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Review

Recent advances and perspectives in molecular epidemiology of *Taenia solium* cysticercosis

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ABSTRACT

Cysticercosis caused by accidental ingestion of eggs of *Taenia solium* is spreading all over the world through globalization and is one of the most neglected, neglected tropical diseases (NTDs) or neglected zoonotic diseases (NZDs). In the present study, the reason why *T. solium* cysticercosis has been neglected is discussed at first, and followed with an overview on the most recent advances and perspectives in molecular approaches for epidemiology of *T. solium* taeniasis/cysticercosis, since although taeniasis does not constitute recognized zoonoses, transmission and complete development are dependent on human definitive hosts. Main topics are discussions on (1) the two, Asian and Afro/American, genotypes of *T. solium*, (2) comparative analysis of mitochondrial (haploid) and nuclear (diploid) genes, and (3) the presence of hybrids of these two genotypes which indicates outcrossing of two genotypes in hermaphrodite tapeworms in Madagascar. Additional topics are on (4) the usefulness of phylogeographic analyses to discuss where the infection was acquired from, and (5) miscellaneous unsolved topics around these genetic diversity of *T. solium*.

Contents

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1. Introduction

1.1. Why is Taenia solium infection neglected? The present situation of cysticercosis in the world

Cysticercosis (CC) including the most potentially lethal neurocysticercosis (NCC), ocular cysticercosis (OCC), subcutaneous cysticercosis (SCC) etc. is caused by the presence of larval stage, cysticercus or cysticerci of the pork tapeworm, *Taenia solium* after accidental ingestion of eggs released from adult tapeworm carriers or autoinfection with eggs in the tapeworm carriers themselves (Figs. 1 and 2). Disseminated cysticercosis cases are caused mainly in tapeworm carriers themselves by autoinfection even if detection of tapeworm(s) is not always easy (Schantz et al., 1983, 1998; Margono et al., 2002; Kobayashi et al., 2013; Ito et al., 2014). The only definitive host of *T. solium* is human, *Homo sapiens* (de Queiroz and Alkire, 1998; Hoberg et al., 1999, 2001; Hoberg, 2002, 2006; Michelet and Dauga, 2012; Zarlenga et al., 2014a, b). Adult tapeworm matures in the human intestine after eating uncooked pork contaminated with cysticercus or cysticerci. The life span of *T. solium* tapeworm is difficult to observe, but is probably within a few years (Yoshino, 1934; Lightowlers, 2013) and critically differs from that of *Taenia saginata* for over 30 years (Pawlowski and Schultz, 1972; Pawlowski, 1982). The size and thickness of the gravid proglottid as well as the whole worm critically differ between *T. saginata* or *Taenia asiatica* and *T. solium*. *T. solium* is much smaller and thinner than *T. saginata* or *T. asiatica* (Fig. 3).

Although the eggs are infective not only to swine and humans but also dogs, and the range of potential intermediate hosts is broader than swine and dogs (Hoberg et al., 2001; Ito et al., 2002a), the life cycle of this parasite is usually completed between humans (tapeworm carriers, definitive host) and pigs (intermediate host). Therefore, *T. solium* is now considered to be the most important foodborne parasite globally (Robertson et al., 2013, 2014) and so, rationally eradicable disease (Schantz et al., 1983; Pawlowski et al., 2005; Flisser et al., 2006; Pawlowski, 2006, 2008; Schantz, 2006; García et al., 2007; WHO, 2010) but difficult due to poverty, lack of education, traditional culture, etc.

In cysticercosis endemic areas in Asia or perhaps in Africa and Americas, pigs and dogs are living together and free roaming. Although our caution towards the control of cysticercosis has been focused on humans and pigs, dogs should be included as risk factor for both humans and pigs which may cause additional life cycle between dogs and humans, and confusion in pigs contaminated not with *T. solium* but with *Taenia hydatigena* (Ito and Budke, 2014; Ito et al., 2014; Ito, 2015; Wandra et al., 2015).

