Human Echinococcosis: A Neglected Disease?

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Abstract: Human echinococcosis is a zoonotic larval cestode disease usually caused by *Echinococcus granulosus* or *E. multilocularis*. Infection is chronic taking years for symptoms to develop. Because diagnosis and treatment are difficult and reservoirs of infection are maintained in domestic livestock, dogs or wildlife, the disease is difficult to assess in terms of public health and requires long-term control interventions. Estimates of numbers of cystic echinococcosis cases that may occur in 2 large endemic zones, North Africa/Middle East and China/Central Asia, indicates > 423,000 and > 484,000 cases respectively. Globally, 3.6 million DALYs could be lost due to echinococcosis. Echinococcosis is therefore a neglected disease which is under-reported and requires urgent attention in common with a number of other zoonoses in order to reduce morbidity and to help alleviate poverty in poor pastoral areas of the sub-tropics and temperate zones.

Key words: neglected disease, echinococcosis, burden

INTRODUCTION

Infectious diseases include those caused by parasitic protozoan and helminthic organisms, and are recognised as a major cause of morbidity in both human and domestic animal populations [1]. The public health impact of parasitic infections is especially significant for under-developed regions or countries, and may also contribute to medical and/or veterinary health deficits in rural areas of developed countries. In 1975 the World Health Organisation was optimistic following the eradication of small-pox, and listed 5 vector-borne parasitic diseases (malaria, leishmaniasis, trypanosomiasis, filariasis and schistosomiasis) together with some bacterial infections (trachoma, leprosy), as neglected and requiring special attention under a Tropical Diseases Research (TDR) initiative to help reduce human morbidity and mortality. Later, soil-transmitted helminths (STH) and dracunculiasis were also included. Global partnerships in the new century to combat the most important three infectious diseases- HIV, malaria and TB, have also provided a platform for a more robust systems-approach to the control of neglected tropical diseases [2]. The number of disability-adjusted life-years (DALYs) lost globally due to HIV/malaria/TB is around 168 million, and for the main group of ‘neglected diseases’ about 57 million [3]. The DALYs lost globally to food-borne trematodiasis and cysticercosis have not been calculated [4, 5] but these two infections have now been identified by WHO for consideration as neglected diseases requiring control/prevention strategies [3].

There is however, another important group of neglected non-vector-borne zoonotic infections, that are currently not sufficiently prioritised, which includes rabies, brucellosis, echinococcosis, anthrax and leptospirosis [5, 6]. Unlike the former list of neglected diseases mentioned above, transmission of these latter zoonoses cannot be controlled by emphasis on drug treatment (or vaccination) of humans- they are thus difficult to formulate interventions and to apply cost-effective control programmes. Further-

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more, these zoonotic infections have varying negative impacts on domestic animal health and production in poor rural/urban zones and thus their control would also indirectly contribute to poverty alleviation [6, 7]. Therefore prevention and/or reduction in the public health impact of these neglected zoonotic, diseases (NZDs), including echinococcosis, requires interventions directed at reducing or eliminating, the parasite biomass in domestic animal and/or wildlife populations [8].

**ECHINOCOCCUS SPECIES**

Human echinococcosis is caused by organ or tissue infection with the larval cystic stages of cestode species in the genus *Echinococcus*. The two most important zoonotic species being *E. granulosus* (sensu strictu), the cause of cystic echinococcosis (CE), and *E. multilocularis* the cause of alveolar echinococcosis (AE). Apart from the worldwide dominant zoonotic domestic sheep strain (G1 genotype) several other genotypes (or species?) of *E. granulosus* may also be zoonotic (ie. *E. ortleppi, E. canadensis*) [9, 10]. In addition two Neotropical species *E. vogeli* and *E. oligarthrus* that infect wildlife hosts, may cause polycystic echinococcosis, a rare but pathogenic infection of humans [11]. The zoonotic potential of *E. equinus* (or G4 horse genotype /strain of *E. granulosus*) and the newly described Tibetan wildlife species *E. shiquicus*, is unknown but they are probably of low infectivity or non-infectious to humans [12, 13]. In all cases the parasite life-cycles of *Echinococcus* species alternate between an adult segmented egg-producing tapeworm stage in the small intestine of a canid (or felid) definitive host, and a larval cystic stage in the tissues of ungulates, lagomorphs or rodents [10, 14]. Predator-prey associations of these hosts propagate the parasitic life-cycles. A wide range of domestic ungulates are also susceptible to infection with *E. granulosus* and the adult worm is highly infective in domestic dogs. Thus human behaviour is instrumental in facilitating transmission between these domestic animal hosts as a result of traditional pastoral and husbandry practices [15, 16, 17]. Dogs are also susceptible to infection with *E. multilocularis* and *E. vogeli* (whose intermediate hosts are principally rodents) and dogs may constitute a greater zoonotic reservoir of infection compared to natural wild canid hosts. Peri-domestic transmission may occur and could for example sustain a level of transmission of *E. multilocularis* in highly endemic communities [18], but is probably not responsible for long-term maintenance of these *Echinococcus* species adapted to small mammals.

