



**Report of the WHO Informal Working Group on cystic
and alveolar echinococcosis surveillance, prevention and control,
with the participation of the Food and Agriculture Organization of
the United Nations and the World Organisation for Animal Health**

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1. Opening session

Dr Lorenzo Savioli, Director, Department of Control of Neglected Tropical Diseases, welcomed the members of the informal working group on echinococcosis and representatives of the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). He extended WHO's thanks to the former coordinator of the informal group, Dr Philip Craig, who had led it for more than 4 years, and to Dr Peter Kern, who had agreed to lead the group for the next 4 years. Dr Savioli thanked all the participants for their dedicated work on a group of parasitic diseases that had a significant public health and economic impact on communities around the world but attracted little attention from decision-makers at national and international levels. He formally opened the Consultation on Cystic and Alveolar Echinococcosis, focusing on the role of veterinary public health in controlling those diseases, the importance of which still is unfortunately often overlooked by both human and veterinary health officers in endemic countries.

Dr François Meslin, Team Leader, Neglected Zoonotic Diseases, said that the purpose of the consultation was to review the current situation of those zoonoses in highly endemic countries, discuss current veterinary public health measures used for their prevention and control, and assess the value of new advances, such as vaccines, and the feasibility of integrated approaches for disease control in intermediate and definitive host species. Dr Meslin also summarized the work of the informal working group on echinococcosis since its creation in 1985 (see section 7).

Dr Philip Craig was nominated Chairman and Dr Thomas Romig Rapporteur of the consultation.

2. Updated global burden of cystic and alveolar echinococcosis

P.R. Torgerson and P. Craig

The diseases caused by these parasites represent a substantial burden on the human population. Present estimates suggest that cystic hydatid disease, caused by *Echinococcus granulosus*, results in the loss of 1–3 million disability-adjusted life years per annum. The annual cost of treating cases and economic losses to the livestock industry probably amounts to US\$ 2 billion. Alveolar echinococcosis, caused by *E. multilocularis*, results in the loss of about 650 000 disability-adjusted life years per year. These diseases are perhaps some of the more important global parasitic diseases, with more than 1 million people affected at any one time, many showing severe clinical syndromes.

3. Human aspects of cystic and alveolar echinococcosis

P. Kern

The term 'echinococcosis' encompasses two diseases, which differ markedly in their presentation, behaviour and clinical management: alveolar echinococcosis, caused by *E. multilocularis*, in which a multivesiculated tumour forms, mainly in the liver; and cystic echinococcosis, caused by *E. granulosus*, in which fluid-filled cysts (also called hydatids) develop, mainly in the liver or lung. The larval growth of the two parasites separates the

‘malignant’ alveolar echinococcosis from the ‘benign’ cystic form. Experts have recently reached consensus on the diagnosis and treatment of alveolar and cystic echinococcosis, and their recommendations offer guidance to clinicians in areas where these diseases are endemic but rarely diagnosed.

Alveolar echinococcosis is characterized by an asymptomatic incubation period of 5–15 years. Precise diagnosis remains a challenge for clinicians and radiologists, and incomplete knowledge of the disease results in misinterpretation of clinical and imaging findings. Serology is helpful, but, again, clinicians and microbiologists are uncertain about the cross-reactivity of antibodies with antigens from *E. multilocularis* or *E. granulosus*. The PNM classification system¹ is based on imaging findings and has become an international benchmark. Larval metastases may form in organs adjacent to the liver *per continuitatem* or in distant locations by a haematogenous or lymphatic route. To avert the potential ‘malignant’ features of alveolar echinococcosis, continuous larval suppression with benzimidazoles remains the backbone of lifelong treatment. If the lesion is confined, radical surgery offers cure. Unfortunately, in many patients, the disease is diagnosed at an advanced stage, and they undergo palliative surgery without benzimidazoles or with incomplete coverage. As a result, relapses are frequent. Immune deficiency appears to have a strong negative impact according to anecdotal observations. The molecular mechanisms leading to progressive disease are still not known.

Cystic echinococcosis, also known as hydatid disease, is relatively frequent on a global scale. Thus, many clinicians are somewhat familiar with the disease. The incubation period can be as long as that for alveolar echinococcosis, but signs and symptoms are often reported within a shorter period, depending on the location of the cyst(s). Besides the liver and lung, other organs can be affected. In contrast to alveolar echinococcosis, the larva forms a single or several fluid-filled cysts—known since ancient times as hydatids, which are always surrounded by a well-organized, compact capsule of host origin. Larval growth occurs inside the cyst (endogenous budding). Young, unruptured cysts often remain serologically negative. The WHO system for classifying hepatic cysts by ultrasound imaging has also become the benchmark,² and its application has much improved both the clinical management and international comparison of clinical data. Experience with interventional procedures, such as percutaneous puncture, is encouraging, and use of this technique for hepatic cysts has been shown to be safe. Surgery may no longer be the treatment of choice; instead, many centres use short-term cycles of benzimidazole, which degenerates the endocyst and results subsequently in a regressive course of cystic echinococcosis. Others favour the ‘watch and wait’ principle and carefully observed natural degeneration of the cyst. Diagnosis of regressive cystic echinococcosis is, however, still a challenge; serology is not well adapted for identifying either the remnants or the viability of the parasite, and imaging findings result in unnecessary surgery, exposing the patients to high risk,

¹ The WHO PNM classification system covers a wide clinical spectrum, with four ‘P’ categories for the distribution of lesions (P for parasite in the liver), two ‘N’ and two ‘M’ categories for the presence or absence of local infiltration including lymph nodes (N) and metastasis (M), respectively. Stages I–IV are derived from those categories.

