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Chapter I

Epidemiology and Microbiology of Hepatic Echinococcosis

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Introduction

Echinococcosis is a disease caused by four out of the six known cestoda species from the genus *Echinococcus sp.*: *E. granulosus*, *E. multilocularis*, *E. vogeli* and *E. oligarthrus.* The two most important species are *E. granulosus* and *E. multilocularis* [1]. The epidemiology of each species of *Echinococcus* sp. varies greatly, although the clinical manifestations they cause are similar. The liver is affected in 75-100% of the cases [2]. We mainly refer to the epidemiology and microbiology of *E. granulosus* infection.

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The Parasite and Its Biological Cycle

Similarly to other cestoda, echinococcus have intermediate and definitive hosts (figure 1). Canidae are the definitive hosts, especially dogs, which form the so-called "domestic" cycle. Some authors have referred to the existence of "wild" cycles in which the wolf is the main definitive host. The intermediate hosts are usually ruminants and particularly sheep and goats, but due to their low specificity for intermediate hosts, *E. granulosus* can also be hosted by a wide range of vertebrates: ungulates, marsupials, primates and humans. The circumstances and the transmission dynamics of this zoonosis depend, among other things, on the availability and the nature of the intermediate hosts, which may vary from one country to another or even from one region to another. As in other zoonosis, the human species is a paratenic host. In intermediate hosts, after the ingestion of eggs, cysts are formed (larval stage). When canines eat entrails that contain cysts, the adult stage develops. The adult tapeworm is small, it resides in the intestine and it has three proglottids: one immature, another mature and a gravid one.

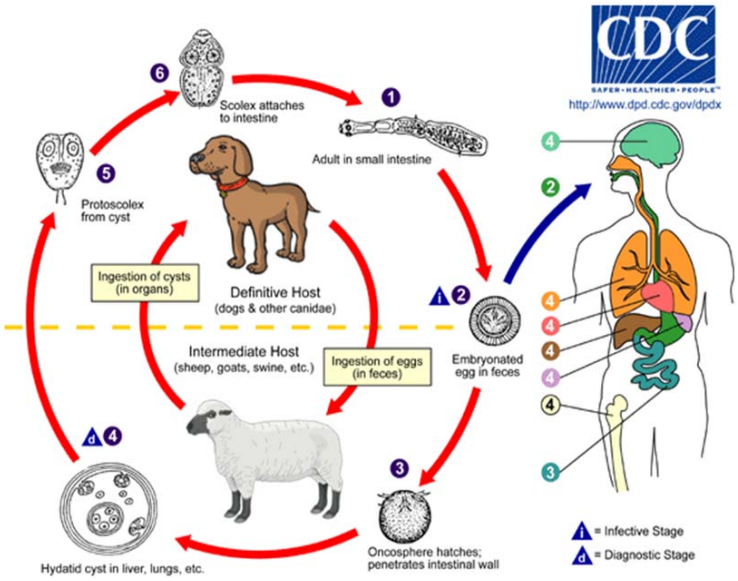

Figure 1. Life cycle of *Echinoccocus* sp.

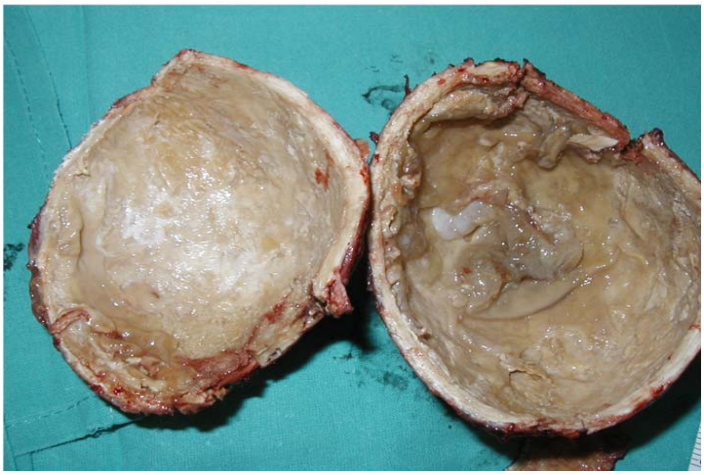

Figure 2. Hydatid cyst.

