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Trichinellosis: A World Health Problem

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Received: Sept 28, 2022 **Accepted: Dec 12, 2022**

INTRODUCTION

The nematodes of the genus *Trichinella* belongs to the Family Trichinellidae. Likewise, *Trichinella* belongs to the Trichinelloidea superfamily which has particular characteristics different from other nematodes (Wu et al. 1998). Currently in the genus *Trichinella* two main clades are recognized, one that includes the species that are encapsulated in the muscular tissue of the host including *Trichinella (T.) spiralis, T. native*, T6, *T. britovi*, T8, *T. murrelli* and T9 and another in which the species are not encapsulated including *T. pseudospiralis*, *T. papuae* and *T. zimbabwensis*. It has been pointed out that although there are no clear morphological differences between species and genotypes, yet these can be differentiated (International Commission on Trichinellosis, 2022).
The disease caused by species of the genus *Trichinella* is known as Trichinellosis or trichinosis. It should be noted, according to the International Organization of Epizootics and the International Commission on Trichinellosis, that the worldwide distribution of *T. spiralis* (the best-known species) has been fundamentally influenced by humans, who passively introduced it into the North, Central, and South of the American continent, as well as in New Zealand and Egypt (World Organization for Animal Health, 2022).
Trichinella is a genus of zoonotic nematode that occurs in carnivores and omnivores (mammals, including people, reptiles and birds) and causes the disease known as Trichinellosis, which has been a public health threat for more than 170 years (Murrell and Pozio 2000). In this context, it has been estimated that only in China more than 40 million people are at risk of *Trichinella* infection (Bai et al. 2017).

Etiological Agent

The recent application of molecular techniques has led to the identification of 10 species including *T. spiralis, T. nativa, T. britovi, T. murrelli, T. nelsoni, T. pseudospiralis, T. papuae, T. patagoniensis, T. zimbabwensis,* and *T. chanchalensis* and three genotypes including T6, T8, T9 which have not yet been given species status (Zarlenga et al. 2020) (Fig. 1, Table 1).
T. patagoniensis was isolated and identified in muscle tissue from cougar in Argentina (Krivokapich et al. 2012). More recently, a new species, *T. chanchalensis*, was described in wolverine (*Gulo gulo*) from northwestern Canada (Sharma et al. 2020). It is important to note that *T. spiralis*, the most studied species, is an intracellular parasite that does not kill the host cell, but induces transformations in cell structure that benefits the survival of the parasite (Despommier 1990).
Trichinella species infect more than 100 species of vertebrates including mammals, birds, and reptiles. In this respect, it is estimated that 10,000 cases of Trichinellosis have been reported from human worldwide on annual basis, with an average mortality of 0.2% (Pozio 2005; Zarlenga et al. 2006). *Trichinella* larvae are located in muscle tissue and the adults in the small intestine for a long period of time, (International Commission on Trichinellosis, 2022).
From the clinical point of view, the effect of *Trichinella* infection in the pig (the most important host in many countries, including Mexico) Ortega-Pierres et al. 2000) is minimal and practically undetectable; however, trichinellosis is considered an important zoonosis due to outbreaks in humans. It should be noted that most cases of human Trichinellosis in México have been due to the consumption of semi-raw meat from backyard pigs (generally in celebrations and family parties) that do not undergo sanitary inspection (Ortega-Pierres et al. 2000).
Generally, it should be noted that the most important risk factors in the domestic cycle of *Trichinella* include: 1) intentional feeding with food scraps containing pig remains or exposure (intentional or unintentional) to dead pig carcasses or wild animals; 2) allow pigs to feed in garbage dumps; 3) feeding wild animals with carcasses or remains of hunted animals; 4) feeding horses with pig carcasses or animal carcasses; 5) feeding sled dogs carcasses from other animals in the arctic; 6) feeding carcasses as food to fur animals; 7) feeding farmed crocodiles with meat from other farmed crocodiles; 8) feeding young crocodiles with pig carcasses. It is worth to mention that, in the domestic cycle of trichinellosis, there is predominate infection of *T. spiralis* in pigs and synanthropic hosts without affecting the health of these animals significantly, except when the infection by *Trichinella* is severe (International Commission on Trichinellosis, 2022).