Dogs are the definitive host of *T. hydatigena* and several other *Taenia* species (Table 1) (Nakao et al., 2013). Among these *Taenia* species, *T. hydatigena* is the commonest species in livestock. Therefore, pigs are commonly infected with cysticercus/cysticerci of *T. hydatigena*. It might be more common than cysticercus/cysticerci of *T. solium* in free roaming pigs where dogs and pigs are living together (Ito et al., 2014; Wandra et al., 2015). This has often been ignored, but many epidemiological survey of pigs where dogs are living together should remind this fact in order to obtain sound "direct evidence of infection". Recent waves to use antigen-ELISA without necropsy of pigs are difficult to evaluate if antigen-ELISA positive pigs really include pigs infected with *T. solium*, since pigs infected with *T. hydatigena* become strongly positive (Fleury et al., 2003; Dorny et al., 2004). Without necropsy of pigs to confirm infection with *T. solium*, it is not clear whether the antigen-ELISA positive results are from contamination with *T. hydatigena*, since the monoclonal antibody was prepared against metacestodes of *T. saginata* and is highly possibly cross-reactive to other *Taenia* species (Brandt et al., 1992; Fleury et al., 2003; Dorny et al., 2004; Ito, 2013, 2015; Ito et al., 2014). Furthermore, local people in many Asian countries love to eat dog meat (Hoberg et al., 2001; Ito et al., 2002a, 2005, 2014; Ito and Budke, 2014). Therefore, there may be additional alternative but minor transmission of *T. solium* between dogs and humans (Ito et al., 2002a).

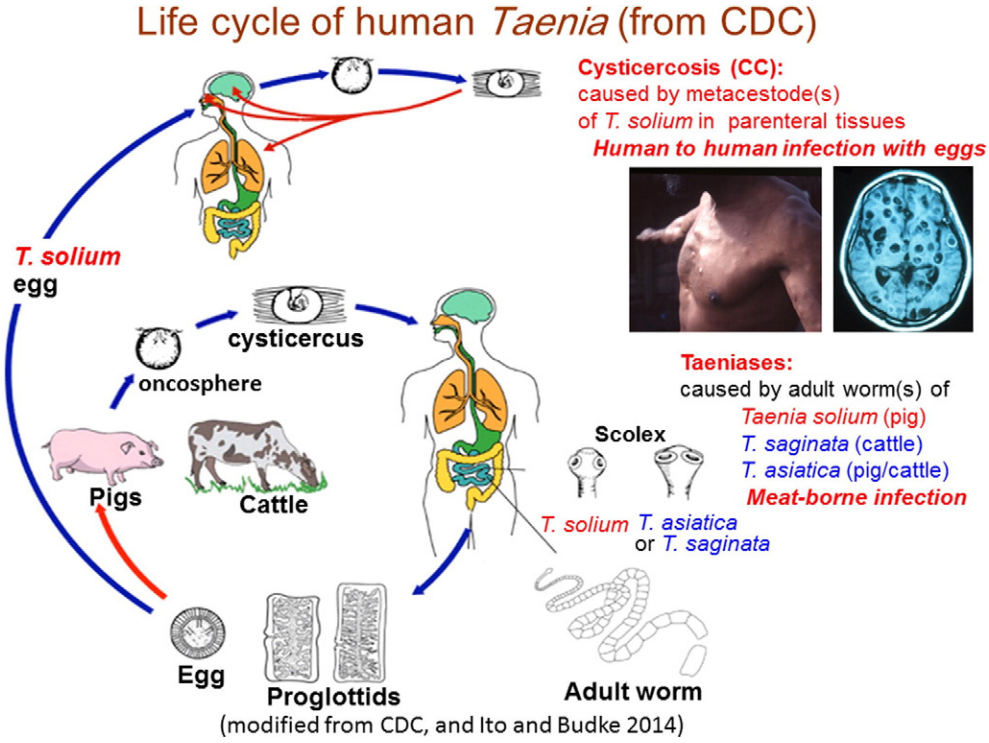

Fig. 1. Life cycles of human *Taenia* species (modified from CDC, and Ito and Budke, 2014; Ito et al., 2014).