The gravid segment breaks away to release extremely hard eggs which are then passed in the feces (>70000 eggs/day). This release takes place every 4-6 weeks during the period in which the worm remains in the host, which usually ranges between 6-20 months [3].

When humans ingest the eggs, the embryos or oncospheres are released; they penetrate the intestinal mucosa, reach the portal circulation system and are move to different organs, starting with the liver and the lungs, if they cross the mucosal barrier, and if they cross the lung filter, any other organ. The final location seems to be related to some characteristics of the host and the size of the oncospheres, the venules and the lymph nodes. Afterwards, the larvae develop and form hydatid cysts filled with liquid (figure 2). These cysts are formed by an outer membrane and an inner germinal layer which generates a series of germinal cystic structures called brood capsules. Inside these brood capsules there is a large number of new larvae, called protoscolices. The rupture of these daughter cysts and the release of the scolices give way to sediment called hydatid sand, which remains in the bottom of the cyst. Some cysts may remain sterile and not produce prolific vesicles, and they are called acephalocysts. The dissemination of scolices within the organ due to the rupture of the cysts originates a secondary echinococcosis. The cysts grow slowly through the years (approximately 1 mm per month) [4]. The evolution of cysts caused by *E. granulosus* is variable: 14% of them die and become

calcified; 20% of the cysts do not grow and in 66% of them there is a progressive growth [5]. Although most patients are asymptomatic for long periods of time, as the cysts grow they can cause complications, none of which are specific, which can be classified into three types: immunological, infectious, and mechanical [6].

Epidemiology

The epidemiological importance of the different species of *Echinococcus* sp. is very variable. The distribution of echinococcosis caused by *E. granulosus* is worldwide spread and cosmopolitan (figure 3), whereas the infection caused by *E. multilocularis* is mainly located in the northern hemisphere, mainly in central Europe, Russia, China, the north of Japan, North America and Alaska (figure 4) [7,8]. The epidemiological repercussion of cases caused by *E. vogeli* and *E. oligarthrus* is insignificant. We will mainly describe the epidemiology of echinococcosis caused by *E. granulosus*

The worldwide incidence and prevalence of cystic echinococcosis have fallen dramatically over the past several decades. Nonetheless, infection with *E. granulosus* remains a major public health issue in several countries and regions, even in places where it was previously at low levels, as a result of a reduction of control programs due to economic problems and lack of resources [9], and given a geographic distribution and extent greater than previously believed; several studies have shown that echinococcosis is currently considered an emerging or re-emerging disease, both for *E. granulosus* and *E. multilocularis* [1,2,8,10-13]. Therefore, the existing data probably underestimate the real dimensions of this zoonosis. This may be partly explained by the growing use of radiodiagnosis techniques (with frequent incidental diagnoses) [14], or by a real increase in the prevalence of the disease. This increase has already been registered in some endemic countries, such as Bulgaria, China and Morocco [7,15], while at the same time new cases are arising in countries that were previously free from the disease, such as Austria or Hungary [16,17]. The reasons that may explain this phenomenon are varied, ranging from climate changes that favor the environmental survival of eggs and cysts to a decrease in the rigor of the health campaigns for the control of the disease. While the infection in adults has been traditionally considered as a rural disease, the data regarding the pediatric population are controversial, with some studies stating that it is predominant in rural areas and others reporting a predominance in the urban population [18,19].