Life Cycle of *Trichinella* spp.

The new-born *Trichinella* larvae (NLs) migrate from adult female worms to host lymphatic vessels, then enter in the

Citation: Bautista-Garfias CR, Aguilar-Marcelino L and Oropeza-Guzmán G, 2023. Trichinellosis: A world health problem. In: Aguilar-Marcelino L, Younus M, Khan A, Saeed NM and Abbas RZ (eds), One Health Triad, Unique Scientific Publishers, Faisalabad, Pakistan, Vol. 3, pp: 15-19. https://doi.org/10.47278/book.oht/2023.71

Table 1: *Trichinella* species or genotype, hosts, and world distribution (Table designed by Carlos R. Bautista-Garfias)

Species or genotype	Hosts	Distribution	Reference
T. spiralis	Mammals	Cosmopolitan	Gottstein et al. 2009
T. nativa	Mammals	Arctic and Subarctic regions of America, Europe and Asia	Uspensky el al. 2019
T. britovi	Mammals	Tempered areas of Europe and Asia Northeast and West Africa	Pavic et al. 2019
T. murrelli	Mammals	Tempered areas of North America	Pozio and La Rosa, 2000
T. nelsoni	Mammals	East and South east Africa	Pozio et al. 1997
T. patagoniensis	Mammals	Patagonian region South America	Krivokapich et al. 2012
T. zimbabwensis	Mammals, Reptils	Africa South of Sahara.	Pozio et al. 2007
T. chanchalensis	Mammals	Nothwestern Canada	Sharma et al. 2020
T. papuae	Mammals, Reptils	Papua New Guinea.	Takahashi et al. 2000
T. pseudospiralis	Mammals, Birds	Cosmopolitan	Santrac et al. 2015
T6	Mammals	Arctic and Subarctic regions of America	Reichard et al. 2008
T8	Mammals	Tempered areas of North America	Gottstein et al. 2009
T9	Mammals	Japan	Tada et al. 2018

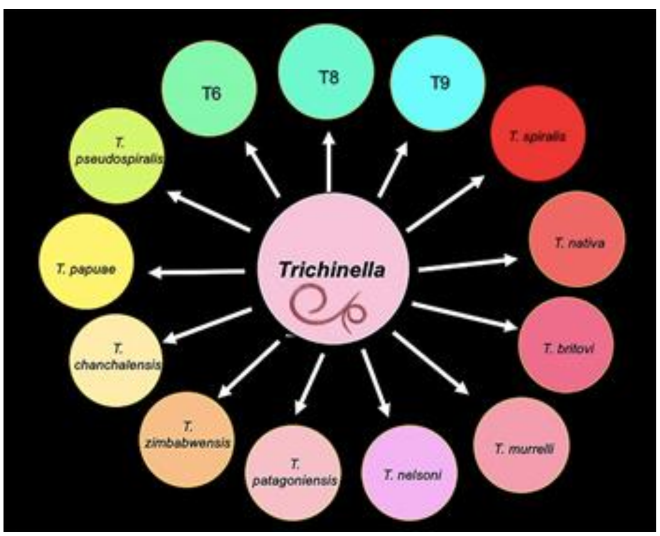

Fig. 1: Known species of genus *Trichinella* (composition by Carlos R. Bautista-Garfias)

blood vessels to be transported to skeletal muscle cells. The NL transform in the muscle cell to stage L_1 larvae. These larvae may survive up to two decades in polar bears and up to four decades in humans. Once the L_1 larvae in muscle tissue are ingested by a new host, they are released from the muscle cells by gastric juices in the stomach; then they reach the duodenum where these penetrate the intestinal villi and transform into adult worms, which mate, and after six to seven days, the females begin to produce NL, whose production continues for at least one to two weeks or longer depending on immune response at intestinal level (International Commission on Trichinellosis, 2022) (Fig. 2). The muscle larvae can be easily recognized in an infected host, while the adult worms are difficult to detect, which can only be obtained from the intestine. It is more difficult to detect NL migrating in the blood of naturally infected host (International Commission on Trichinellosis, 2022).

