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An Overview about Trichinosis; Morphology, Pathogenesis and Presentation

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Abstract: Trichinosis is a re-emerging zoonotic disease that has develops a public health concern since its reported human outbreaks in many countries. Both male and female are colorless. The cuticle is smooth, but shows pseudo segmentation and is disturbed by dorsal and ventral pairs of hypodermal gland cells. The somatic musculature consists of a single layer of muscle cells. Muscle cells contain mitochondria, prominent contractile filaments and a large nucleus. The alimentary tract involves an oral cavity, capillary oesophagus, midgut with brush border and hind gut. An inflammatory response is prompted at the intestinal level in the host, playing a crucial role in the expulsion and elimination of the parasite during the course of infection with T. spiralis. However, many studies have proved that this inflammatory response is harmful to the host. Through the enteral phase of the infection, the existence of the adult and larvae in the mucosal and submucosal layers causes an inflammatory response and functional changes in the motility of small intestine. Obviously, light infection causes slight damage but, with more severe infections, hyperemia, petechiae of the serosa, excessive mucous secretion, enlarged Peyer's patches and dilatation of loops of bowel occur. Histopathology of the small intestine shows that there is strong inflammatory response with mixed cellular infiltration mainly neutrophils, eosinophils and lymphocytes in the jejunum. The onset of symptoms can range from 12 hours and two days after ingestion of infected meat. Movement of worms in the intestinal epithelium can cause severe damage to the host tissue and the waste products they excrete can provoke an immunological reaction. 5-7 days after the presence of symptoms, facial edema and fever may occur. After 10 days, weakening of pulse, blood pressure, intense muscular pain, difficulty in breathing, heart damage and various nervous disorders may occur, eventually leading to death due to heart failure, respiratory complications or kidney malfunction. Low-intensity infection can remain asymptomatic.

Keywords: *Trichinosis*

Introduction

Trichinosis is a re-emerging zoonotic disease that has develops a public health concern since its reported human outbreaks in many countries **(1)**.

Two main groups are recognized in the genus:

1. **Capsulated group** *T. spiralis*, T1: *T. nativa*, T2; *T. britovi*, T3; *T. murrelli*, T5; *T. nelsoni*, T7; *T. patagoniensis*, T12; and *Trichinella* genotypes T6, T8 and T9; they infect mammals only.

2. **Non-capsulated group** *T. pseudospiralis, T4 (infecting birds and mammals); T. papuae, T10; and T. zimbabwensis, T11 (infecting mammals and reptiles).* **(2)**.

Morphology

Both male and female are colorless. The cuticle is smooth, but shows pseudo segmentation and is disturbed by dorsal and ventral pairs of hypodermal gland cells. The somatic musculature consists of a single layer of muscle cells. Muscle cells contain mitochondria, prominent contractile filaments and a large nucleus. The alimentary tract involves an oral cavity, capillary oesophagus, midgut with brush border and hind gut **(3)**.

Male of *T. spiralis:* measures between 1.4 and 1.6 mm long, and is flat anteriorly than posteriorly. The anus can be found in the terminal end. It has a large copulatory pseudo bursa on each side. The reproductive tract is composed of a single testis. **Female of *T. spiralis:*** is about twice the size of the male. It has an anus found terminally and the vulva is located near the oesophagus. The single uterus is full with developing eggs in the posterior portion, while the anterior portion contains the fully developed juveniles **(4)**.

The larvae of *T. spiralis*:

- **Muscle larva**

Muscle larvae (ML) are known as first-stage (L1) larvae as developmental moults happen only after their penetration in the gut mucosa of a new host **(2)**.

They are 0.7 to 1.5 mm long and approximately 0.3 mm in width. The esophagus is narrow and has a slightly rounded end. The cuticle is smooth. In the anterior half of the body cavity, the stichosome, a structure instituted of a long slender tube surrounded by a row of 45 to 55 large cells (stichocytes), can be observed. The rectum is also rounded without any projections or appendages **(5)**.

- **Newborn larvae (2)**.

