General Overview about Trichinella and Trichinellosis

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Abstract

Background: Trichinella had infected humans long before its discovery in the 1800's. In ancient Egypt, trichinellosis was highly prevalent and was found in many mummies as one of the earliest human infections documented around 1300 Before Christ (BC). Human trichinellosis is one of the most common parasitic zoonosis worldwide caused by nematodes infection of genus Trichinella. After the consumption of pork from a domestic pig in 1975, a human trichinellosis outbreak occurred among French tourists. A prevalence of 4.5% in domestic pigs slaughtered at the Cairo abattoir was observed at that time. In addition, several cases were reported in various Egyptian localities including Tanta. After consumption of infected meat, the enzymes pepsin and hydrochloric acid act in the stomach and lead to the release of the first stage larvae (L1). These larvae penetrate the small intestine. Invasion may be asymptomatic or may be associated with abdominal pain, diarrhea, nausea and vomiting. Larvae then become adults and mate. Larvae are produced by female Trichinella which complete the gastrointestinal or enteric stage. Larvae join the lymphatic circulation and then enter the blood to reach organs with high oxygen content, skeletal muscles, myocardium and brain. This phase results in systemic symptoms as fever, myalgias, myositis, periorbital edema and may cause myocarditis and encephalitis up to death. The larvae cause significant eosinophilia, especially in patients with cardiac and CNS dysfunction. The severity of the clinical course depends mainly on parasitic factors, such as the type of species involved and the number of infective larvae consumed as well as host factors, such as age, sex and immune status. In humans, T. spiralis infection may remain asymptomatic if it involves a few number of larvae ingested, but in case of ingestion of hundreds of larvae, gastrointestinal symptoms appear as soon as 2 days post ingestion (p.i). subsequently a sever, rarely fatal, disease develops. Trichinellosis usually has a benign and self-limiting course. Complete recovery of patients is expected within 2 to 6 months of infection. Some cases may be severe, and even death may occur. However, death is unlikely if the heart and CNS are uninvolved. Many people with CNS involvement may have residual long standing deficits. Trichinellosis prognosis correlates proportionately to the parasite load. Some complications may occur in untreated cases such as chronic diarrhea myocarditis, pneumonitis, nephritis or neurotrichinellosis

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Introduction

Trichinella larva in a human diaphragm was first described in 1835 by Richard Owen and James**.** Virchow and Leukart had briefly described *T. spiralis'* complete life cycle in 1860. *Trichinella* had infected humans long before its discovery in the 1800's. In ancient Egypt, trichinellosis was highly prevalent and was found in many mummies as one of the earliest human infections documented around 1300 Before Christ (BC)**.** Since the name *Trichina* was given to a genus of flies in 1895, the worm was renamed *Trichinella* by Railliet **(1).**

Human trichinellosis is one of the most common parasitic zoonosis worldwide caused by nematodes infection of genus *Trichinella***.** Human infections occur after consumption of raw or undercooked meat containing encysted larvae. Pigs are a major source of infection in humans**.** It has been documented in 55 (27.8 %) countries throughout the world including the United States, China, Argentina and Russia. About 11 million people are infected with the genus *Trichinella*, of which the species *T. spiralis* is responsible for most of these infections**.** Generally, about 10,000 *Trichinella* infections occur annually worldwide**,** making them one of the most prevalent infectious agents that are responsible for various diseases in both animal and human hosts, being a global health problem **(2).**

Two known outbreaks occurred in 2015. In the first outbreak, about 40 people were infected during a New Year's Eve in Liguria, Italy. The second one was linked with Corsican pork sausages consumed raw in France. China is considered of the highest number of *Trichinella* infections where pork consumption is the highest worldwide. In recent years, there is an increase in Trichinellosis in Europe because consumer preferences for eating antibiotic-free meat **(3).**

Trichinellosis in Egypt

After the consumption of pork from a domestic pig in 1975, a human trichinellosis outbreak occurred among French tourists. A prevalence of 4.5% in domestic pigs slaughtered at the Cairo abattoir was observed at that time. In addition, several cases were reported in various Egyptian localities including Tanta. The prevalence dropped to 1.7% in 2000. High infection prevalence levels (up to 13.3%) were observed among Alexandria abattoirs synanthropic rats. Larvae of the genus *Trichinella* were also found in Sinai wolves. These epidemiological data suggest that Egypt has both a domestic and a sylvatic cycle **(4).**

Youssef and Uga (5) stated that there were only few reports of *T. spiralis* infection in pigs in Egypt. **Abdel-hafeez *et al*. (6)** concluded that there was no *T. spiralis* infection of pigs in El-Minia, Egypt, using the various techniques throughout governorate.

