia

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Cysticercosis due to *Taenia solium* has been reported in Papua and Bali and several other islands, Indonesia. Cysticercosis is now sporadic in Bali. Field surveys to detect taeniasis carriers for eradication of cysticercosis in Bali have been carried out the past one decade. When we worked in Bali 2002-2010, we confirmed many tapeworm carriers of *Taenia saginata*, but no carrier of *T. solium*. Nonetheless, when we treated those tapeworm carriers, some carriers were confirmed to be neurocysticercosis (NCC) of *T. solium*. Several

patients showed epileptic seizures within half day after treatment with praziquantel to expel adult *T. saginata*. Both serology and neuro imaging figures revealed these patients were asymptomatic NCC before treatment. In December 2010, we found an ocular cysticercosis case of 9 years old girl in Karangasem. Then, we did epidemiological survey in this area in January and September 2011, and detected 3 tapeworm carriers of *T. solium* and one pig full of cysticerci of *T. solium*. It is the first time for us to detect taeniasis carriers of *T. solium*. The integrated health education program with serology and molecular tools for epidemiological survey are important to prevent and control this disease.

Pig Cysticercosis in Karangasem, Bali, Indonesia

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Cysticercosis in pigs and taeniasis due to *Taenia solium* have not been reported for years in Bali, Indonesia. In early 2011, we found two *T. solium* taeniasis cases in Karangasem, Bali. In September-October 2011 we conducted pig serological survey at Dukuh and Datah Villages, Karangasem. When we applied ELISA in the villages using purified native antigens for a total of 64 pigs' sera, we found only one strong positive

by our naked eyes. We slaughtered it. *T. solium* cysticerci were observed from almost all of the carcasses and brain and eyes. Two cysticerci of *T. hydatigena* were also observed from mesentery. We later repeated ELISA using ELISA reader in the laboratory. The results revealed 0.093% (6/64) of the samples were positive. The pig full of cysticerci showed OD = 1.319. Another pig showing OD = 0.103 (cut off point 0.046) was slaughtered in 2012. It was infected with only one *T. hydatigena* cysticercus in mesentery. Although it has been confirmed that serology using the purified antigens is highly useful for detection of human cysticercosis, we have to evaluate its usefulness for pig survey. Pigs infected with *T. hydatigena* may show at least weak cross reaction to the diagnostic antigens.

Taeniasis and Cysticercosis on the Thai-Myanmar border: an update

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Taeniasis and cysticercosis are found in many parts of Thailand, but rarely in the South. A previous collaborative project was conducted among Karen refugees in a central province along the Thai-Myanmar border. Since 2011, field studies have been conducted at a village in the northern province of Tak, also on the Thai-Myanmar border. Human feces were examined by Kato thick-smear technique, while human and swine (intermediate host) sera were tested by ELISA, periodically confirmed by

immunoblot. Fecal-smear testing found 3.09% (15/486) positive for taeniasis. At Asahikawa Medical University (AMU), the first batch of human serum samples were tested for antibody against solium antigen; ELISA gave a positive rate of 5.17% (6/116). Immunoblot testing positively confirmed 66.67% (4/6). Of a total of 135 swine sera, 50 were found positive at a rate of 40% (20/50) by ELISA. Immunoblot positively confirmed 60% (12/20). In Tak Province, 12.9% (11/85) were positive by using ELISA only. By ELISA, 22.9% (31/135) were positive. Nine of the positive swine (5 at AMU; 4 at Tak) were killed to observe the cysticerci in the carcasses, which were only found in the 4 at Tak. Using parasitic agents for molecular identification, most were *Taenia solium*; one was *T. saginata*.

Teniasis in Mongolia, 2002–2011

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We have aimed to evaluate a total of 185 proglottids of *Taenia* spp, 31 fecal samples and 59 serum samples from 187 taeniasis cases that were submitted to the Mongolian National Center for Communicable Diseases from 2002 to 2011 and to confirm the source of infection for human. Mitochondrial DNA was used to identify parasite species, with the goal of assessing the epidemiological situation of taeniasis in Mongolia.

All of the proglottids and stool samples were confirmed to be *T. saginata*. There was no evidence of *Taenia solium* taeniasis/cysticercosis or *Taenia asiatica* taeniasis.