Newborn larvae (NBL) (about 7 µm in width, 110 µm in length) show rudimentary morphological features. They are L1 larvae as the muscle larvae. At this stage, the sex cannot be identified. The newborn larva is the only stage of the parasite that has a sword-like stylet, located in its oral cavity. It uses it to create an entry hole in potential host cells.

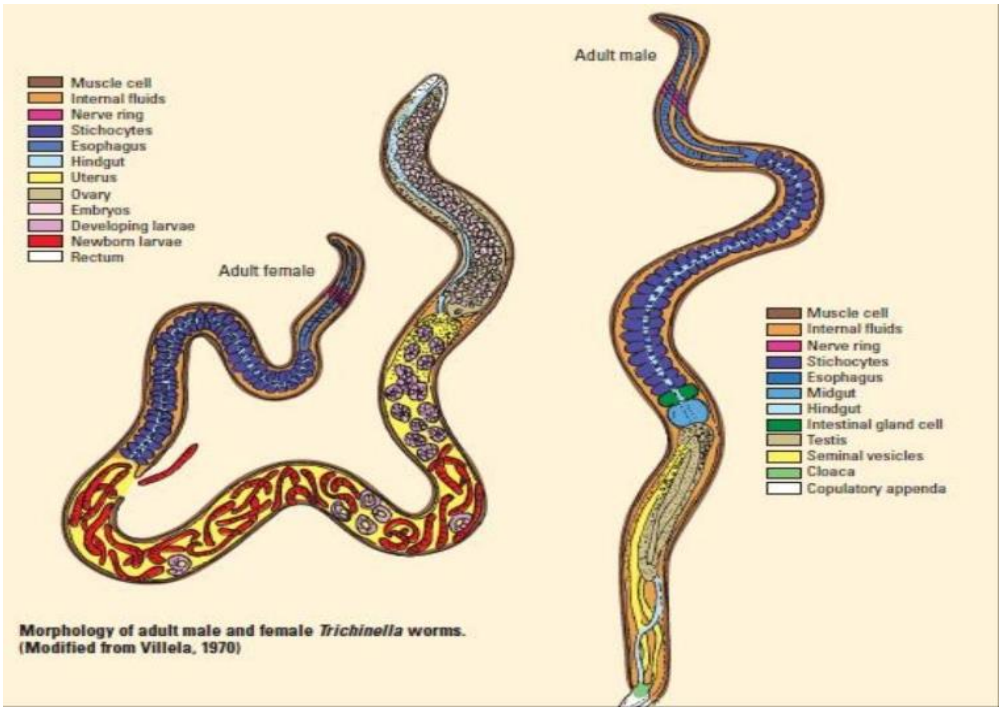

Fig (1): Morphology of *T. spiralis* male and female **(6).**

Life cycle

The *Trichinella* parasite, the smallest of the human nematode parasites, has a unique life cycle. The small adult worms grow in the small intestine of a definitive host, such as pigs. Each adult female yields huge number of live larvae that penetrate the intestinal wall to enter the blood and lymphatic systems to be carried to striated muscle to encyst **(4)**.

T. spiralis infection in humans is primarily due to ingestion of raw or semi-raw meat or meat products infected with the encapsulated muscle larvae. When being eaten, *T. spiralis* ML encapsulated in the skeletal muscles are released from their capsules in the stomach, where they develop into intestinal infective L1 larvae (IIL1) within the intestines. The IIL1 larvae disturb into enteral epithelia. They continue to grow into adult worms by molting four times **(7)**.

The female is ovo-viviparous. This means that she yields eggs, but doesn't lay them until they have already hatched in her uterus. She lays her living larvae inside the small intestine beginning at the fifth or sixth day after infection. In 2 to 3 weeks, the fertilized females discharge ~1500 NBL which penetrate the intestine and migrate via the blood and lymphatic systems to skeletal muscles. The NBL afterthat develops into infective ML in addition the infected muscle cells develop into nurse cells that contain a collagen capsule **(7)**.