² Annex 1 in *PAIR: puncture, aspiration, injection, re-aspiration: an option for the treatment of cystic echinococcosis*. Geneva, World Health Organization, 2001 (WHO/CDS/CSR/APH/2001.6).

particularly in regions where both cystic and alveolar echinococcosis are diagnosed. Consultation at specialized centres is recommended.

4. Veterinary public health and veterinary surveillance

F.X. Meslin and P. Craig

Veterinary public health is listed as one of the five strategies for overcoming neglected tropical diseases in the report entitled *Working to overcome the global impact of neglected tropical diseases*¹ launched by the WHO Director-General on 14 October 2010. In her speech, Dr Chan acknowledged the importance of veterinary public health, particularly for the prevention and control of zoonotic diseases. This Neglected Tropical Diseases report, which was well received by the public health and donor communities, provides technical information on 17 diseases, including three zoonoses: porcine cysticercosis (taeniosis), human and dog rabies and cystic echinococcosis (hydatidosis). Inclusion of these infections on the Neglected Tropical Diseases list has raised interest and should help to improve the visibility of both cystic and alveolar echinococcosis.

Annual surveillance of infection rates in dogs, livestock and humans is critical for establishing a pre-intervention baseline, assessing the efficacy of control programmes and providing data to control authorities and organizations for forward planning and budget approval. Purging of owned dogs with arecoline and necropsy of strays may largely be replaced by testing of faeces with a coproantigen enzyme-linked immunosorbent assay. Livestock slaughter inspection records (from local slaughterhouses or purchased animals) remains the gold standard, but cysts <1 cm require histological verification or DNA analysis. Livestock serology is of limited use—probably only for imported or exported live animals and possibly for herd testing for consolidation or maintenance of eradication phases. Surveillance tools are widely available for control of *E. granulosus*.

5. Review of control programmes and disease epidemiology

5.1 Control of *Echinococcus granulosus* and cystic echinococcosis

5.1.1 General aspects

P. Craig

The disease caused by *E. granulosus*, cystic echinococcosis, is one of the neglected zoonotic diseases recognized by WHO. It represents a significant global human disease burden in resource-poor pastoral communities. Transmission occurs from dogs to humans but not directly between humans. Interventions should therefore be targeted to animal hosts; however, both definitive (dogs) and intermediate animal hosts (sheep, other livestock) are asymptomatic, and cystic echinococcosis is not of significant economic importance to livestock owners or governments. The chronicity of human cystic echinococcosis, fragmented medical records, its

¹ *Working to overcome the global impact of neglected tropical diseases*. Geneva, World Health Organization, 2010 (WHO/HTM/NTD/2010.1).

complicated diagnosis and difficult and costly treatment result in further neglect. Interventions to reduce the zoonotic risk and human cases are necessarily directed to treating domestic dogs and to changes in husbandry, which require veterinary action and surveillance. Control should be a concern of public health rather than animal health; however, it has low priority and intersectoral cooperation is often poor. An active programme for cystic echinococcosis case management, treatment and follow-up is vital. Hydatid control programmes begun during the 1960s and 1980s indicate that effective intervention is possible with established tools but requires time (more than 5–10 years).

Supervised treatment of owned dogs four to eight times a year with praziquantel is the single most important intervention. Its effectiveness depends on the percentage of the dog population registered and treated, access to households, the efficiency of the dosing team, community acceptance, logistics and management. Other interventions include changing livestock husbandry and home-slaughter practices, meat inspection and dog management. Health education can increase participation and maintain the continuity of long-term control, especially in the consolidation phase. Vaccination of sheep with EG95 vaccine should reduce transmission to dogs and the time required to achieve control. Control end-points should be defined. Simulations of animal prevalence and frequency distributions, intervention parameters, cost–benefit and other factors should be modelled before and during control. Veterinary surveillance is described in section 4; medical surveillance, from hospital records (surgical, medical, outpatient), provides a basis for health impact assessment, with community-based mass ultrasound examinations annually, especially among people aged <15 years. Human serological screening alone is not always helpful and may result in large numbers of false-positives for long-term follow-up. Recognized hydatid treatment centres should be identified in endemic areas, in which surgical, chemotherapeutic, PAIR (puncture, aspiration, injection, re-aspiration) and ‘watch-and-wait’ approaches are available (for in- or outpatients) for the various clinico-pathological presentations.

The success of a hydatid programme often depends on the structure, effectiveness and sustainable funding of the control authority and team and the willingness of target communities to participate, rather than on the technical tools and approaches available. Integrated dosing of dogs with praziquantel (at a defined frequency) combined with vaccination of livestock with EG95, with effective surveillance, have not yet been adequately assessed. Guidelines for successful control require clarification in relation to attack, consolidation and maintenance of elimination phases, and best practice must be identified for monitoring the parasite in transboundary situations. Identification of exposure of young livestock and children to cystic echinococcosis during and after control is difficult. An effective vaccine against *E. granulosus* for dogs remains to be found.

Combined control of cystic echinococcosis with other zoonotic diseases should be investigated for cost–effectiveness, especially in hard-to-reach traditional or semi-nomadic populations where the disease is endemic.

5.1.2 Control in China

Q. Wang

Echinococcosis is widely distributed in western China, Sichuan Province, Xinjiang Region, Qinghai Province and the Tibet Region being highly endemic. Cystic echinococcosis caused by *E. granulosus* is more widespread than alveolar echinococcosis caused by *E. multilocularis*. A national survey in 2001 estimated that the prevalence of human cystic echinococcosis in western China was >0.5%, with 380 000 patients, constituting >75% of all Chinese echinococcosis cases. Herdsmen had the highest prevalence (>2.3%) among all occupational groups, and Tibetans constituted 69.3% of all patients. The intermediate and definitive hosts are abundant in these vast, extremely sparsely populated areas. *E. multilocularis* and *E. granulosus* have complex life cycles due to the involvement of domestic and wild animal hosts. Sheep and goats are the commonest intermediate hosts of *E. granulosus* in Gansu, Ningxia and Inner Mongolia, whereas yaks are the hosts in Qinghai, Sichuan and Tibet. In China, dogs are common definitive hosts and the most important source of human alveolar and cystic echinococcosis infections.