Transmission

Briefly, *Trichinella* transmission occurs when a susceptible host (carnivorous or omnivorous, including man) eats meat of a *Trichinella* infected host which harbours infective larvae in muscle cells. Then, the life cycle of this parasite begins again as depicted in Fig. 2. (International Commission on Trichinellosis, 2022).

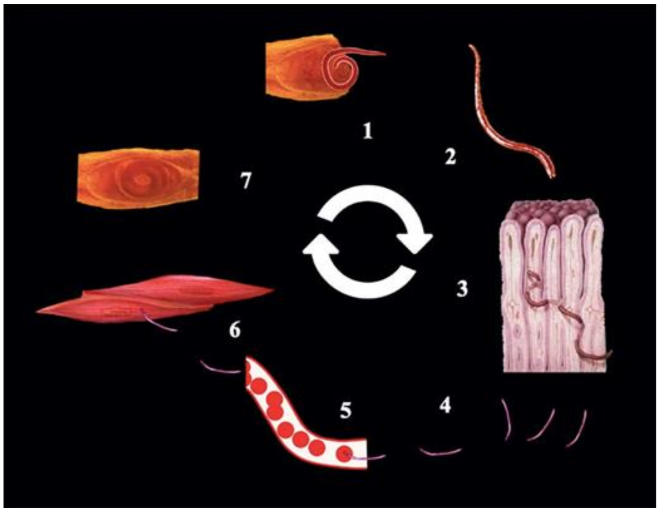

Fig. 2: Biologic cycle of *Trichinella spiralis*: 1) After a muscle cyst is ingested by a new host, the larva is liberated by the gastric fluids of the new host. 2) Infective larvae transform into adults in the intestine. 3) After copulation the female sheds live newborn larvae (NL). 4, 5) NL migrate through lymph and blood. 6,7) NL penetrates a skeletal muscle cell and induces the formation of a nurse cell which will become a muscle cyst. (Figure designed by Carlos R. Bautista-Garfias)

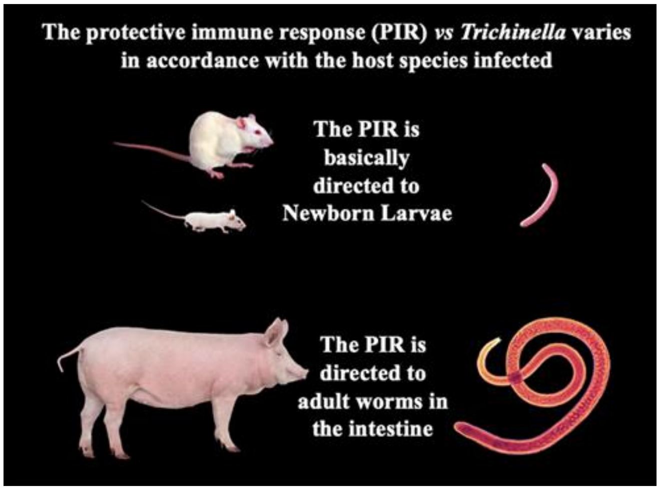

Fig. 3: The protective immune response against *Trichinella spiralis* in rodents and swine (Figure designed by Carlos R. Bautista-Garfias; based on: Murrell 1985; Bell and Wang 1987; Zhang et al. 2018).

Epidemiology of Trichinellosis

T. spiralis parasitize the domestic animals, while the other species in this genus mostly infect wild animals. When there is improper management of domestic and wild animals, other *Trichinella* species are also transmitted from the wild to the domestic environment. Alternatively, *T. spiralis* can also be transmitted from domestic animals to wildlife. In this respect, it should be noted that no systematic epidemiological studies of Trichinellosis have been carried out in some countries such as México. A very limited epidemiological information available regarding the prevalence of *T. spiralis* yet (International Commission on Trichinellosis, 2022).

Pathogenesis/Clinical Signs

Pathogenesis usually refers to humans rather than animals and involves two phases of the *Trichinella* life cycle including an intestinal (or enteric) phase and a muscular (parenteral or systemic) phase. During intestinal phase, symptoms like fever, myalgia, eosinophilia, and diarrhoea occur. In the muscle phase inflammatory and allergic responses due to invasion of skeletal muscle cells by larva migrans may occur. In this phase, either there will be direct damage to muscle cells or indirect stimulation of eosinophils. In this regard, there is a correlation between the levels of eosinophils and muscle serum enzymes such as lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) (Bruschi and Murrell 2002; Dupouy-Camet et al. 2002).

