DISCONTOOLS

Echinococcosis
Summary

Introduction

This note provides a brief summary of an analysis undertaken by a DISCONTOOLS group of experts on Echinococcosis. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details can be downloaded from the web site here.

Disease profile

Cystic echinococcosis (CE), also known as hydatidosis or hydatid disease, is caused by the larval stages of various species of the *Echinococcus granulosus* (sensu lato) complex. Taxa within this complex were formerly identified as genotypes (G1-10) or strains of *E. granulosus*, but the substantial biological and genetic differences between them have led to a subdivision into at least five species. For the European situation, this complex comprises *E. granulosus* sensu stricto (s.s.) (G1, G3 and other variants), *E. equinus* (G4, 'horse strain'), *E. ortleppi* (G5, 'cattle strain'), *E. canadensis* (G8, G10) and *E. intermedius* (G7). In Europe, *Echinococcus granulosus* s.s. is the most important in South and Southeast Europe and primarily maintained via a sheep/dog cycle. *E. intermedius* is responsible for CE in the Baltic countries and Poland and is also focally distributed in South Europe (Portugal, Italy, Corsica), this species circulates between pigs (additionally wild boars in Corsica) and farm dogs. The other *Echinococcus* species are of minor importance for CE in Europe. The latest estimate of the global public health impact of CE is 188,079 new cases per year, with a disease burden of 183,573 DALYs. The far lower health burden per patient compared with alveolar echinococcosis (AE) is due to the low mortality. In contrast to AE, there is an economic impact caused by CE in livestock, which is often difficult to quantify.

E. multilocularis occurs across the northern hemisphere and causes AE. The adult tapeworm resides in the small intestine of the definitive hosts (foxes, dogs and other wild canids) and worms, segments and eggs are passed in the faeces and contaminate the environment. In the intermediate rodent host (mainly voles) the larval alveolar form occurs mainly in the liver. Based on published data, it was estimated that 18,451 true AE cases (including underdiagnoses and underreporting) occurred in 2010 worldwide, resulting in a global disease burden of 687,823 DALYs. The large number of DALYs per patient reflects the severity and limited treatment options of AE (as compared with CE with <1 DALY per case (see above). In Switzerland, the number of DALYs per AE patient was estimated at 3.7, ten times less than the global estimate.

Humans acquire the infection via ingestion of *Echinococcus* eggs excreted in the faeces of infected definitive hosts. The eggs are well adapted to survive in the environment for as long as a year in cool moist conditions. Direct contact with infected definitive hosts represents another way of transmission. Both, CE and AE in humans may remain silent for years before the enlarging cysts in the affected organs cause symptoms. *E. granulosus* affects mostly the liver and the lungs forming expansive growing cysts, *E. multilocularis* predominantly affects the liver as a slow growing, invasive and destructive tumour-like lesion.

Control

Traditional control strategies have focused on breaking the life cycle of the parasite. Approaches against CE in Europe, in theory a preventable disease, included: meat inspection, controlled home slaughter of livestock, correct disposal of offal, preventing dogs having access to raw viscera, treating dogs with praziquantel and practicing good hygiene when handling animals and in slaughterhouses. So far, with the exception of an old successful control program in Iceland, these measures were insufficient for the control of CE in continental Europe. New approaches are urgently needed including elimination of old

infected sheep and vaccination of young lambs before exposure. Integrated control programmes have a high potential to be successful but require a long period of intervention (>5-10 years). This is expensive with the necessity to reach high cover rates for the deworming of dogs as well as for the vaccination of lambs.

Treatment of dogs with praziquantel before movement may be required to avoid introducing *Echinococcus* species into infection-free regions. There are few or no specific signs of disease in carnivores or farm animals, but the detection of cysts of *E. granulosus* at meat inspection allows the identification of infected farms or communities. Dog access to offal should be prevented during home slaughter.
For *E. multilocularis*, which is transmitted in a wild animal cycle, control strategies are more complex. The use of praziquantel baits for foxes reduced significantly the environmental contamination with eggs in rural and urban areas. So far, no continuous control programmes have been established in Europe.

Risk
CE is a serious zoonosis, with rates of human infection ranging from less than 1 to more than 200 cases per 100,000 inhabitants in certain rural populations where there is close contact with domestic dogs (in Asia). CE is considered to be a major neglected zoonosis in southern Europe where the cycle of *E. granulosus* s.s. is allowed to continue.
The incidence of human AE is usually less than 0.5 per 100,000 but can reach >100 cases per 100,000 inhabitants in certain communities. The gradual spread of *E. multilocularis* in Europe is associated with a strong increase of fox populations even in urban areas, posing an increasing risk to the population.
In an endemic area, where CE is uncontrolled, the infection rate in sheep can be >50% and in dogs rates may be >10%. In the case of *E. multilocularis*, endemic areas can have >50% prevalence in foxes.