These endemic areas have poorer socioeconomic development, sparser populations, poorer infrastructure and more minority populations than eastern China. In Buddhist areas, stray dogs represent a major source of both *E. multilocularis* and *E. granulosus*. High illiteracy and the variety of dialects represent additional challenges for the dissemination of health information. A systematic, long-term national prevention and control programme was budgeted in 2005 and implemented in 2006 in 10 counties in Sichuan Province. In 2010, the programme was extended to 170 counties in seven provinces or regions, namely Sichuan, Xinjiang, Inner Mongolia, Gansu, Qinghai, Ningxia and Tibet. The goals were to decrease the seropositivity rate in children aged <12 years by more than 40% and the infestation rate in dogs by 50% in each county by the end of 2010. The measures adopted include human population screening, patient treatment, health education, capacity-strengthening and deworming of dogs. Many mostly asymptomatic patients were found and treated, and unprecedented large-scale health education targeting all people and dog deworming programmes were started. In Sichuan Province, the rate of patients found positive during mass screening dropped to 3% (717/237 399) in 2010 from 2.4% (4247/178 358) in 2008. Population screening is the best way to increase awareness among local people and officials. Health education of the public requires the sustained involvement of local people. In the same province, the overall dog infection rate, as measured by the coproantigen enzyme-linked immunoassay, dropped to 15.9% (4638/29 109) in 2010 from 28% (4190/14 964) in 2008. Deworming dogs monthly is not easy, and reducing the number of stray dogs is difficult. The human consequences of the disease are more relevant than animal echinococcosis for both governments and people.

5.1.3 Control in Cyprus and the Mediterranean area

G. Christofi

E. granulosus is the only member of the genus *Echinococcus* reported in Cyprus. During the past century, several programmes for controlling *E. granulosus* have been used, with two main control strategies. The first is a horizontal approach, which includes education, sanitation and meat inspection; and the second is a vertical approach, which targets the parasite and involves dog control, testing with arecoline or coproantigen and/or treatment with praziquantel.

The main provisions of the Cyprus programme were:

registration of owned dogs and control of stray dogs throughout the island,
testing of dogs with arecoline or the coproantigen enzyme-linked immunoassay,
treatment of dogs with praziquantel at 5 mg/kg body weight,
control of the movements of food animals and dogs,
education of owners about proper feeding of their dogs,
education of the public to secure their cooperation and assistance to the plan,
control and supervision of all slaughtered animals, and safe disposal and destruction of all infested viscera,
organized disposal of dead animals by burning or burial,
making hydatid disease a notifiable disease in both humans and animals and
drafting appropriate legislation to cover all the relevant provisions of the programme.

As a result of these activities, the last infected dog was found in 1996. The last cases of hydatid disease were recorded in goats in 2003, in sheep in 2004, in cows in 2005 and in mouflons in 2010.

A. Dakkak¹

Both cystic echinococcosis caused by *E. granulosus* and alveolar echinococcosis caused by *E. multilocularis* have been reported in several countries of the Mediterranean area. *E. granulosus* has always been present in the area and is the most common species. This parasite depends on the dog–sheep cycle and is actively transmitted in all pastoral regions where sheep, cattle and camelids predominate. *E. multilocularis* occurs only sporadically in limited areas of France, Serbia and Montenegro, Turkey, Tunisia and Morocco. However, recent evidence indicates its spread into other regions of the Mediterranean. Given the lack of well-documented data and the fact that cystic echinococcosis is not a notifiable disease in the majority of Mediterranean countries, the precise incidence and prevalence of the disease in humans and animals are not known. Published data suggest that prevalence is rather high in North Africa, Turkey, Greece and in several regions of Italy and Spain. A number of factors contribute to the increased prevalence and the spread of cystic echinococcosis in the area. These include the diversity of livestock production systems (predominantly extensive, traditional animal husbandry), small, ill-equipped and unsupervised slaughter-houses, illegal and family slaughtering practices, low public awareness of hydatid diseases, and the high population of stray dogs. Cyprus is the only country where an eradication programme has been successfully implemented. There have been, however, important developments during the past decade in the epidemiology of cystic echinococcosis, the diagnosis of canine infection, in strain characterization and in immune strategies against the disease in animals.

¹ Dakkak A. Echinococcosis/hydatidosis: A severe Threat in Mediterranean countries. *Veterinary Parasitology*, 2010, 174:2–11.

5.1.4 Control in Kyrgyzstan

K. Abdykerimov

Echinococcosis is the most important zoonosis in Kyrgyzstan, with 700–800 human cases reported each year. Human echinococcosis in Kyrgyzstan is caused by two parasites, *E. granulosus* and *E. multilocularis*. The prevalence of cystic echinococcosis has increased since 1991: in sheep from 30.6% to 58.7%, in cattle from 20.7% to 36.7%, in yaks from 0.5% to 12.7% and in pigs from 0.9% to 4.7%. The prevalence in dogs is highest in central Kyrgyzstan and Naryn Oblast, with 20% *E. granulosus* and 19% *E. multilocularis*. The World Bank has committed US\$ 10 million to a project for the control of cystic echinococcosis, brucellosis, anthrax and rabies and two animal diseases: foot and mouth disease and peste des petits ruminants. The strategy encompasses an information, education and communication programme to provide brief information about echinococcosis via the media; collecting baseline data from 200 randomly sampled dog faecal samples in each district and city; dog registration and deworming four times a year and treatment with praziquantel; elimination of stray dogs; encouraging the slaughter of all livestock in slaughterhouses; and vaccinating lambs with the EG95 vaccine. A pilot vaccination programme is being implemented in Ak Talinsky district, Naryn Oblast, and the results will be analysed after 2 and 3 years.