Echinococcosis can thus be considered as a cyclozoonosis or ‘Stage 2’ pathogen where humans may acquire infection from wild or domestic animal hosts- but the parasite cannot be directly transmitted between humans [19]. Therefore from a control viewpoint, treatment of human echinococcosis cases will have no effect on pathogen transmission. Rather, interventions to reduce human exposure or break transmission cycles, by necessity require to be targeted at the animal hosts or reservoirs. This places echinococcosis in a ‘difficult-to-deal-with’ category on at least two counts (also see below). Firstly, unlike the other neglected parasitic diseases humans can not act as a definitive host, and secondly, echinococcosis in livestock (or dogs) is not perceived as an animal health problem. Therefore responsibility for research support and cooperation (eg. medical vs veterinary) and for intervention approaches is not sufficiently clear or prioritised.

**HUMAN ECHINOCOCCOSIS**

The medical impact of the late stages of human cystic or alveolar echinococcosis may be significant though morbidity and mortality are usually grossly under-reported in endemic areas. Pathology and clinical symptoms of human echinococcosis have been described in several recent reviews or papers [20, 21, 22]. These zoonotic cestodiasis are chronic infections in humans with an initial asymptomatic period, usually of several years prior to onset of clinical signs associated with pressure effects or tissue fibrosis/necrosis in the affected organ(s) (primarily liver and other abdominal viscera, but also including lungs, brain, bones or other sites) (Fig. 1). In common with human cesticeriosis, most clinical symptoms and subsequent diagnoses of echinococcosis occur in adults (20-60 years) (Fig.2) but infections in children may also become symptomatic. Imaging techniques (ultrasound, CT scan, MRI, X-ray) are the basis for diagnosis preferably accompanied by a specific serological test [22, 23]. Surgical removal of cysts/cystic masses, cyst drainage or organ resection, are the main form of treatment, often supported by high dose albendazole cover; the latter also has a benefit in medically-only treated cases [24]. Albendazole therapy results in only 5-35% cure or significant improvement for CE/AE but therapeutic benefit, quality and prolongation of life may be significant for 50% of drug treated cases. The cost of surgical treatment for human echinococcosis is high compared to other neglected parasitic diseases ie. approximately US$ 700-7000 in under-developed countries increasing to US$ 20,000->250,000 in Europe or USA [25]. A standard 6 month course (10-15 mg/kg/day) of albendazole for human echinococcosis is approximately US $100-500.

In the commonest form cystic echinococcosis (CE), due to infection with *E. granulosus*, slow growing cysts (hydatids) usually occur in the liver (~70-80% cases) or
Fig. 1. CE case from a) Turkana (Kenya); b) CE, and c) AE cases from Tibetan Sichuan (China); d) ultrasound screening of CE case in Xinjiang (China); e) ultrasound image of CE liver cyst with daughter cysts (Ningxia, China); f) AE case from Gansu (China); g) hepatic ultrasound image of late stage AE (Ningxia, China)
lungs (~5-15% cases) but in some cases anaphylactic shock from acute cyst rupture can be life-threatening. Human alveolar echinococcosis (AE) affects the liver (>98% cases) with eventual tissue fibrosis and necrosis with usually very poor prognosis. Progression of untreated hepatic CE often causes palpable or noticeable large upper abdominal protrusions—for example in children<10 years of age (Fig.1 a,c). In contrast, untreated AE progresses more slowly (5-15 years) and does not usually cause obvious abdominal distension so that the main symptoms of chronic upper abdominal discomfort and jaundice may be tolerated until late end-stage disease (Fig.1 f,g) which has a high fatality rate (50-90%) [23, 24]. There is usually a large discrepancy between hospital records (surgical, medical and out-patient wards) and the real community prevalence of human AE or CE that is determined following active mass ultrasound screening in endemic rural areas [26].