Diagnostics
Highly sensitive and specific molecular tests are available for the detection and genotyping of *Echinococcus spp*. in clinical material. Diagnostic kits or antigens to detect specific serum antibodies are commercially available for human CE and AE. The specificity of these tests is variable and the sensitivity for early detection is low for both diseases.
The diagnosis of intestinal infections in dogs or other carnivores requires the demonstration of the adult cestodes in the small intestine or the detection of specific coproantigens or parasite DNA in faeces. Coproantigen ELISAs for *E. multilocularis* or *E. granulosus* have been applied in control programmes, but are not commercially available to date. Molecular tools applying commercial DNA-isolation kits are state of the art for the specific diagnosis in definitive host faeces. There are no sufficiently specific and sensitive serological tests for the diagnosis of cystic echinococcosis in livestock.

Vaccines
An effective recombinant vaccine “EG95” for livestock animals has been developed and is available as a commercial product in China and in South America. The vaccine is currently used in the Chinese National Program for Control of Echinococcosis with 155 million doses of vaccine applied in 7 provinces in the years 2016-8. An 8-year long trial of the vaccine in Rio Negro province in Argentina has shown promising results. The vaccine is not registered for use in Europe. It is effective against *E. granulosus* s.s. in sheep, goats and cattle. It is not known if it is effective against other species in the *E. granulosus* s.l. group. Mathematical modelling of the transmission of the parasite suggests that a combined approach to control, involving both medication of dogs and vaccination of livestock, can be effective. Culling of old livestock as part of such a programme would reduce the time required for the livestock population to be free of infection and unable to transmit the parasite to dogs. Vaccines for the definitive hosts may have advantages, particularly an

oral vaccine for foxes to prevent infection with *E. multilocularis*, however attempts to develop a vaccine for the definitive hosts have not been successful so far.

Pharmaceuticals

Treatment for human AE patients is restricted to surgical removal of the metacestode at an early stage of development. At later stages of the disease (around 50% of cases at first diagnosis), further metacestode growth can be prevented in most patients by continuous (life-long) treatment with benzimidazoles (usually albendazole). Survival analyses of AE patient cohorts in France and Switzerland documented that nowadays the patient survival time after first diagnosis is reduced by only 2-3 years. However, the survival time of patients is still much shorter in Lithuania; in 34.4% of AE cases survival was less than one year from diagnosis because the initial diagnosis was only obtained at an advanced stage of the disease. For CE, surgical removal is usually possible, even in advanced stages of the disease. US-guided, percutaneous treatment and antiparasitic medication with benzimidazoles are alternative or accompanying treatment options.

Infection in dogs can be treated with high efficiency with praziquantel (so far no resistance has been documented). *E. granulosus* s.l. control programmes based on several praziquantel treatments a year have been implemented. In the case of *E. multilocularis*, reduction in transmission has been achieved by use of praziquantel baits for foxes monthly over several years.

Knowledge

In Europe, data on human CE are fragmentary due to the lack of dedicated reporting and documentation systems. The epidemiology and distribution of *E. granulosus* s.l. in animals in Europe is partially outdated and fragmented, however, sufficient knowledge is available for the design of advanced integrated control programmes in large parts of southern and southeastern Europe. The reported number of cases of AE in humans is difficult to interpret and it is not possible to compare between European countries as AE is not notifiable in all countries, or in all EU Member States, in addition to diverging systems of diagnostic effort and reporting.

Conclusions

Human cystic echinococcosis (caused by *E. granulosus* s.l.) and alveolar echinococcosis (caused by *E. multilocularis*) are important public health threats in many parts of the world including most parts of Europe. The gradual increase of *E. multilocularis* infection pressure due to the increasing fox populations and the spread to Western, Northern and Eastern Europe is causing concern. Some areas in Europe have an incidence of CE in humans among the highest in the world. There is an urgent need to begin new, active steps to reduce this burden on human health. The necessary tools and knowledge are both available to control the disease. What is needed is European manufacture and registration of the EG95 vaccine for livestock and political will and funding to undertake control programs.

For *E. granulosus* s.l. the best control measure is to interrupt the domestic life cycle of the parasite. This can be achieved with well-designed, integrated control programs based on deworming of dogs and vaccination of lambs over the long-term. Control of *E. multilocularis* is more complex because the cycle occurs within wildlife. The development of (i) improved diagnostic tests to use in monitoring of control programmes and for the individual fast diagnosis in dogs and (i) improved methods to control the infection in wildlife are needed.