5.1.5 Control in South America

C. Gavidia

All the control programmes used in South America are based on experience accumulated in successful programmes elsewhere. Most programmes started in the 1970s, with the exception of Uruguay where a programme began in the 1990s. The programmes have required extensive field infrastructure, training of personnel and high transportation costs to deworm a large dog population (e.g. Uruguay) or to deworm a smaller number of dogs widely distributed over vast regions inaccessible by car for part of the year (Argentina and Peru). Overall implementation therefore required massive funding both at the beginning and for maintenance throughout the operational period.

The countries and areas that have attempted control programmes are: Argentina (Rio Negro, Chubut, Tierra del Fuego, Neuquen), Brazil (Rio Grande do Sul), Chile (Regions XI and XII), Peru (Junin) and Uruguay. Unfortunately, many of these programmes have been either discontinued (partially or completely) or modified from the original design, losing the important advances that had been obtained in a few years, such as in the case of Peru. The other programmes, although continued, have not reached the main objective of eliminating *E. granulosus* as the activities have not been maintained over time; that is the situation in Argentina. The partially successful programmes in Argentina and Chile are working in only a small part of the endemic areas in these countries.

Why is it so difficult to implement and maintain a successful control programme? Possible answers, not necessarily in order of importance, are that farmers, most at a low socioeconomic and educational level, do not perceive *E. granulosus* as a health problem for their livestock. They do not recognize that losses in wool, meat or milk are a consequence of the parasite, and most do

not even associate the parasite with the cysts found in the lungs and livers of their animals. They do not even correlate the presence of the parasite with the cysts in themselves, their family members or friends. Secondly, there is lack of political interest, and the governments and health authorities have been unable to organize and implement appropriate control programmes against this zoonosis. Therefore, there is no planning, funds are insufficient, personnel have not been adequately trained, and there is lack of experience and knowledge. Thirdly, there has been no interaction between the government, research groups (such as universities) and local authorities in endemic communities or villages. Finally, unforeseen situations (regional violence and terrorism) and geographical and climatological difficulties (snow, lack of roads, landslides, rain) have interfered with the success of the programmes.

More than 30 years after the beginning of the South American control programmes and use of a 100% efficient, safe drug, praziquantel, not one endemic area on the continent has reached elimination or eradication status. Only two programmes (Region XII in Chile and Uruguay) have been able to maintain the attack stage; nevertheless, the programmes have been partially discontinued or modified. It has been impossible to organize a consistent control programme in Brazil, Peru and many endemic areas of Argentina and Chile. Serious difficulties are still encountered in using praziquantel as a control strategy. The recommended programme (eight times at year) is economically and politically unsustainable, not only because of the cost (e.g. for pills, transport, salaries and infrastructure) but also because of the vast territory over which dogs live, owners' reluctance to treat their dogs frequently or complete lack of interest in treating their dogs, inability to ensure complete ingestion of the pills by dogs and inaccessible roads (due to adverse weather).

Use of the intermediate host vaccine (EG95) is being evaluated in Argentina. The problems identified by experts working in endemic areas of Argentina include the fact that sheep farmers do not recognize cystic echinococcosis as a problem and are therefore not interested in vaccinating their flocks. They often do not vaccinate their sheep against other diseases, are reluctant to corral their animals on the vaccination day and have limited infrastructure for carrying out the vaccination.

5.1.6 Control in sub-Saharan Africa

T. Romig

Cystic echinococcosis occurs in most regions of sub-Saharan Africa, but the frequency differs considerably among and within countries. Human cases in particular appear to be focally distributed, due to a number of environmental and behavioural factors, i.e. density of livestock, presence of dogs, uncontrolled slaughter and insufficient hygiene. In addition, the various taxa of *Echinococcus* spp. differ considerably in their infectivity to different host species, including humans. Genetic characterization of isolates, which is necessary to evaluate their infectivity, has so far been done in only a few countries; the results indicate that the diversity of *Echinococcus* spp. is greater than on any other continent. The incomplete data available show that sympatric taxa may infect different hosts, others may be geographically restricted, some life cycles involve livestock and others wild animals. Despite considerable economic losses, the political will to control cystic echinococcosis effectively is often lacking, as the disease does not seriously affect

the health of the urban population or cause significant losses in intensely managed meat production schemes. It is a typical affliction of rural pastoral societies with little access to health facilities, whose economic losses are rarely considered and are difficult to quantify.

Control programmes against cystic echinococcosis have been successful, even in remote areas, but have proven difficult to maintain for financial and logistic reasons. Identification of the locally prevailing *Echinococcus* taxa, their distribution, host preferences and pathogenicity is urgently needed to increase cost-efficiency by targeting control and preventive efforts to those transmission cycles that are locally most important for human health and the production of vital animal resources. The interaction between wildlife and livestock transmitted forms is likely to affect human and animal health in the vicinity of national parks and game reserves, but may also pose risks for wildlife species, which may be faced with additional infection pressure from surrounding and encroaching pastoral communities.