**DISTRIBUTION OF ECHINOCOCCUS**

*Echinococcus* spp. are among the most geographically widespread of the zoonotic parasites, with active transmission in Arctic tundra, boreal, high plateaux, temperate, Mediterranean, semi-desert, savannah, sub-tropical and tropical biomes. The genus occurs in regions of all continents (and many islands) and may involve indigenous or introduced/imported wildlife/domestic mammals. It appears that the *Echinococcus* genus probably evolved as parasites of rodents and their canid or felid predators either in North America or Asia respectively [10]. Wildlife cycles exclusively or predominantly still maintain transmission of *E. oligarthrus* and *E. vogeli* in the Amazonian region and Central America, of *E. multilocularis* in the holarctic/palaearctic region, and for *E. shiquicus* on the Tibetan Plateau. While *E. granulosus* sensu strictu is still maintained within archetypal wolf-cervid cycles in North America and Eurasia [14, 27] and between lions and large herbivores in Africa [28]. Importantly *E. granulosus* has also become very well adapted throughout the world to a number of synanthropic cycles involving dogs and domestic livestock and it is these host-parasite associations that represent the main zoonotic risk. All pastoral regions from arid to temperate or mountain to plateau, where predominantly sheep, but also bovids, camelds or other livestock occur, support domestic cycles of *E. granulosus* with resultant risk of human exposure to echinococcosis. Thus human CE is particularly endemic in rural communities across regions of southern South America, the Mediterranean littoral, Eastern Europe, North and East Africa, the Near and Middle East, Central Asia, the Indian sub-continent, Russia, China, Mongolia, and Australasia [29]. Within endemic zones or countries the presence of *E. granulosus* may be known from occurrence of human CE cases in provincial/district clinics or city hospitals, and/or through detection of hydatid cysts in the viscera of slaughtered livestock at abattoir, butcher, farm or homestead level. Canine echinococcosis is rarely apparent in endemic areas unless dog culling and necropsy is performed, though active ante-mortem screening can be achieved by arecoline purgation or more efficiently by coproantigen ELISA testing of dog faecal samples [23].

Human AE caused by *E. multilocularis*, occurs only sporadically and in most of its northern hemisphere range represents a rare disease. However, relative hotspots of transmission resulting in regular diagnosis of human AE cases occur in parts of western Alaska, central/eastern Europe, the Near East (eastern Turkey and neighbours), eastern Russia, western China (including Tibet) and northern Japan [29]. As mentioned the long asymptomatic period in human AE often means that only a proportion of cases (usually late stage presentations) present at clinics or hospitals. The most practical evidence to assess presence of *E. multilocularis* transmission within a region is from fox (mainly *Vulpes vulpes* in most of the Palearctic endemic zone) necropsies/gut inspection or coproantigen ELISA [30]. Usually prevalence of *E. multilocularis* in foxes is sufficiently high (10-50%) to be more useful in epidemiological studies, rather than the normally low prevalence (1-5%) in rodents [31].

Within the known distribution of echinococcosis, emergence or re-emergence of human cases has occurred over the last 50 years. For example emergence of human CE has become a significant public health problem in sev-
eral ex-Soviet countries of Central Asia (eg. Kazakhstan, Kyrgyzstan, Uzbekistan, Turkmenistan), in the Middle East (Syria, Jordan, Israeli, Arab communities), in western China, the Central Andes (Peru, Bolivia), eastern Europe (Romania, Bulgaria), North Africa (Morocco, Tunisia) and Eastern Africa (Kenya) [17, 18, 29, 31-33]. Furthermore, there is evidence for the spread of *E. multilocularis* in Europe, northern Japan and western China (including eastern Tibet) [9, 31, 34, 35].