Clinical signs generally are not detectable in animals such as pigs; however, in humans symptoms may appear during the acute phase of Trichinellosis, which include palpebral or facial oedema, and myalgia, which is aggravated by myocarditis, thromboembolic disease and encephalitis (Bruschi and Murrell 2002).

Immune Response of Mammals to *Trichinella* spp. Infection

The immune response of the host against *Trichinella* infection is of both nonspecific and acquired type and depends on the species of infected host (Ottesen et al. 1975; Murrell 1985; Bell and Wang 1987). In mice and rats the protective immune response in a reinfection is directed against new born larvae (Bell and Wang 1987; Zhang et al. 2018), while in swine it is directed against the adults in the intestine (Murrell 1985) as mentioned in Fig. 3. It also depends on the *Trichinella* infective dose (Martínez-Gómez et al. 2011; Wang et al. 2020) and the *Trichinella* species (Wakelin et al. 1994). It must bear in mind that during infection, T. spiralis is also capable of modulate the immune response of the host; for example, depressing the production of effector immune molecules, such as cytokines. (Song et al. 2019; Xu et al. 2021).

On the other hand, based on the acquired immune response against *Trichinella*, several antigens are being evaluated as possible vaccines (Zhang et al. 2018). However, other approaches to induce protection of the host have been developed; for example, the use of *Lactobacillus casei* that generates a non-specific protection against *T. spiralis* infection (Bautista-Garfias et al. 1999; Bautista-Garfias et al. 2001; Martínez-Gómez et al. 2009) and, recently, against *T. britovi* (Boros et al. 2022).

Diagnosis

In order to detect *Trichinella* infection in the hosts, several tests have been implemented, either to observe directly the parasite, or to evaluate indirectly the effector immune molecules (for example, antibodies) elicited by this. In accordance with Ruitenberg et al. (1983), in order to detect *Trichinella* larvae per gram in pigs, the less sensitive test is the Trichinoscopy, while the best techniques *available* are the digestion test (5 x 20g), pooled sample digestion (Van der Giessen et al. 2013; Riehn et al. 2013), and the Enzyme Linked Immunosorbent assay (ELISA) (Venturiello et al. 1998; Gamble et al. 2004). In this context, it has been demonstrated that western blot is a useful diagnostic technique for differentiating *T. spiralis* or *T. britovi* from *T. pseudospiralis* (Gómez-Morales et al. 2018). For diagnosing *Trichinella* infection in human, serological tests, such as ELISA (Bruschi et al. 2001; Gómez-Morales et al. 2008) and Western blot (Yera et al. 2003) have been employed.

Control

The International Commission of Trichinellosis has recommended the following points for the control of Trichinellosis (Gamble et al. 2000; Dupouy-Camet and Murrell 2007):

1- Detection at slaughterhouse level (in order of importance i.e., pigs, horses and game animals.

2- Meat processing by cooking, freezing, or irradiation.

In this respect, China has pointed out the need to carry out effective control measures (for example, educating and informing the public) for controlling Trichinellosis (Liu and Boireau 2002). Contrary to this, when control measures fail due to social, political and economic factors, Trichinellosis re-emerges (Djordjevic et al. 2003). It has been suggested that for controlling Trichinellosis, monitoring *Trichinella* infection in wildlife could help (Van Knapen 2000). The changing global condition such as demographic, climate change, and socioeconomic change affected the parasitic diseases, so there is the need for new transdisciplinary control approaches (Thoisy et al. 2021).

Conclusion and Perspectives

The published information about *Trichinella* and Trichinellosis indicates that this neglected zoonosis is not completely understood. Several advances have been achieved, including, the discovery of new Trichinella species, although their life cycles are partially known only. It is also true that the diagnostic techniques have improved (serological and molecular), and treatment of the disease in humans is effective. However, we do not know how socioeconomic changes, climate change and the continuously growing human population invading wildlife will impact on animal and human trichinellosis, so much research should be carried out under the One Health scheme to implement effective control measures.

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