5.1.7 Control in Tunisia

L. Samia

Cystic echinococcosis remains the most important parasitic disease in Tunisia, leading to veterinary, public health and socioeconomic problems. Cystic echinococcosis is predominantly a rural disease. The overall cost of the disease is about US\$ 15 million annually. In 1986, the ministries of public health and agriculture decided to implement a national control programme. In the planning phase, several baseline surveys were conducted to obtain epidemiological data on cystic echinococcosis in the human population and in definitive and intermediate hosts. Over 30 years (1977–2005), the average annual incidence rate in humans dropped only slightly, from 15 to 12.6 per 100 000, showing that this zoonosis remains a public health problem in Tunisia. A retrospective study to determine the annual surgical incidence of human cystic hydatidosis between January 2001 and December 2005 showed a total of 6249 surgical interventions. The highest proportion was recorded in the hospitals of Tunis District (42.9%), with 95% of them in Ariana Hospital alone. The annual incidence was 11–13.6 per 100 000, and the 5-year incidence was 63.2 per 100 000 inhabitants, giving an average annual incidence rate of 12.6 per 100 000. Governorates of the northwest and western–central regions of the country are the most highly endemic areas, with average annual incidence rates of 19.2–33.9 per 100 000 population.

The mean prevalence rate was 24% of examined dogs, with the highest prevalence rate among young dogs, which are massively infected. The prevalence decreases in older dogs because they develop acquired immunity to re-infection in endemic areas. Among livestock, sheep are the most commonly infected with hydatid larvae (16.5%), followed by cattle (8.6%), donkeys (7.9%), camels (5.9%) and goats (2.9%). Sheep are the principal source of *E. granulosus* infection in the north and centre of the country, while camels act as an important reservoir of the parasite in the south. The prevalence and intensity of infection with hydatids increases with age in all intermediate hosts, with linearly increasing age–prevalence and age–intensity curves, indicating that *E. granulosus* is in an endemic steady-state equilibrium in Tunisia and therefore amenable to control. Ultrasonography confirmed the high prevalence of ovine hydatid cysts (40.4%), indicating a mass screening approach for cystic echinococcosis in a hydatid control programme.

The 'domestic rural' life cycle in which dogs are in close contact with flocks predominates, contributing to the highest infection rates in dogs, sheep and humans. A sylvatic cycle involving jackals (9.7%) and wild boar (15.8%) has been confirmed.

No cystic echinococcosis control measures have been undertaken by the national authorities yet. The high rate of dog *E. granulosus* re-infection 2 months after taenicial treatment requires frequent (every 6 weeks) praziquantel treatment to decrease *E. granulosus* pressure and prevent increased larval populations in sheep. Sheep vaccination against hydatidosis could reduce the length of the attack phase, and health education could change the attitude of rural inhabitants and thereby also reduce infection of dogs.

5.2 Control of *Echinococcus multilocularis*

T. Romig

Throughout its geographical range, the life cycle of *E. multilocularis* is based on wildlife hosts, involving canids (foxes, coyotes, jackals, wolves) as definitive hosts and arvicoline rodents as intermediate hosts. Domestic carnivores (dogs, cats) do not contribute substantially to the maintenance of the parasite's life cycle, except under special circumstances (Tibetan plateau and, formerly, Saint Lawrence Island off Alaska).

The parasite shows great plasticity in adapting to different regional conditions and host species, including man-made environments in temperate zones (meadows, agricultural lands, e.g. in central Europe); arctic and subarctic natural environments (circumpolar); high-altitude semi-natural grassland (China); natural forests and bushland (Japan) and urban areas (central Europe). In addition, the parasite readily exploits newly introduced species as hosts, such as raccoon dogs, coypu and muskrats in central Europe and introduced voles on Svalbard archipelago, Norway. Owing to this diversity, any control strategy must be tailored for regional specificities.

In principle, there are four options for prevention and control. Information and education has no impact on the life cycle but may reduce the risk for human infection. In Europe, however, the risks are difficult to specify or cannot be avoided (e.g. working in agriculture). Regular deworming of domestic carnivores again has no or only a minor impact on the life cycle, but the risk of humans is reduced. Because of the effort involved, this option should be restricted to the subpopulation of pet animals that catch wild rodents. Culling of host species is applicable only to definitive hosts (e.g. foxes, stray dogs), but it appears to be highly inefficient for a variety of reasons (effort, social acceptance). Deworming of wild and stray definitive hosts resulted in drastic reductions in prevalence in European and Japanese studies in which anthelmintic baits were distributed, but its sustainability and cost-benefit are controversial.

Anthelmintic baiting has been the subject of a number of studies. Two large-scale studies in Germany, covering 3400–5000 km² and with bait distribution by aircraft, reduced the prevalence in foxes from 67% to 15% and from 26% to 3% in the two studies. The prevalence relapsed to pre-control levels after termination of baiting. Small-scale studies of local bait distribution in peri-urban areas (as small as 1 km²) proved effective in reducing the prevalence in foxes but was labour-intensive as bait was distributed by hand. Bait distribution by aircraft combined with

distribution by hand in human settlements reduced the prevalence in foxes to detection threshold in a 250-km² area in southeast Germany. The long-term sustainability of this integrated approach is under evaluation.

The accumulated experience of bait distribution studies shows that tools for large-scale and focal application of anthelmintic baits are available and ready for application. As the studies have shown that long-term application is necessary, the relevant political and financial commitment must be available from funding bodies (communes, counties, local government). This is usually difficult to obtain in view of the relative rarity of human cases.

6. Advances in programme execution and a proposal for an integrated pilot project for control of cystic echinococcosis

6.1 EG95 vaccine and immunization and evaluation of new strategies and regimes

M. Lightowers

After the 1950–1970s, when there was intense interest in controlling cystic echinococcosis, efforts to control the disease declined markedly, even though the infection remained highly prevalent in large areas of Africa, Asia and South America. The decrease in interest might have been due to the poor efficacy of the many attempts to control the disease in continental areas. The only available control methods have been treatment of dogs with anthelmintics, dog population control, control of livestock slaughter, disposal of offal and public education. Limitations inherent to these methods, particularly in continental areas, restricted the effectiveness of disease control efforts.