**HOW MUCH HUMAN ECHINOCCOCCOSIS IS THERE?**

Establishing the burden of a particular zoonotic infectious disease is not straightforward, and echinococcosis is no exception [4]. For zoonoses there may also be animal health costs in addition to the human health impacts. The latter can be measured in terms of morbidity indices and/or mortality, but for chronic zoonoses like echinococcosis morbidity levels are more useful. The disability adjusted life year (DALY) was developed by WHO as a preferred measure for comparison of both infectious and non-communicable chronic diseases, and between developed

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**Table 1. Estimate based on prevalence and population at risk of numbers of human CE cases in North Africa/Middle East endemic zone (including refs 25, 29, 33, 50).**

<table>
<thead>
<tr>
<th>Country</th>
<th>Surgical incid./10^6 (range)</th>
<th>Prev. % (range)</th>
<th>Pop@ risk (00,000's)</th>
<th>Predicted cases endemic areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morocco</td>
<td>7.4 (0.7 - 15.8)</td>
<td>1.1 (0.9 - 1.3)</td>
<td>82</td>
<td>90,000</td>
</tr>
<tr>
<td>Algeria</td>
<td>3.4 - 4.6</td>
<td>[1]</td>
<td>82</td>
<td>82,000</td>
</tr>
<tr>
<td>Tunisia</td>
<td>15 - 56</td>
<td>2.3 (0.4 - 3.6)</td>
<td>25</td>
<td>57,500</td>
</tr>
<tr>
<td>Libya</td>
<td>1.7 (&lt;0.3 - 4.5)</td>
<td>14</td>
<td>24,000</td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>0 - 2.6</td>
<td>[0.2]</td>
<td>15</td>
<td>3000</td>
</tr>
<tr>
<td>Palestine</td>
<td>3.1</td>
<td>[1]</td>
<td>2</td>
<td>2000</td>
</tr>
<tr>
<td>Israel</td>
<td>(1.4 - 7.1)</td>
<td>[1]</td>
<td>2</td>
<td>2000</td>
</tr>
<tr>
<td>Lebanon</td>
<td>3.8</td>
<td>[1]</td>
<td>1.6</td>
<td>1600</td>
</tr>
<tr>
<td>Syria</td>
<td>900 in 4 yrs</td>
<td>[2]</td>
<td>45</td>
<td>90,000</td>
</tr>
<tr>
<td>Iran</td>
<td>6 (5 - 10)</td>
<td>1.5</td>
<td>17</td>
<td>25,000</td>
</tr>
<tr>
<td>Turkey</td>
<td>3.4</td>
<td>[2]</td>
<td>17</td>
<td>34,000</td>
</tr>
<tr>
<td>Jordan</td>
<td>2.3 (1.4 - 3.6)</td>
<td>[1]</td>
<td>12</td>
<td>12,000</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>31,460,000</strong></td>
<td><strong>423,100 (1.3%)</strong></td>
</tr>
</tbody>
</table>

*Excludes some countries; [ ] estimated prevalence

**Table 2. Estimate based on prevalence and population at risk of numbers of human CE cases in China/Central Asia endemic zone (including refs 18, 25, 26, 29, 33, 36).**