Dyab *et al*. (7) reported that the prevalence of *T. spiralis* infection in pigs at the Albasatin slaughterhouse in the Cairo Governorate (Egypt) was 1.08 percent. In Upper Egypt, *T. spiralis* infection rate is 5% & 2% in Assiut and Sohage Governorates, respectively. The low prevalence rate of trichinellosis in pigs in Egypt may be related to hygienic conditions for raising pigs in private farms. Also, raising Egyptian pigs are mainly indoors away from the infection source. There is no doubt that there is a lack of accuracy in slaughterhouses during the examination of pig trichinoscopy, which is more or less unreliable and needs a trained technician **(7).**

- **Adult:**

T. spiralis adult is one of the smallest nematodes infecting man and is white in colour**.** The cuticle is smooth, but it shows pseudosegmentation and is regularly interrupted by ventral and dorsal pairs of hypodermal cells. The somatic musculature is made of one layer of muscle cells. They involve a large nucleus, prominent contractile filaments

and mitochondria. The alimentary tract is made of an oral cavity, capillary oesophagus, midgut with brush border and hind gut**.** Life span of adult worm is very short. The male after fertilizing the female dies about one week after infection. The female lives for about 16 weeks **(8)**.

The male of *T. spiralis* measures 1.4 - 1.6 mm in length and 0.04 mm in diameter, and is more flat anteriorly than posteriorly. The copulatory sheath and spicules are absent in males but there are two conspicuous conical papillae called claspers on either side of the tail's tip used to hold on to the female worm while mating. The reproductive system consists of a single testis. While, the females measure 3-4 mm in length and 0.06 mm in diameter. They are viviparous and release the first stage of the larvae into the intestinal mucosa. The vulva is located near the oesophagus. The single uterus is packed with eggs that mature in the posterior part, while the anterior portion includes fully developed juveniles **(9).**

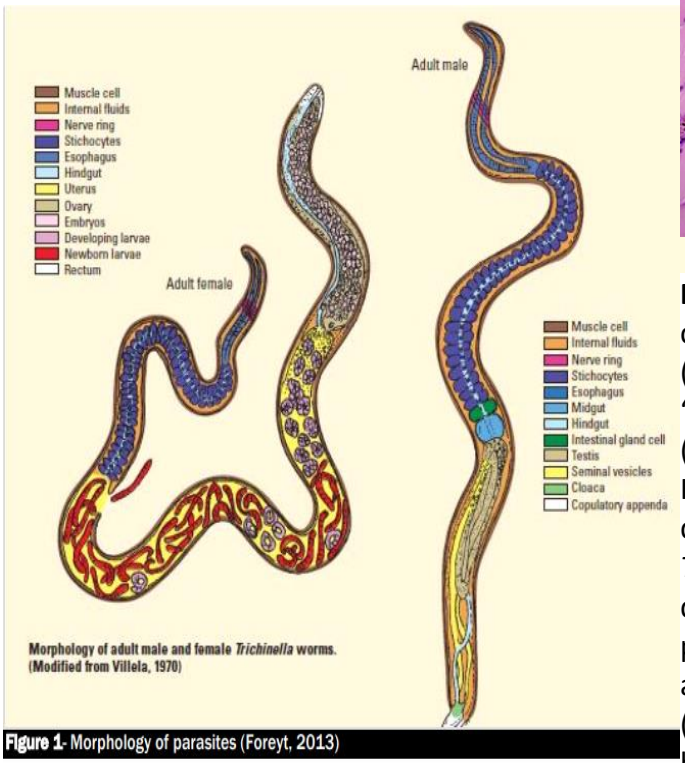

Fig. (1): The morphology of adult (male & female) of *T. spiralis* **(10).**

- **Larva:**

The larva of *T. spiralis* measures about 100µm and 6µm in diameter and remain encysted in stri ated host muscles**.** It grows inside the cyst until sexual differentiation occurs, to become 10 times its original size from 100 µm to 1000 µm (1 mm). Maximum size is reached by the 35th day and normally only one larva is present in a single cyst. Larva encapsulation begins on day 21 and is completed in 3 months. An ellipsoidal lemon-shaped sheath (0.4 by 0.25 mm) develops as a result of an interaction between the host tissues around the tightly coiled larva. The long axis of the capsule is parallel to the muscle fiber**.** Calcification takes place in 6-18 months **(11)**.