The EG95 vaccine for use in livestock is a new tool for the control of cystic echinococcosis transmission. Numerous trials of the vaccine have been undertaken in many countries, all of which showed the vaccine to be highly effective and reliable. The vaccine has not yet been incorporated into any wide-scale control programme, perhaps because no new programmes have been initiated since its development. The EG95 vaccine has been evaluated in field trials in Argentina, China and Italy, but, because of their limitations, these trials will not provide clear scientific evidence of the value of EG95 vaccination for the control of cystic echinococcosis. The principal limitations are the accuracy of the methods for measuring disease prevalence and intensity before control activities and for evaluating disease transmission during and after interventions.

Scientifically rigorous evaluation is needed of potential new regimes for the control of cystic echinococcosis incorporating livestock vaccination. The results of such evaluations would form the basis for a clear, evidence-based plan for future control activities and attract renewed investment in cystic echinococcosis control. The control options would be evaluated on the basis of their effectiveness, cost, feasibility and sustainability, and selection would be guided by data from mathematical models. Four scenarios should be evaluated, representing different levels of investment:

option A: EG95 + praziquantel:

- *Option A₁*: vaccination of all young animals (twice), one annual booster immunization of all previously vaccinated livestock, 6-monthly treatment of all dogs with praziquantel;
- *Option A₂*: vaccination of all young animals (twice), one booster immunization of previously vaccinated livestock at 1 year of age, 6-monthly treatment of all dogs with praziquantel;

option B: EG95 only:

- *Option B₁*: vaccination of all young animals (twice), one annual booster immunization of all previously vaccinated animals; or
- *Option B₂*: vaccination of all young animals (twice), a single booster immunization of previously vaccinated livestock at 1 year of age.

The controls would consist of 6-monthly treatment of all owned dogs with praziquantel only or no intervention. The methods of assessing pre- and post-control levels of cystic echinococcosis transmission would be critical aspects of the design of an evaluation trial.

6.2 Integrated approaches for cystic echinococcosis control

P. Torgerson

A number of approaches could be used to control or eliminate cystic echinococcosis: anthelmintic treatment of dogs, improvement of slaughter facilities, use of EG95 vaccine, dog population management (registration, reproduction control, humane culling), culling of old or infected sheep, community education, and combination of cystic echinococcosis control activities with those for other diseases. None of these approaches alone would result in control or elimination, and an integrated approach is required. The advantages and disadvantages of each of these approaches and programme components were reviewed.

6.2.1 Programme components

Intensive programmes for anthelmintic treatment of dogs have been successful, leading to rapid cessation of transmission to humans. The limitations are the high number (eight) of treatments per year, the cost and logistics of carrying out intensive programmes, the low compliance of dog owners, and the difficulty of treating stray dogs.

Improvement of slaughter facilities ensures that animals are slaughtered under veterinary supervision, and this should improve the safe disposal of offal in order to interrupt the disease cycle. Slaughterhouses provide opportunities for surveillance of echinococcosis and other diseases; however, such facilities are found in only a few endemic areas. Modern slaughterhouses are usually expensive, but building low-cost concrete-slab buildings in remote areas is a viable alternative.

The trials with EG95 vaccine indicate that it is highly effective in sheep and that vaccinated lambs do not become infected with *E. granulosus*. Vaccination therefore interrupts the cycle. Farmers are, however, reluctant to vaccinate sheep when there is no apparent improvement in animal health and also because of the complex logistics of vaccination. The vaccine might also be blamed for losses due to concomitant disease. Costs and licensing represent other challenges to its use.

A source of funding must be identified for proper dog population management, as dog owners will be more likely to cooperate if interventions (registration and deworming) are free. If dog owners are obliged to pay for registration, additional 'stray' dogs may result. Legislation is required and should be adapted to the local conditions and to the behaviour of dog owners and dog status in order to control both unregistered owned dogs and ownerless dogs. Culling dog would immediately prevent transmission from dogs and have other potential benefits, such as fewer dog bites and transmission of other zoonoses. However social reluctance to indiscriminate large-sale dog elimination is likely to lead to opposition to culling operations as well as other dog-related interventions including testing and deworming. Selective dog elimination and promotion of responsible dog ownership for proper dog population management including reproduction control should be carried out instead.

Culling sheep immediately reduces transmission to dogs, and this approach might be cost-effective. It may, however, require heavy financial input early in the programme, and many farmers may be reluctant to allow culling of older proven stock. An alternative option would be to treat sheep with oxfendazole, an antiparasitic drug that might reduce the number of viable protoscolices in cysts, although further studies are required to determine the appropriate dosage.

Education can be relatively cheap and might facilitate other parts of the programme, improving community involvement and participation. It is, however, of questionable efficacy on its own.

6.2.2 Integration

The activities of the different sectors involved must be integrated, particularly agricultural and veterinary services and the health sector. This will reduce costs, facilitate implementation of all parts of the programme and improve participation. Integrating certain programme components, such as use of praziquantel in dogs, EG95 vaccination of sheep and culling of older sheep, can be cost-effective.

Integration with control programmes for other zoonoses, such as dog rabies (vaccinate against rabies and treat dogs with praziquantel), brucellosis (vaccinate sheep with both rev 1 and EG95 vaccine or identify pregnant and infected ewes by ultrasound) and clostridial disease (infect sheep with clostridial toxoids and EG95 vaccine). The advantages would be shared logistics, which would in principle decrease costs, and possibly greater compliance, as more than one service is provided at one point. The different vertical programmes may, however, be reluctant to share resources, and the different 'cultures' associated with different diseases or interventions might hamper implementation.