<table>
<thead>
<tr>
<th>Country/Province</th>
<th>Incid./10^6 (range)</th>
<th>Prev. % (range)</th>
<th>Pop@ risk (00,000's)</th>
<th>Predicted cases endemic areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xinjiang (Ch)</td>
<td>8.7 (1 - 80)</td>
<td>2 (0.6 - 4)</td>
<td>16</td>
<td>32,000</td>
</tr>
<tr>
<td>Qinghai (Ch)</td>
<td>3.8 (0.2 - 8.3)</td>
<td></td>
<td>12</td>
<td>45,000</td>
</tr>
<tr>
<td>Sichuan (Ch)</td>
<td>6.6 (0.2 - 12)</td>
<td>17</td>
<td>112,200</td>
<td></td>
</tr>
<tr>
<td>Ningxia (Ch)</td>
<td>4.6 (1 - 7)</td>
<td>3.6 (0.2 - 8.1)</td>
<td>20</td>
<td>72,000</td>
</tr>
<tr>
<td>Tibet AR (Ch)</td>
<td>2 (1 - 4)</td>
<td>15</td>
<td>30,000</td>
<td></td>
</tr>
<tr>
<td>Gansu (Ch)</td>
<td>1.8*</td>
<td>5</td>
<td>9000</td>
<td></td>
</tr>
<tr>
<td>Shaanxi (Ch)</td>
<td>[1]</td>
<td>7</td>
<td>7000</td>
<td></td>
</tr>
<tr>
<td>Nei Mongol (Ch)</td>
<td>[2]</td>
<td>20</td>
<td>40,000</td>
<td></td>
</tr>
<tr>
<td><strong>Total China</strong></td>
<td></td>
<td></td>
<td><strong>11,200,000</strong></td>
<td><strong>347,200 (3.1%)</strong></td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>6.5 (1.3 - 13.3)</td>
<td>1.5</td>
<td>30</td>
<td>45,000</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>19</td>
<td>1.5</td>
<td>10</td>
<td>20,000</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>10 (0.2 - 14.6)</td>
<td>[1.5]</td>
<td>20</td>
<td>30,000</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>27</td>
<td>[1.5]</td>
<td>15</td>
<td>22,500</td>
</tr>
<tr>
<td>Mongolia</td>
<td>(1 - 13)</td>
<td>1 (0.2 - 2.7)</td>
<td>20</td>
<td>20,000</td>
</tr>
<tr>
<td><strong>Total Central Asia</strong></td>
<td></td>
<td></td>
<td><strong>9,500,000</strong></td>
<td><strong>137,500 (1.4%)</strong></td>
</tr>
</tbody>
</table>

*Mainly Tibetan Communities; [ ] estimated prevalence; (Ch) Main endemic provinces of China
and under-developed regions. It is calculated as healthy years (whole years or fraction) of life lost due to a particular pathogen/disease. Interviews with patients and analyses of treatment measures, survival times and incapacity can be used to calculate DALYs, then extrapolated to disease/case frequency data. For example in Shiqu County of eastern Tibet (pop. 63,000), where both CE and AE are co-endemic, >50,000 DALYs were calculated lost due to echinococcosis, equivalent to 0.85 for every person in the County [36]. Establishing the numbers and/or incidence of CE or AE cases in a particular country, region or district however is not easy because records are not always kept, are not accurate and/or are dispersed across different treatment/ward/unit specialities (e.g. surgical units for abdominal, hepatic, gastroenterology, thoracic, orthopaedics, neurology, also paediatrics, general medicine and microbiology). Even when echinococcosis is a notifiable disease by law, records may not be properly collated and centrally reported. Human echinococcosis is therefore usually significantly under-reported. Surgical incidence rates and/or ultrasound based prevalence values are the most useful measures to quantify human echinococcosis cases (Fig. 2) [23] and can be used to determine the burden of disease or health impact [36]. Mass ultrasound abdominal screening (Fig. 1d, e) at community level is the gold-standard to assess prevalence of hepatic echinococcosis (usually 70 to >95% cases of CE and AE) [37] and may indicate a significantly greater community prevalence than surgical incidence data [26]. Based on a crude assessment of regional incidence/prevalence data in the early 1990s it was estimated that 2-3 million cases of human CE occurred at any one time in the world [38]. More specifically, using incidence/prevalence data, and allowing for 10% under-reporting, the total global burden was recently calculated to be 1,009,662 DALYs lost to human CE [25]. This was similar to the total combined DALYs lost for onchocerciasis and American trypanosomiasis, and only slightly lower than the total number of lost DALYs due to African trypanosomiasis. More than 75% of the CE impact in lost DALYs was estimated to occur in 2 of the 8 endemic world regions i.e., Middle East Crescent and China [25]. How many cases of CE occur in these two regions? We have now taken the main endemic countries or provinces in these two regions plus 5 ex-Soviet Republics (Central Asia and Mongolia), and using published incidence/prevalence data and/or unpublished prevalence data from mass screenings, or using estimated prevalence data for similar regional endemic communities, and estimating the proportion of the total population at risk (by ethnic group, pastoral life-style and/or rural area in endemic zone), we have estimated the total numbers of human CE cases that could occur in these two broad geographic regions (Tables 1, 2). Based on that rather conservative analysis, a minimum of 907,000 CE cases would occur across the two regions, of which 423,000 CE cases would occur in the Middle Eastern Crescent, and 484,000 CE cases in the China/Central Asia zone. The average number of DALYs lost per symptomatic CE case may be conservatively estimated to be around 3 years, therefore under that estimation nearly 3 million DALYs in total could be lost in the endemic communities of those two endemic zones. If these cases represent around 75% of the burden, then the number of CE cases globally would be approximately 1.2 million cases i.e., equivalent to 3,600,000 lost DALYs.