T. saginata infections were identified in individuals from 15 of Mongolia's 21 provinces. *T.saginata* cysticercosis in beef represents a significant source for human infection. Lifestyle and food preparation

choices among Mongolians are believed to be the primary reasons for these infections.

Keywords: *Taenia saginata*, taeniasis, multiplex PCR, LAMP assay, Mongolia

Transmission of Taeniasis and cysticercosis in Southeast Asia

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Taeniasis is an intestinal infection caused by the adult stage of the large tapeworm. Carriers of *T. solium* acquire infection through eating undercooked pork contaminated with cysticerci (larvae). Cysticercosis, a tissue infection caused by accidental ingestion of eggs released from humans harboring the pork tapeworm, *Taenia solium*, is one of the most serious reemerging parasitic diseases worldwide. This report will introduce the transmission of taeniasis and cysticercosis in some southeast Asian countries, such as Indonesia, Vietnam, Philippines, Lao People's Democratic Republic etc..

Parallel Session 3

Current research and Control strategy in echinococcosis

Recent advances in serodiagnosis of both alveolar and cystic echinococcoses and monitoring of progression of AE

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One of the most important and informative tools for diagnosis and monitoring the prognosis of echinococcosis is serology. Recent trends in serodiagnosis past two decades are how to detect specific and sensitive antigens through the course of infection, either alveolar (AE) or cystic echinococcosis (CE). Through blind tests based on international collaboration projects, Em18, one of ELPs especially recombinant Em18 (RecEm18), has been confirmed to be one of the best candidates to detect almost all active AE cases (PNM classification) and highly useful for monitoring the progression of AE, whereas recombinant Antigen B8/1 (RecAgB8/1) is a good candidate to detect the majority of CE2, CE3a and CE3b (WHO-IWGE US classification). We have developed rapid immunochromatographic kits for both AE

and CE using recEm18 and RecAgB8/1, respectively. In this talk, I will introduce the outlines of our international joint projects and recent preliminary work in Mongolia and unexpected rapid drop in titers through surgery in radically cured AE cases. This is a brief overview of several joint projects with German, Chinese and Mongolian groups.

Seasonal infection pattern of echinococcus spp. in dogs in Tibetan communities in Sichuan Province

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Abstract: Tibetan communities are endemic with alveolar echinococcosis or/and cystic echinococcosis on the Qinghai-Tibet Plateau in western Sichuan Province . Since 2006, Chinese government initiated an echinococcosis control programme in the province firstly, which in turn included other provinces and regions e.g. Qinghai , Tibet ,

Gansu , Ningxia, Xinjiang and Inner Mongolia . A major component of the programme is to dose dogs with praziquantel monthly. The dosage is 200mg for body weight (BW) less than 15kg and 400mg for BW more than 15kg . Due to lack of public infrastructure and facilities in township and village levels, it is very difficult to dose the dogs monthly. Therefore it is highly necessary to understand if it is possible to reduce times of dosing. According literature review and field observation, a seasonal re-infection pattern was assumed for dogs. After 1 years of testing, it was revealed that the major seasons for re-infection of dogs were spring and winter. The results indicated a simplified dog deworming scheme is possible, which will be cost-effective and easy to carry out.

Study on the Distribution Characteristics of Intermediate Host of *Echinococcus multilocularis*

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The study conducted in the southern Qinghai Plateau and proved that the two species of small mammals-*Ochotona curzoniae* and *Microtus fuscus* are the intermediate host animals of *Echinococcus multilocularis* and are abundant in this area.

The results revealed that the aggregation and spatial autocorrelation in the

distribution of *Ochotona curzoniae* and *Microtus fuscus*, and verified that their distribution conformed to the negative binomial distribution. So we investigated the environmental factors influencing the distribution of *Ochotona curzoniae* and *Microtus fuscus* by field survey and collection of RS/GIS information, and established a regression model of negative binomial distribution. Multivariate analysis was used to determine environmental factors that combine best to provide favorable conditions for *Ochotona curzoniae* and *Microtus fuscus*. We developed a discriminatory model by using stepwise discrimination method and evaluated its efficacy. The negative binominal regression model and the discrimination model developed through this study provided a useful tool for the estimation of distribution of the intermediate hosts for alveolar echinococcosis according to the geographic environment, and for the rodent and Lagomorpha control by the sectors involved.

