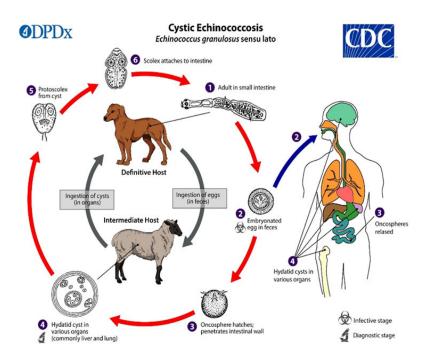
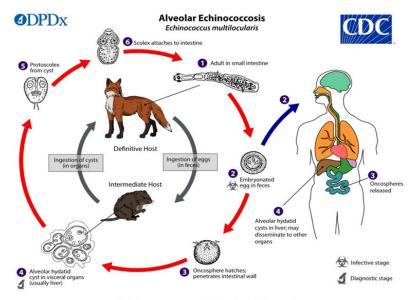
## **CLINICAL CONTEXT**

## **Echinococcosis**

Echinococcosis are parasitic zoonoses due to tapeworm larvae belonging to the *Echinococcus* genus, parasiting the intestine of wild and domestic canines. Beside canines (mostly dogs and foxes for *E. multilocularis*), cats are sometimes found as accidental definitive hosts. Humans, as the other omnivorous and herbivore intermediate hosts, gets infected by ingestion of eggs, eliminated in nature or present on the fur of definitive host. Transmission in humans usually occur by ingestion of unsufficiently rinsed fruits or vegetables contaminated by feces of the definitive host. The egg releases a larva which migrates through blood or lymphatic stream before being stopped mostly by the liver, but also other organs such as lungs. Larvae develop in cysts, which can either grow progressively larger (*E. granulosus*) or form buds, which upon detachment form secondary cysts (*E. multilocularis*) (Woolsey & Miller, 2021).



Echinococcus granulosus life cycle



Echinococcus multilocularis life cycle

Four species are responsible of human chronic and severe diseases, infecting between 2 and 3 million people (<u>Cerda et al., 2018</u>). There is a clinical latency of several years between infection and symptoms onset.

- *E. granulosus*, present worldwide, is responsible of cystic echinococcosis, and is frequent in places where veterinary surveillance is lacking. It is the cause of important economic losses, as the infection also reaches livestock.
- E. multilocularis, that circulates in the northern hemisphere, is the agent of alveolar echinococcosis.
- *E. vogeli* and *E. oligarthus* are responsible of polycystic echinococcosis in Latin America, where they are considered as emergent parasitoses.
- central Europe, Russia and China (McManus et al., 2003).

  The infection is often of poor prognosis, lethal if untreated. In humans, Echinococcus spp. multiply and reorganize to form larvae with complex structures. The endogenous/exogenous development as well as the intra-visceral organization differ from one species to another (Thompson, 2017). In 70% of cases E. granulosus embryos are located in the liver, but can also be found in the lungs or in other organs (heart, bones, spleen or central nervous system). Its cells bud and form vesicles containing protoscolexes and a clear liquid. At least for the hepatic locations, the larva develops in a hydatid cyst. Clinical manifestations differ according to the location, size and number of cysts. They are directly linked to the progressive invasion of the organs or their compression. Accidental rupture of a cyst may result in immediate hypersensitivity manifestations, triggered by the cystic liquid, and in the formation of secondary cysts from protoscolex newly externalized (Higuita et al., 2016).
- E. multilocularis, the most pathogenic of the Echinococcus species, mainly invades the liver. The
  proliferation of its cells is exogenous. The larva progressively infects the organ and causes an
  intense granulomatous reaction followed by a diffuse fibrosis. As a result, parasitic cells can also
  create secondary cysts. Clinically, alveolar echinococcosis mimicking hepatocarcinoma (Brunetti et
  al., 2010).

 E. vogeli and E. oligarthus multiply mainly endogenously, but sometimes exogenously. They form liquid vesicles that remain linked to the index cyst, giving a grapefruit aspect. The hepatic location is more frequent than isolated pulmonary, cardiac, mesenteric, ocular locations or multi-visceral forms. The prognosis of polycystic echinococcosis is close to the one of alveolar echinococcosis. (D'Alessandro, 1997).

Direct parasitological examination of echinococcosis is very invasive and therefore rarely possible. Puncture of a cyst for diagnosis is contraindicated because of the high risk of anaphylactic incident due to the rupture of the cyst, but may be done in a curative surgical context. The diagnosis, guided by biological abnormalities (especially for alveolar echinococcosis) and morphological abnormalities (detected with imagery, mainly by ultrasound), relies on serology. Serodiagnosis is essential for the rapid medical support of patients.

Treatment is both medical and surgical: albendazole for several years if not for life, and whenever possible, surgery. This surgery depends on the size, location and number of lesions. It consists in removing the cyst content by PAIR technique (Puncture, Aspiration of the parasitic mass, Injection of salt serum and Re-aspiration), or removing the infected part of the organ (partial hepatectomy for instance).

Amongst classical serology techniques, the most frequently used is ELISA. Frequent cross-reactions (with other helminthiases and during other pathologies, in particular other hepatic diseases) observed with non-purified antigens lead to the use of synthetic antigens (synthetic peptides, recombinant antigens). These ELISAs may lack of sensitivity (Wen et al., 2019). Due to these limitations, a positive or equivocal serological diagnosis must be verified by Western Blot to confirm the diagnosis.

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## **ECHINOCOCCUS Western Blot IgG TEST**

Specificity and sensitivity of the immunoblot lead to propose this technique as confirmation of screening tests, and as a differentiating assay for the two main human echinococcosis: alveolar and cystic echinococcosis.

The Haute Autorité de Santé (HAS) in France as well as the American Center for Disease Control (CDC) recommend the immunoblot for the confirmation of serodiagnoses (<u>Argumentaire HAS</u>, <u>2017</u>, <u>DDPx Echinococcus</u>, <u>2019</u>).

In order to meet this demand, we developed a reliable test based on the Western Blot technique. Associated with highly sensitive natural antigens, the **ECHINOCOCCUS Western Blot IgG** test is a robust confirmation technique of classical screening tests (<u>Liance et al., 2000</u>, <u>Yamano et al., 2004</u>, <u>Bart et al., 2007</u>, <u>Vola et al., 2019</u>). It allows the differential diagnosis between *E. granulosus* and *E. multilocularis* infections.

Several studies reported its pertinence in the follow-up of patients with alveolar echinococcosis (<u>Tappe et al., 2008</u>), and post-surgery follow-up of cystic echinococcosis (<u>Makni et al., 2007</u>). It also seems to be more sensitive than other commercial kits (<u>Deininger & Wellinghausen, 2019</u>, <u>Tamarozzi et al., 2019</u>).