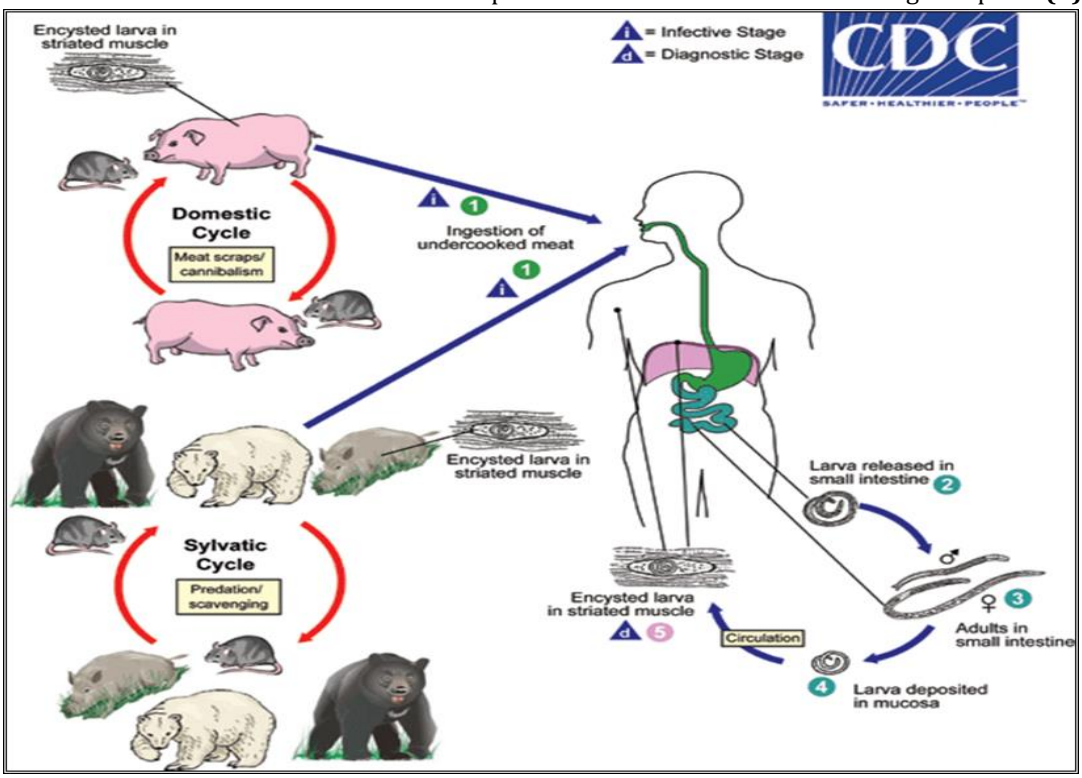

Fig. (2): The life cycle of *T. spiralis* **(8).**

Nurse cell:

T. spiralis is a multicellular parasite that inhabits within a single muscle cell, and is highly adaptable to its host's needs **(9)**.

Nurse cell is made from a normal part of striated skeletal muscle cell. It develops in 15 to 20 day after the larval penetration of that cell type. The parasite is causing alteration of muscle cell through secretion of several proteins into its intracellular niche, leading to reprogramming of host genomic expression**.** The sticocyte-specific secreted polypeptides of the L1 larva (43kDa peptide) localizes in the cytoplasm of nurse cell from day 12 through day 15 of nurse cell development **(10).**

Invasion of *Trichinella* larva causes complete loss of myofibrillar organization, then satellite cells are activated and basophilic transformation occurs in the infected muscle cell then a septum is formed to limit

damaged area. A septum is designed to separate the affected area (basophilic cytoplasm) from the intact area of the same muscle cell**.** Infection leads to the proliferation, differentiation and activation of satellite cells, which develop into eosinophilic cytoplasm **(11).**

The developed nurse cell has as many as 100 greatly enlarged nuclei with well developed nucleoli. It is surrounded by a collagenous capsule wall and a circulatory rete **(12).**

Epidemiology of trichinosis in Egypt

A human outbreak of trichinosis arisen among French tourists after the consumption of pork from a domestic pig in 1975. At that time, an incidence of 4.5% was found in domestic pigs slaughtered at the Cairo abattoir. In addition numerous cases have been reported in different localities in Egypt including Tanta **(13)**.