**WHY IS ECHINOCOCCOSIS NEGLECTED?**

Human echinococcosis is globally a neglected zoonotic parasitic disease by the standards of reasonable public health concern [6, 29]. As described, its impact on human health is significant when compared to vector-borne parasitic diseases with higher priority in the under-developed world [25]. Then why is this disease not of greater concern to provincial, national or regional authorities within endemic zones?

There are several reasons, some of which have already been touched on, that can be considered to lower the awareness of the disease and that mitigates against proactive interventions that could reduce parasite transmission. Ten key factors that contribute to the neglect of human echinococcosis are summarised below.

1) Human echinococcosis is a zoonosis, and a non-vector-borne zoonosis at that. It is also a Stage 2 type zoonosis [19] which is not transmitted between humans. Together this equates to a disease with animal host reservoirs (livestock, dogs, or wildlife), that is not amenable to vector-based control nor to direct human-treatment-approaches for case prevention, unlike say schistosomiasis, filariasis or malaria.

2) Human CE and AE are chronic diseases with very long asymptomatic periods so that endemic communities and health authorities fail to properly recognise the negative health impacts. Prevalence values represent infection events some years previously.

3) Echinococcosis is difficult to detect or diagnose in humans without access to imaging tools (e.g., ultrasound, CT scan), furthermore the basis for confirmatory laboratory diagnosis is usually expensive serological tests.

4) Treatment is very difficult and not always very effective, relying largely on costly major surgical or percutaneous hospital-based interventions to remove or sterilise cystic lesions. Furthermore, anthelmintic therapy is not as
highly effective as for other helminthic diseases (eg. gastrointestinal helminthiases, schistosomiasis or onchocerciasis), and is based on long-term high dose albendazole usually requiring a minimum 6 months daily course, for which follow-up is very difficult especially in resource-poor areas. In this regard echinococcosis treatment more closely resembles tumour treatments or TB therapy, than that for a parasitic disease.

5) Medical records are usually not very explicit/specific, may involve complex follow-up notes, and may be dispersed across several specialities within/between hospitals/clinics and therefore data is not usually properly collated.

6) In under-developed regions, human echinococcosis generally occurs in poor, often remote marginalised pastoral societies that may be ethnically/socio-culturally isolated from the general population. Consequently they are not usually very well prioritised by the predominant agricultural-based community district health authorities, and so access to affordable health care is also poor and/or difficult [7].

7) The burden of echinococcosis disease is therefore difficult to quantify, and official hospital or district records often inaccurate, and in any case represent gross under-estimates of the real burden in an endemic area.

8) CE is a chronic, asymptomatic infection in domestic animals and is therefore also not recognised by livestock owners as an animal health or economic problem. Pastoralists usually are unaware of the link between livestock and human echinococcosis, nor the zoonotic role of dogs.

9) Dogs are the main carrier and spreader of the parasite, but are asymptomatic. In contrast to livestock numbers, official accurate estimates of dog population sizes (owned and stray) are almost never kept/known by municipal, veterinary or agricultural authorities. In some regions stray/feral/wild dogs are also an important reservoir of the parasite but may be protected on animal welfare or cultural/religious grounds [39, 40]. Canine echinococcosis is treatable with the anthelmintic praziquantel but requires frequent dosing. Unlike for rabies, there is currently no dog vaccine against canine echinococcosis.