A study on dynamic changes of Cytokines in BALB/c mice infected with *Echinococcus granulosus*

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To build optimal model of animal infected with *Echinococcus granulosus*, and to observe the dynamic changes of Cytokines in BALB/c mice infected with Eg in difference period of time, and to explore host's immune regulation. The Eg was collected from the sheep in Qinghai province. Rabbit, Guinea pig, SD Rat and BALB/c Mice were infected with Eg. After 6 months later, all animals were dissected and found that BALB/c was the optimal model of animal

infected with Eg. SD Rat and Rabbit were infected with Eg, but the cyst of Eg did not have a good growth. Guinea pig was not infected with Eg. Each BALB/c mice was injected 2000 Egs into peritoneal cavity, the infection lasted and was followed up to 28 weeks. Serum sample was collected from BALB/c mice infected with Eg in difference period time. IgG/IgM/IgE, IFN- γ , IL-2, IL-4, IL-10 and TNF- α were determined by ELISA. After infected with Eg, IgE was rise from first week to 28th week. IL-4 had a marked rise from 10th weeks to 16th week. IFN- γ showed a rise from 10th week to 14th week. IL-10 went up during 16th week to 20th week, and TNF- α showed a rise after 4 weeks later infected with Eg. IL-2 did not have apparent change during infection period. After infected with Eg, Th1 is the major response in the early stage of infection. Th2 is the major response between 8th week and 16th week.

Parallel Session 4

Clinical treatment and case study

Usefulness of pumpkin seeds combined with areca nut extract in community-based treatment of human taeniasis in northwest Sichuan Province, China

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Currently the most commonly applied anthelmintics for treatment of taeniasis are praziquantel and niclosamide. Praziquantel is very effective, but has the risk of induction of epileptic seizures or convulsions in carriers with asymptomatic concurrent neurocysticercosis. In contrast, niclosamide is safe and effective, but is not readily available in many endemic countries including China. In the present study, we assessed and compared the efficacy of treatment with combination of pumpkin seeds and areca nut extract, either pumpkin seeds or areca nut extract alone in taeniasis cases in a known endemic area of Sichuan Province. Results from this study implied

that the traditional Chinese herbal treatment consisting of pumpkin seeds followed by areca nut extract was safe and highly effective in eliminating intact tapeworms in more 89% of taeniasis cases.

Vaccine development against alveolar echinococcosis using tetraspanin

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Vaccine efficacies of *Echinococcus multilocularis* Tetraspanins (TSP) against primary alveolar echinococcosis in BALB/c mice were evaluated. Cyst lesion number reduction (CLNR) in the liver of vaccinated vis-à-vis non-vaccinated mice by subcutaneous (s.c.) administration of 7 recombinant TSPs (rTSP1-rTSP7) with Freund's adjuvant were 87.9%, 65.8%, 85.1%, 66.9%, 73.7%, 72.9% and 37.6%, respectively. Intranasal (i.n.) immunizations with rTSP1 and rTSP3 with CpG ODN achieved a CLNR of 37.1% and 62.1%. Moreover, both s.c. and i.n. administration with rTSP3 evoked strong serum IgG, IgG1

and IgG2 α responses; i.n. immunization induced significantly higher IgA responses in nasal cavity and intestine compared with s.c. immunization. Both immunization routes induced extremely strong liver IgA responses; s.c. immunization resulted in a reduction in the IgG1/IgG2 α ratio (Th1 tendency), whereas i.n. immunization caused a shift from Th1 to Th2. More interestingly, i.n. immunization of rTSP3-FBP (TSP3 fused with fibronectin-bonding peptide (FBP) of *Mycobacterium avium* fibronectin attachment protein (FAP)) and rTSP3+CpG evoked strong serum IgG and IgG1 responses, whereas only the latter induced a high level of IgG2 α production; rTSP3-FBP resulted in a Th2 tendency and provoked significantly stronger IgA antibody responses in intestine, lung and spleen compared with those by rTSP3+CpG; significant IgA antibodies were detected in nasal cavity and liver samples from both groups.