In 2000, the prevalence dropped to 1.7%. High incidence rates of infection (up to 13.3%) have been noticed among synanthropic rats of Alexandria abattoirs. *T. spiralis* has been recognized in two stray domestic pigs and dog. *Trichinella* species larvae have been also perceived in wolves from Sinai. These epidemiological data recommend that both a domestic and asylvatic cycles occur in Egypt **(2)**.

Sayed *et al.* (14): reported that the incidence of Trichinosis in human was 60.8% with a rate of 67.7% in Assiut governorate and 46.7% in Sohage governorate. However, domestic trichinosis (*T. spiralis*) is present in Egypt. Little reports of *T. spiralis* infection in fresh and processed pork in Egypt are available **(15).**

Mohammed *et al.* (16): reported that the seroprevalence rate of *T. spiralis* infection in humans tested by Enzyme linked immune-sorbent assay (ELISA) was 10% and the overall prevalence was 1.06% in pigs by trichinoscope in Sohag and Qena governorate.

Pathology and pathogenesis

1. **Gastro intestinal tract phase:**

An inflammatory response is prompted at the intestinal level in the host, playing a crucial role in the expulsion and elimination of the parasite during the course of infection with *T. spiralis*. However, many studies have proved that this inflammatory response is harmful to the host **(17)**.

Through the enteral phase of the infection, the existence of the adult and larvae in the mucosal and submucosal layers causes an inflammatory response and functional changes in the motility of small intestine. Obviously, light infection causes slight damage but, with more severe infections, hyperemia, petechiae of the serosa, excessive mucous secretion, enlarged Peyer's patches and dilatation of loops of bowel occur. Histopathology of the small intestine shows that there is strong inflammatory response with mixed cellular infiltration mainly neutrophils, eosinophils and lymphocytes in the jejunum **(18)**.

Furthermore, *T. spiralis* infection leads to trophic changes in both circular and longitudinal smooth muscle layers of both jejunum and ileum with increased thickness of the jejunal and ileal muscle layers due to both hypertrophy and hyperplasia **(19)**.

2. **Muscular phase:**

In the muscle stage, larvae cause a similar inflammatory response when they invade the skeletal muscle bundles. This type of inflammation can be considered a response of the tissue immune system against the invasion. Nevertheless, extreme regulation signals of inflammation can lead to cellular destruction and tissue damage, which is responsible for inflammation-associated diseases **(20)**.

Nuclear infiltration is responsible for a mark of early muscle inflammation. Histological study of muscle inflammation exhibited that the decrease in muscle strength was accompanied by an inflammatory response **(21)**.

3. **Central nervous system:**

Neuro-trichinellosis represents a major complication of human trichinellosis. It is caused primarily by vasculitis and granulomatous inflammatory reactions. NBL wanders, triggering tissue damage before re-entering the blood stream, or remains trapped and destroyed by the following granulomatous reaction. The lesions involve acute non-suppurative meningitis with perivascular lymphocytic and monocytic infiltration, local granulomatous lesions and capillary thrombosis **(22)**.

There are many mechanisms responsible for the contribution of the nervous system through direct or indirect involvement of the parasite. In the latter, inflammatory cells, especially eosinophils, appear to play a crucial role **(22)**.

4. Lung:

The lung is one of the main organs for the holding and destruction of NBL. Larval migration through the lung exacerbates an inflammatory allergic response together with bronchus associated-lymphoid tissue and goblet cell hyperplasia **(23).**

Ierna *et al.* (24): showed that inflammatory process during trichinosis in the lung caused from a signal originated in the gut due to larval penetration into its epithelium with development of an inflammatory process with the rejection of the adult worms from such mucosa.

5. Liver:

There are two main causes of liver damage. The first is that the adult *T. spiralis* leads to extensive damage to the intestinal epithelium, giving the chance for normal intestinal bacteria to reach the liver through the portal system. The second is that NBL which is excreted by adult female in the intestine may elicit an immune response that affects the liver **(25)**.

Farid *et al.,* (26) observed acute hepatitis in response to infection with *T. spiralis* in rats.