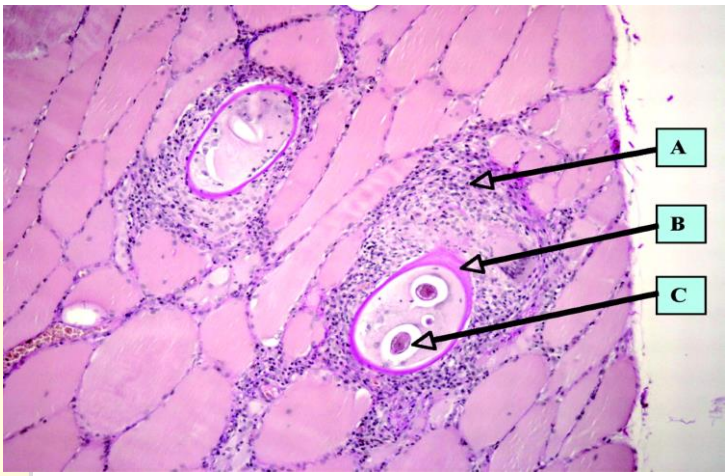

Fig. (2): *T. spiralis* larvae encapsulated in nurse cells within the skeletal muscle tissue of the host (A) Cellular infiltrates; (B) collagen capsule of a "nurse cell"; (C) intersected muscle larva. (Photograph courtesy of Dietrich-Bonhoeffer-Klinikum, Neubrandenburg, Germany. Among the different helminths, the entire life cycle of *Trichinella spp* is unique, involving the development of all three life cycle stages of the parasite, infective muscle larvae (ML), adult(AD) and new born larvae (NBL) within the same host (man, pig or rat). Although one animal serves as both a definitive and an intermediate host, two hosts are needed to complete the life cycle **(9).**

Human infection occurs by ingestion of infected raw or undercooked meat containing encysted first stage larvae (L1). Upon ingestion, they decapsulate in the stomach of the host then invade the small intestine mucosa where they molt four times within 24–30 hours. Upon sexual maturity, the adult worms mate in the intestinal epithelium and produce NBL. The adult females start to release larvae as early as day 5 after infection. The NBL penetrate the intestine and migrate via the blood and lymphatic systems all over the host's body. Finally, they rest in striated muscle cells where they develop into infective ML encysted in muscle tissue **(12).**

The heavy larval burdens are present in highly active muscles, such as the diaphragm, intercostal, pectoralis major, biceps, deltoid and gastrocnemic muscles. There are 1000 *Trichinella* larvae per gram of the muscle. Both larvae as well as the infected muscle cells undergo severe modifications upon penetration of the muscle cells. The larvae undergo rapid growth with a 40% daily increase in volume over a period of 2 weeks. During this period, host cells biochemistry and biosynthetic capabilities, transforming them into a new type of cells, "nurse cells" (NC). These new cells are used to house, protect and feed larvae **(13).**

The capsule consists of a collagen wall and cellular component. The wall protects the parasite and the cellular component is responsible for the metabolism of the parasite. Due to its function, the name "nurse cell" has been given to cellular component**.** Majority of the larvae in muscle die within 6 months but some may survive up to 10 to 31 years **(11)**.

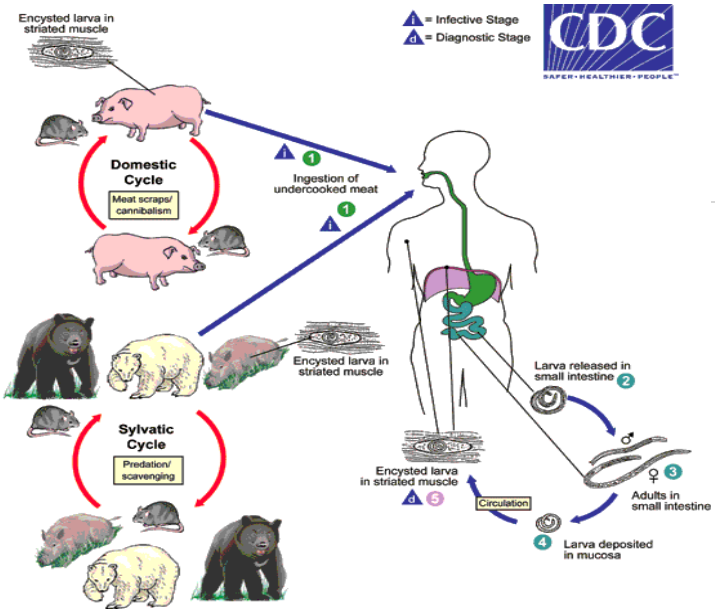

Fig. (3): Life cycle of *T. spiralis* **(1)4.**

Pathology and pathogenesis of trichinellosis

1. Enteric or gastrointestinal phase:

After consumption of infected meat, the enzymes pepsin and hydrochloric acid act in the stomach and lead to the release of the first stage larvae (L1). These larvae penetrate the small intestine. Invasion may be asymptomatic or may be associated with abdominal pain, diarrhea, nausea and vomiting. Larvae then become adults and mate. Larvae are produced by female *Trichinella* which complete the gastrointestinal or enteric stage**.** The presence of the adult and larvae in the mucosal and submucosal layers during the enteric phase of the infection results in an intense inflammatory response with mixed cellular infiltration. This occurs mainly in the jejunum, with neutrophils, eosinophils and lymphocytes as well as functional changes in the motility of the small intestine. Severe infections cause hyperemia, serosa petechiae, excessive mucous secretion, enlarged Peyer patches and bowel loop dilation **(15).**