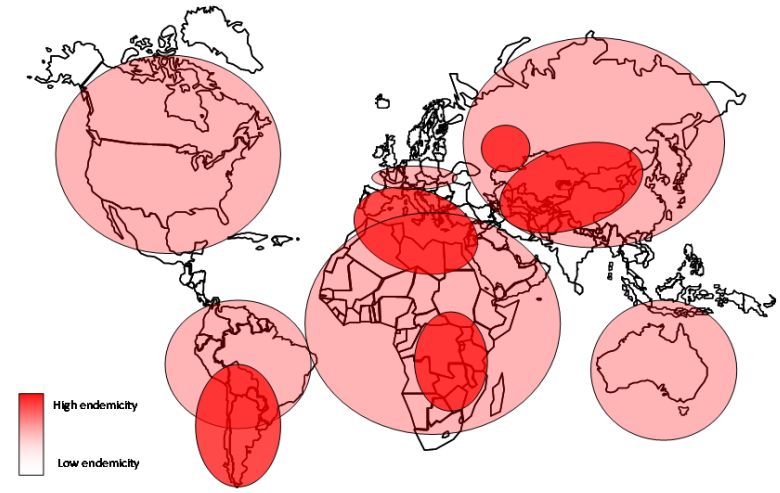

Figure 3. Worldwide distribution of *Echinococcus granulosus*.

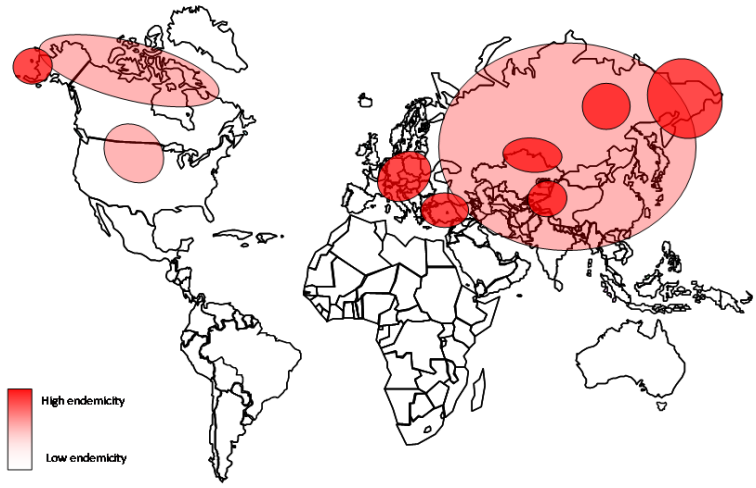

Figure 4. Worldwide distribution *of Echinococcus multilocularis.*

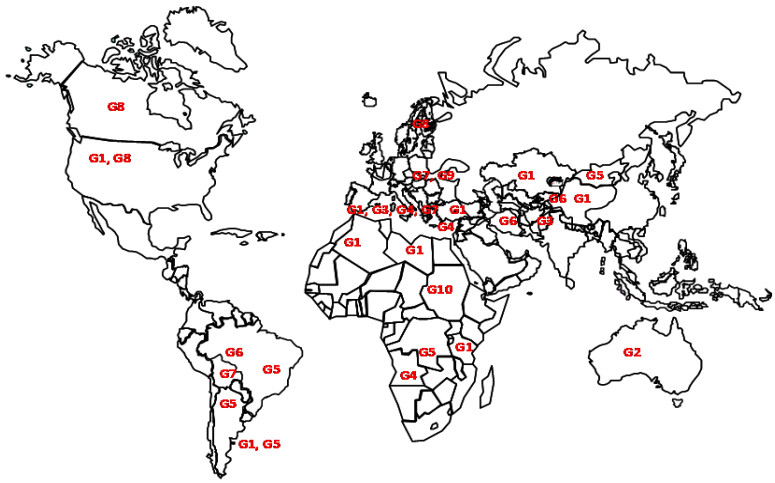

Figure 5. Worldwide distribution of the zoonotic strains of *Echinococcus granulosus.*

Geographic distribution differs by country and region depending on the presence in that country of large numbers of nomadic or semi-nomadic sheep and goat flocks that represent the intermediate host of the parasite, and their close contact with the final host, the dog, which mostly provides the transmission of infection to humans [9].