6. Heart:

Myocarditis is primarily caused through invasion of the migrating larvae, then by immunopathological responses as activated eosinophil infiltration and mast cell degranulation, according to experimental results in rats and histopathological observations **(27)**.

The larvae of *T. spiralis* are neither fixed nor encapsulated in heart muscle tissue but their transitory stay in the heart leads to morphological changes. The focal cellular infiltrates consist primarily of eosinophils and mononuclear cells. Eosinophilic myocarditis characterized by granuloma formation and proliferation of the connective tissue, leading to interstitial myocarditis **(28**).

Clinical picture

The onset of symptoms can range from 12 hours and two days after ingestion of infected meat. Movement of worms in the intestinal epithelium can cause severe damage to the host tissue and the waste products they excrete can provoke an immunological reaction**.** 5-7 days after the presence of symptoms, facial edema and fever may occur. After 10 days, weakening of pulse, blood pressure, intense muscular pain, difficulty in breathing, heart damage and various nervous disorders may occur, eventually leading to death due to heart failure, respiratory complications or kidney malfunction. Low-intensity infection can remain asymptomatic **(4)**.

***Trichinella* infection in the human host can be divided into two phases:**

1. Intestinal (or enteral) phase:

This clinical presentation is characteristic of many enteral disorders (e.g., food poisoning or uncomplicated indigestion) and thus it is easily misdiagnosed. Trichinosis usually begins with a feeling of general discomfort and headache, increasing fever, chills, and sometimes diarrhea and/or abdominal pain. Fever, eyelid, or facial edema and myalgia are the principal signs and symptoms of the acute stage, which can be complicated by myocarditis, thromboembolic disease, and encephalitis **(29)**.

2. Muscular phase:

Parenteral or muscular phase presents by periorbital edema, myalgia and muscle weakness**.** Months or even years after the acute stage, chronic trichinosis may yield persistent formication, numbness and excessive sweating as well as impaired muscle strength and conjunctivitis, which may persist up to 10 years post infection in people not treated early during the acute phase of infection **(30)**.

Complications

Complications advance within the first 2 weeks. They are detected primarily in severe cases. In moderate cases such as people who were inadequately treated or those started treatment so late and old people may also suffer complications. There is a strong correlation found between age and the frequency and severity of

complications. Myocarditis and encephalitis, which are both life-threatening, are frequently simultaneously present **(31)**.

1. **Cardiovascular complications (myocarditis):**

Although cardiac involvement in trichinosis is uncommon, it is the most common cause of mortality. It happens in moderate and severe cases of the disease. It occurs between the 3rd and 4th weeks post infection **(32)**.

Myocarditis develops in 5–20 % of all patients. The symptoms include tachycardia, pericardial pain and electrocardiogram abnormalities **(23)**.

Thromboembolic disease like deep thrombophlebitis, intraventricular thrombi and/or pulmonary embolism is another fatal cardiovascular complication. Paroxysmal tachycardia or pulmonary embolisms are two possible causes of sudden death. Additionally, hypo-albuminemia may happen as a sequel of cardiac complication leading to edema in lower extremities **(33)**.

2. **Neurological complications:**

One of the most significant complications of severe trichinellosis in humans and occasionally fatal is neuro-trichinellosis **(33)**.

Neurological symptoms like excessive excitement, frequent somnolence, consciousness disorders and apathy; some patients with these symptoms show signs of meningitis or encephalopathy. In severe cases, facial nerve paresis, anisocoria, and Babinski reflexes have also been observed. Brain injury, which is often detected within a few days after the onset of fever, can result in diffuse encephalopathy or focal signs such as disorientation, memory disturbances, behavioral disturbances, transient hemiparesis or hemiplegia, oculomotor dysfunction, aphasia and cerebellar syndrome **(23)**.

3. **Respiratory complications:**

Respiratory complications are less frequent. They might occur in both early and late stages of the disease. Dyspnea is relatively common. It is caused mostly due to parasite invasion and subsequent inflammation of respiratory muscles such as the diaphragm. Obstructive bronchitis, pneumonia, Loffler-type infiltrates, ventilation failure and bacterial pleurisy are among the complications **(34)**.

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