7. History of the informal working group on echinococcosis

F.X. Meslin and D. Vuitton

WHO first established informal working groups on echinococcosis in 1985, and for 10 years, under the leadership of Professor J. Eckert (Zurich, Switzerland), they facilitated communication among interested scientists working in specialized echinococcosis areas. In 1995, the Veterinary Public Health Unit at WHO created an informal working group on echinococcosis, bringing together scientists involved in research on echinococcosis – irrespective of their specialty, field of interest or type of echinococcosis studied – to assist WHO in establishing international networks on relevant, important problems in echinococcosis, and reporting their findings to WHO for review and appropriate action.

WHO identifies and nominates the coordinator of the group for a 4-year term. He or she is assisted by a coordinating board, which is also renewed every 4 years. In principle, the next coordinator is chosen by members of the informal working group to ensure a certain continuity. Professor Dominique A. Vuitton, WHO Collaborating Centre for Prevention and Control of Human Echinococcosis, University Hospital, Besançon, France, was coordinator for 1995–1999; Dr Peter Schantz, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, for 2000–2004; and Dr Philip Craig, Cestode Zoonoses Research Group, School of Environment and Life Sciences, University of Salford, Manchester, United Kingdom, for 2005–2010. Dr Peter Kern, Section of Infectology and Clinical Immunology, Department of Internal Medicine, Ulm University, Germany, has agreed to be coordinator for 2011–2015.

The informal working group on echinococcosis is an open group of researchers and experts. People interested in participating in this network or wishing to establish a new network should send their name, a description of their research team and the part they plan to play in the proposed network. All proposals are submitted to the coordinating board and to WHO. If the work undertaken by a network leads to a proposal for international classification or standardization or major recommendations for treatment, prevention and control, it must be submitted to WHO for review.

The WHO informal working group on echinococcosis is expected to continue to play a major role in information exchange and in stimulating research of public and veterinary public health interest for the prevention and control of these diseases. The products of the group have dealt mostly with the treatment of cystic and alveolar echinococcosis in humans. In 1993,¹ WHO published the report of the WHO working group meeting on echinococcosis research and control in Beijing, China. In 1996, the group published *Guidelines for treatment of cystic and alveolar echinococcosis in humans*² on the basis of the outcome of two previous meetings, one held in Besançon, France, in 1992³ and one organized in Al-Ain, United Arab Emirates in 1994.

¹ *Report of WHO working group meeting on echinococcus research and control, Beijing, China, 12 October 1993* Geneva, World Health Organization, 1993 (VPH/93.131) http://www.who.int/hq/1993/vph_93.131.pdf.

² WHO Informal Working Group on Echinococcosis. Guidelines for treatment of cystic and alveolar echinococcosis in humans. *Bulletin of the World Health Organization*, 1996; 74:231–242.

³ *Report of the WHO working group meeting on clinical medicine and chemotherapy of alveolar and cystic echinococcosis, Besançon, France, 10 October 1992*. Geneva, World Health Organization (WHO/CDS/VPH/93.118).

In 2001, WHO published guidelines on PAIR.¹ Annex 1 of that document contained the group's classification of ultrasound images of cystic echinococcosis cysts, which is recognized internationally. In 2001, the PNM classification of alveolar echinococcosis was proposed in an WHO/OIE manual on echinococcosis and published as the WHO classification of alveolar echinococcosis.² In 2007, consensus on the diagnosis and treatment of cystic and alveolar echinococcosis was achieved during a WHO co-sponsored meeting in Besançon and Salines Royales d'Arc-et-Senans, France, and published in 2010.³

In the field of human and animal echinococcosis, WHO and the OIE published a manual on echinococcosis in humans and animals.⁴ The section of the guidelines on animals was in need of updating, and Dr Philip Craig of the informal working group on echinococcosis initiated the task. An advanced draft was discussed at the consultation in June 2011 (see section 8.6).

8. Conclusions and recommendations

8.1 Intersectoral collaboration

Good, effective medical and veterinary interaction is needed for echinococcosis prevention and control. As the impact of the disease on livestock health and production is not obvious, farmers and official veterinary and livestock services often do not see the relevance of a programme. In endemic areas, however, the impact of these zoonoses on human health is significant, and the health sector often leads in echinococcosis control, trying to involve the veterinary sector for animal-related interventions. Dedicated veterinary public health services should be strengthened or established, preferably in the health sector, for effective collaboration with the veterinary sector in order to prevent and control echinococcosis and other zoonoses effectively.

8.2 Surveillance, case definition and classification

The consultation recommends that both cystic and alveolar echinococcosis be made notifiable to national authorities as named diseases. The effect of making them notifiable, particularly with regard to under- and multiple reporting, should be further studied. Studies should also be conducted on the reliability of data on echinococcosis collected in community surveys and from hospital records and the relation between disease prevalence and incidence.

A number of synonyms are used for the two diseases, which are confusing for unspecialized physicians or clinicians, who are only sporadically involved in the management of cases. The

¹ PAIR: *puncture, aspiration, injection, re-aspiration: an option for the treatment of cystic echinococcosis*. Geneva, World Health Organization, 2001 (WHO/CDS/CSR/APH/2001.6).

² Kern P et al. WHO classification of alveolar echinococcosis: principles and application. *Parasitology International*, 2006; 55(Suppl.):S283–287.

³ Brunetti E, Kern P, Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Tropica*, 2010; 114:1–16.

⁴ Eckert J et al., eds. *WHO/OIE manual on echinococcosis in humans and animals: a public health problem of global concern*. Geneva, World Health Organization, and Paris, World Organisation for Animal Health, 2001.

case definitions recently proposed by the WHO informal working group on echinococcosis¹ should therefore be used. WHO classifications are available for alveolar echinococcosis and for hepatic cysts of cystic echinococcosis. The consultation recommends that a classification of extrahepatic involvement of cystic echinococcosis be developed rapidly, and that a relevant subgroup of the working group design a graphical decision-tree for differentiating alveolar from cystic echinococcosis.