The distinct genetic types of *E. granulosus* include G1-G10 (figure 5) [20-22]. Among these strains, we have available data for preliminary epidemiological analyses only for some strains. In fact, some of them are still poorly characterized and further research is needed to determine with higher detail their host and geographic ranges and whether their genetic characteristics are conserved between different endemic regions.

The most frequent strain associated with human echinococcosis appears to be the common sheep strain (G1) and, to a lesser degree, G2. This G1 strain appears to be widely distributed in all continents. Highest rates of infection are recorded in communities involved in extensive sheep farming and epidemiological studies suggest that this genetic variant is the principal strain infecting humans [1,23]. Consequently, its presence coincides with areas which have high prevalence of human echinoccocis such as in Morocco, Tunisia, Kenya, Kazakhstan, western China and Argentina [9]. The G2 strain is known to be transmitted among sheep and infect humans also, but genetic

differences biologically distinguish it from the G1 strain, conferring a different life cycle. It has been found in Australia and previously also documented in Tasmania. The remaining strains are more poorly characterized (G3-G10), and they are of lower epidemiological interest.

The prevalence of echinococcosis caused by *E. granulosus* is high in some areas of Eurasia. It is mainly described in countries of the Mediterranean region (except for Malta and the south of Cyprus): Greece, Italy, Portugal, Tunisia, Morocco, Algeria, Turkey and Spain [10,24-26].

In Asia, it is important mainly in southern and central parts of Russia, central Asia and China [9]. It is considered an emerging or re-emerging disease in some countries of central Asia. In Kazakhstan, human infection has increased since the middle 1990s till present time from 200 surgical cases annually to the current level of nearly 1000 cases per year [27]. Similar trends in human cases have been assessed in all other Central Asian countries. However, no detailed data is available about transmission and diffusion of *E. granulosus* infection in Central Asian countries [9]. China is one of the most important endemic regions of echinococcosis and now, it has been estimated that about one million existing cases of human echinococcosis occur in China [28]. In some regions, the prevalence rate reaches 2.1% [29].

Although most regions of Africa are poorly researched and limited information is available, several taxa have been found in the African countries. We have found seroprevalence levels of 3.5% in countries from Eastern and Western Africa such as Sudan, Uganda or Kenya [9,30].

In America, the highest prevalence rates are found in countries from the Southern Cone (Peru, Argentina, Brazil, Chile and Uruguay), where in regions with high endemism they can range between 5-10% [9,31-35].

In some regions of Australia, the disease has a medium importance. Annually, new cases of human echinococcosis appear stable, numbering between 80 and 100 among the entire country [9,36].

Socioeconomic Impact

Echinococcosis represents an increasing public health and socioeconomic concern, and it is a cause of loss of DALY (disability-adjusted life years) in many areas of the world [37-39]. According to a global study on this subject, the global economic loss reaches $193,529,740 annually. If this figure is adjusted with the estimate of undeclared cases and the per capita income, they

increase to $1,918,318,955. In Spain, the global figures for the cost of echinococcosis are estimated in €148,964,534 annually [40].

In view of the relevance of these figures, it is essential to control this disease, trying to reduce its prevalence, both in the definitive and the intermediate hosts, in order to interrupt its transmission. Ever since the 80s, some regions in Spain develop programs for the control and prevention of this disease, which proves that these measures are cost-effective [41].

Conclusion

Given the wide geographic distribution, echinococcosis caused by *E. granulosus* is a re-emerging disease in several countries and regions, even in places where it was previously at low levels. Evidence suggests this is a result of a reduction of control programs due to economic problems and lack of resources, leading to severe disease, considerable economic loss and, definitely, a public health problem of increasing concern [9].

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