10) Control of echinococcosis is difficult and exacerbated by the requirement of cooperation between agricultural/veterinary services and medical authorities. Attacking the dog reservoir is the best approach, but requires very long intervention and consolidation periods (15- > 50 years) that are organisationally/logistically difficult and expensive [40]. Furthermore, pastoral populations in endemic areas may not easily accept measures for an animal disease they fail to prioritise; health education is therefore important but on its own may not result in significant behavioural changes that reduce transmission [7, 40].

**FUTURE DEVELOPMENTS AND PROSPECTS**

Echinococcosis is a chronic zoonotic infection that occurs in remote pastoral communities, is difficult to detect and treat, to estimate disease burden, and to control transmission. It is therefore neglected by health authorities and national or international bodies. Despite this several countries or states have listed human CE (and some also AE) as a priority endemic disease requiring special attention for treatment, prevention and control [17, 29, 30, 41]. There is an urgent need for echinococcosis to be formally included in the growing list of neglected diseases under one of the Neglected (Tropical) Diseases initiatives [3] though currently it does not appear. A number of neglected zoonotic pathogens ie. anthrax, brucellosis, bovine TB, rabies, African trypanosomiasis, cysticercosis and echinococcosis, have however begun to be targeted by WHO in relation to human health, livestock production and poverty alleviation [6]. This will help to prioritise those zoonoses that are widespread in tropical as well as under-developed non-tropical regions, that are currently in ‘orphan-neglect-status’, for example, brucellosis, cysticercosis and echinococcosis. In the meantime there is a need to ensure research and development can be sustained and funded to help tackle these zoonoses.

There are several problem areas, as well as recent and future developments that have or would greatly benefit our ability to deal with human echinococcosis and to improve control options. Some have recently been highlighted [17] and include the following. Better treatment approaches for human echinococcosis are an urgent requirement in resource-poor endemic areas in order to replace surgical interventions. Albendazole (ABZ) therapy though not always effective, has been very useful as an alternative non-invasive option [42] and can be provided on an out-patient basis in remote areas with poor health facilities. Recommendation of regular liver function tests to check for side-effects in ABZ treated patients is not however always possible and patients may not self-medicate correctly over the required treatment periods of several months. In areas where TB and CE are co-endemic combined patient observation/management and follow-up within communities could be productive. Annual ultrasound check-ups are equally important to assess Echinococcus cyst/lesion status but image characteristics though useful do not always correlate well with therapeutic efficacy of ABZ or percutaneous treatment [43]. Practical serological tests that correlate with treatment efficacy would be useful in post-treatment surveillance. For human echinococcosis and AE in particular, ABZ therapy though beneficial, is usually not curative and therefore alternative drugs are required [44].
Ante-mortem serological detection of CE in livestock is currently not very useful but the application of more specific and sensitive recombinant antigens could improve tests especially for young animals with small lesions and/or in low prevalence situations eg. a post-control consolidation phase. Detection of canine echinococcosis has been greatly improved with the advent of coproantigen ELISA in particular, and also development of specific coproPCR confirmatory tests [45, 46]. There is a need to make such tests affordable and widely available from commercial sources.

A highly protective recombinant vaccine (EG95) to prevent CE infection in livestock has been developed and extensively assessed [17, 47]. The CE vaccine now requires to be adopted by commercial or international agencies to ensure GMP status and production for widespread use in domestic animal populations in endemic zones. Combination of PZQ dog dosing, livestock vaccination, parasite surveillance and health education could dramatically reduce the time required to interrupt transmission and eliminate CE as a public health problem [40]. Two recent reports of prototype recombinant vaccines against canine echinococcosis have resurrected the notion that an anti-worm vaccine could be developed [17, 48]. However, extensive research is now required on putative dog vaccines to establish protective characteristics, efficacy, and optimal modes of administration.

Control of chronic zoonoses like echinococcosis, requires cost-effective veterinary based inter-sectoral approaches that are sustainable over several years in resource-poor communities. A systems-approach in which echinococcosis control/prevention can be linked to control/prevention of other zoonotic or infectious diseases has merit and could result in more effective public health and animal health improvements/delivery, and help poverty alleviation (Fig. 3). For example, combination of interventions against leishmaniasis, rabies and echinococcosis in co-endemic areas of North Africa; for TB, rabies and echinococcosis interventions in East Africa and China; or for brucellosis, rabies and echinococcosis in Mongolia [7, 40, 49].

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