Sensible, informed use of serology (with a high positive predictive value) should be encouraged. Its sole use in surveillance was discouraged by this consultation, as imaging findings are the primary source for determining the prevalence and incidence of cystic echinococcosis. Specific training is needed, and the consultation is encouraging specialized courses at the WHO collaborating centre in Pavia, Italy, and at the Instituto de Medicina Tropical, Alexander von Humboldt, Cayetano Heredia, Lima, Peru.

A comparative evaluation of coproantigen tests is needed, with double-blinding.

8.3 EG95 study protocol

Highly intensive intervention programmes that have been successful in developed countries are not likely to be feasible in low-income or middle-income countries, where most of the disease burden occurs. The consultation assessed the results obtained with a vaccine against cystic echinococcosis (developed by Dr M. Lightowlers) and identified potential sites in Kyrgyzstan, Peru and Tunisia, where well-controlled efficacy and feasibility studies could be conducted.

The consultation proposed that “alternative strategies involving vaccination of sheep in addition to classical interventions would have a much greater chance of success in these countries. It concluded that it is time to initiate a definitive field trial.”

The consultation recommended the inclusion of a praziquantel-only group in the vaccine field trial and double-blinding to avoid including a community with no treatment. It also recommended inclusion of the culling of old sheep, depending on the location of the trial.

The inclusion of praziquantel for dog deworming in the EG95 immunization trials should reduce transmission to humans more rapidly and may therefore be required from an ethical point of view. If human ultrasound surveys are part of the programme, enough drugs must be available to treat identified cases as per WHO guidelines, for obvious ethical reasons.

The timing of sheep vaccination should be chosen to avoid problems of concomitant disease. The issue of whether infection occurs early in lambs or accumulates over a lifetime was debated, as it has important implications for the effectiveness of vaccination. If infection accumulates over a lifetime, vaccination of old animals may be effective, but the possible benefits of vaccinating older sheep should be weighed against the effort involved.

¹ Brunetti E, Kern P, Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Tropica*, 2010; 114:1–16.

Culling of old sheep may, however, be difficult for legal or cultural reasons. Compensation or replacement by younger, naive animals should be considered in the programme, with its financial implications. Removing animals aged over 5 years would certainly have a positive impact on disease transmission but would have negative consequences on the cost–benefit ratio if the costs are high. One-year-old lambs could be used as indicators of transmission.

The consultation requested Dr Lightowlers to revise the proposal on the basis of the discussion and to include cost estimates. He will share the draft at the 24th International Congress of Hydatidology in September in Urumqi, China. The consultation estimated that a multicentric pilot study in the three countries, lasting 5 years, would cost about US\$ 10 million. Potential sources of funding with an interest in neglected tropical diseases are the Bill & Melinda Gates Foundation, the European Union Seventh Framework Programme, the United Kingdom Department for International Development, the United States Agency for International Development, the World Bank and FAO. A letter of intent for potential donors should be prepared, presenting echinococcosis as a major neglected tropical disease.

8.4 Implementing control programmes

8.4.1 Dog registration, culling and population management

Dog registration must be handled sensibly. Imposing a fee is likely to discourage registration and increase the number of free-roaming dogs without a responsible owner. Indiscriminate mass dog culling is not recommended, as it has no long-term effect on the size of the dog population; furthermore, as many so-called stray dogs are likely to have an owner, culling may antagonize part of the local community. Use of inhumane methods for dog elimination may elicit opposition from communities to the entire control programme. Dog reproduction control and other measures for reducing the carrying capacity of the environment for dogs, such as eliminating food and water sources, are viable sustainable alternatives to dog elimination.

8.4.2 Education of communities

Community awareness-raising and education facilitate acceptance of control measures and stimulate community involvement in programme planning and implementation.

8.4.3 Integrated control

Combination with other control programmes, such as for rabies and leishmaniasis, may involve changing ‘culture’. Integrated control projects are being conducted within the framework of the European Union-funded Integrated Control of Neglected Zoonoses programme in Africa.

8.5 Definition of elimination

The consultation discussed a precise definition of cystic echinococcosis elimination. The issues involved include geographical scope (elimination at country level or by administrative division), human age groups, and animal species (sheep only, other livestock, dogs). They discussed whether elimination should cover both humans and animals and the definition of elimination of human cystic echinococcosis as a public health problem. Control and elimination thresholds in humans, sheep and dogs should be defined.

The consultation proposed a definition of 'elimination of human cystic echinococcosis as a public health problem' at national level or in areas within a country as follows:

No cases in humans <15 years of age,

<0.1% cystic echinococcosis cases in sheep aged <3 years and other key livestock species and

<0.01% dog infection rate with *E. granulosus*.

After the criteria are met, a consolidation phase should be initiated.

8.6 WHO guidelines for the control of echinococcosis

The document presented by Dr P. Craig is comprehensive, and each of the nine chapters constitutes a review. Guidelines are expected to provide synthesized evidence and guidance for action. The consultation discussed the expected target audience of the document and requested a more 'user friendly' document. Professor Kachani proposed writing a summary, with an appendix or supplement containing more concise, practical information. The summary should also include definitions of control, stages and end-points, information on identification methods for tracing animals and culling older livestock, and specify minimum requirements for infrastructure and data collection. The dog vaccine section was considered highly contentious, as was the section on dog culling. 'One Health' should be added to the structures in chapter 5. The dog population management options in chapter 4 should be revised, taking into consideration principles for animal welfare (World Society for the Protection of Animals, WHO, FAO, OIE) and guidelines for dog rabies control (WHO/World Society for the Protection of Animals and the Alliance for Rabies Control).

The document should be a combined product of WHO, OIE and FAO. OIE might be offered the possibility of publishing it, although that would mean that it would have a cost.

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