Echinococcus granulosus- a treatment report: Combination use of praziquantel and albendazole in a patient with multi-infected organs

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The clinical treatment for human echinococcosis includes surgery, percutaneous drainage and antiparasitic medication. Albendazole is recommended to treat this disease by WHO and is widely adopted for patients in the National Hydatid Control Programme of China, although it has also been associated with treatment failure in some cases. Praziquantel has recently shown value in the treatment of human echinococcosis and its use in combination with albendazole is recommended in

some patients with complicated Cystic Echinococcosis infections. It was possible to monitor closely the treatment of a 15-year-old patient with three large liver cysts and one lung cyst. The treatment was a cyclic combination therapy of albendazole (400mg, twice a day for 5 days a week) and praziquantel (800mg per day for the other two days of the week). The regimen was repeated for 10 courses with a 2-week interval between each one. Response to treatment was monitored by abdominal sonography, chest X-ray and titer of serum IgG against *Echinococcus granulosus* in ELISA. After 18 months from the beginning of treatment, the size of the lung cyst was reduced from 24.5×21.6cm to 11.5×10.5cm, the size of the biggest cyst (11.4×8.2cm) in liver had reduced to 8.6×7.5cm. The image type varied from CE1 (active) to CE4 (inactive) Two small cysts in liver disappeared. The specific IgG level initially increased but showed a decline after 6 months treatment. The liver function during the treatment will be described. After 12 months treatment regime the size of remaining cysts and the IgG level seemed to remain static. No side effects were observed during the treatment course or during the following 18 months. At present, although there is insufficient published evidence to support a clear recommendation for the use of albendazole combined with praziquantel in chemotherapy for hydatid disease, the combination therapy can be considered to be an option.

Outbreak of *Taenia asiatica* infection in Japan

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Taenia asiatica is found in several countries in Asia; however, until recently, it has been thought that this species does not occur in Japan. Surprisingly, infection with *T. asiatica* has been confirmed in several patients from the Kanto region, including Tokyo, since June 2010. To date, the number of infected patients has reached 25, including 24 Japanese and one Filipino. All the Japanese patients had either never been overseas, or if they had undertaken any travel, it was not to any country where *T. asiatica* is endemic. The epidemiology of these *T. asiatica* infections is not clear, but it is possibly linked to the consumption of raw

pig's liver, from animals that were probably produced and slaughtered in the Kanto region. In fact, 21 patients did have a history of eating raw pig's liver. However, *T. asiatica* metacestodes have not yet been detected in pigs from this area, despite careful examination at local meat inspection centers. In all cases, the disease was diagnosed by analysis of both mitochondrial and nuclear DNA extracted from expelled proglottids. Interestingly, the DNA analysis revealed that the etiologic *T. asiatica* were derived from different tapeworm populations, but the origins could not be specified due to lack of geographical variations in the DNA markers examined.

Enhancement Effect of Oily Dispersion Phases on Benzimidazoles' Bioavailability and Cysticidal Efficacy

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As we know, the albendazole and mebendazole are only two antihydatid drugs recommended by WHO. But their low solubility limits their bioavailability and efficacy. To explore the possibility to increase the bioavailability and cysticidal efficacy of benzimidazoles, several drug-oily solvent suspensions were prepared and their bioavailability was evaluated. Their solubility in different oily solvents was also measured. Chosen three solvents in which the benzimidazoles have high, middle

and low solubility respectively as accessory ingredients to prepare corresponding suspensions and evaluated their bioavailability. By analyzing the correlations of solubility in vitro and the bioavailability of the corresponding suspensions in vivo, the solubility of benzimidazoles in media on the whole positive correlative to their MRT, C_{max}, AUC and F in mice, the medium with best bioavailability to benzimidazoles was selected to prepare the mebendazole-suspension for further studies on pharmacodynamics test. The mebendazole suspension was administered in mice with secondary cyst *Echinococcus granulosus*. Take mice infected with secondary cysts of *E. granulosus* for 8 months treated orally with MBZ-1 % tragacanth at a daily dose of 25 mg/kg, 12.5 mg/kg, 6.25mg/kg and 3.125mg/kg for 14 consecutive days as positive control and the mean cyst weights were lower than that of untreated control, but the difference was not statistically significant. When the infected mice received MBZ-oily solvent preparation at the same oral dose schedule as aforementioned, the mean cyst weights were significantly lower than those in MBZ-1 % tragacanth group or control group. The results indicate that the solubility and bioavailability of MBZ or other benzimidazoles in oils may increase to various degrees according to the kind of oil used. Meanwhile, MBZ-oil preparations administered orally to mice not only improve the bioavailability of MBZ relative to that of MBZ suspended in 1 % tragacanth, but their effects against hydatid cysts also significantly enhanced.