Larvae of *T. spiralis* do not have specialized organ for mechanical invasion of enterocytes. It has been assumed that the molecules on the parasite surface, or excreted-secreted, may be responsible for the initial contact with enterocytes and cell penetration. Several proteases present in ES L1 of *T. spiralis*, such as serine, cysteine and metalloproteases are involved in host tissue and cell invasion and are likely to play an important role in nematode molting **(16).**

- **Systemic (parenteral) phase:**

The migration of *Trichinella* larvae into various organs induces an immediate reaction that causes immunological, pathological and metabolic abnormalities**.** Larvae join the lymphatic circulation and then enter the blood to reach organs with high oxygen content, skeletal muscles, myocardium and brain. This phase results in systemic symptoms as fever, myalgias, myositis, periorbital edema and may cause myocarditis and encephalitis up to death. The larvae cause significant eosinophilia, especially in patients with cardiac and CNS dysfunction. The presence of larvae in the striated muscle cells results in three major cell modifications: 1) The disappearance of sarcomere myofibrils, 2) The encystation of larvae and 3) The development of a capillary network around the infected cell **(17).**

Bai *et al.* (14) reported that the muscular phase of *T. spiralis* involves the change of the host muscle cell into a completely new type, the nurse cell. Alterations in infected muscle cells are controlled by the invasive parasite through secreted proteins released into the matrix of the cell; however, the identity of these molecules is still unknown. It has been shown that ES L1 facilitates the proliferation of myoblasts and at the same time suppresses their differentiation.

- **Central nervous system (Neuro-trichinellosis):**

It is a major complication of human trichinellosis which is mainly caused by vasculitis and granulomatous inflammatory reactions**.** Additionally, neural cells may be damaged by eosinophilic degranulation products such as eosinophil-derived neurotoxin **(18).**

- **Heart:**

Myocarditis is caused by invasion of the migrating larvae, followed by immunopathological responses as activated eosinophil infiltration and mast cell degranulation**.** *T. spiralis* larvae don't encapsulate in heart muscle tissue but their transient stay in the heart results in morphological changes. Focal cellular infiltrates are mainly composed of eosinophils and mononuclear cells **(19).**

Clinical picture

The severity of the clinical course depends mainly on parasitic factors, such as the type of species involved and the number of infective larvae consumed as well as host factors, such as age, sex and immune status. In humans, *T. spiralis* infection may remain asymptomatic if it involves a few number of larvae ingested, but in case of ingestion of hundreds of larvae, gastrointestinal symptoms appear as soon as 2 days post ingestion (p.i). subsequently a sever, rarely fatal, disease develops**.** The clinical signs of trichinellosis are characterized by two stages: an enteral and a parenteral stage, referring to the presence of parasites in the intestine and in the circulation and/or muscle tissue, respectively **(20).**

- **Intestinal (or enteral) phase:**

The first symptoms may occur between 12 hours and 2 days after ingestion of raw or under cooked meat containing encysted larvae**.** The most common findings during the enteral phase of a mild infection are nausea and transient diarrhea. In moderate to severe infections, the first signs

are upper abdominal pain, vomiting, malaise, diarrhea or constipation and mild fever. The enteral phase lasts for 6 weeks **(21).**

- **Migratory phase:**

From 2nd to 6th week post infection, the enteral phase is often present, but the predominant signs occur from the parenteral phase due to the migrating larvae and their penetration of various tissues. Fever is one of the most common and earliest signs of the trichinellosis. Eyelid and facial oedema are typical signs and their severity relies on intensity of the infection. Other prominent manifestations are eosinophilia, conjunctivitis and splinter hemorrhage. Endocarditis, myocarditis, and cardiac failure may complicate this phase **(22).**

- **Muscular phase:**

Months or even years after the acute stage, chronic trichinellosis may yield symptoms due to an invasion of muscle cells. Characteristic signs include muscle pain, weakness and even paralysis**.** These may persist up to 10 years post infection in people not treated early during the acute phase of infection **(23).**

Prognosis & Complications

Trichinellosis usually has a benign and self-limiting course. Complete recovery of patients is expected within 2 to 6 months of infection. Some cases may be severe, and even death may occur. However, death is unlikely if the heart and CNS are uninvolved. Many people with CNS involvement may have residual long standing deficits. Trichinellosis prognosis correlates proportionately to the parasite load**.** Some complications may occur in untreated cases such as chronic diarrhea myocarditis**,** pneumonitis**,** nephritis or neurotrichinellosis **(3).**

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