Summary

- Trichinellosis = Trichinosis
- *Trichinella*: adult worm in intestinal wall (not in the lumen), larvae in muscles and heart
- Transmission by eating infected meat, so there is never a free-living parasite
- Hypereosinophilia, fever, muscle pain, oedema chiefly peri-orbital
- Faeces negative for parasites (no eggs)
- Muscle biopsy positive for larvae
- Filaria are part of tissue nematodes

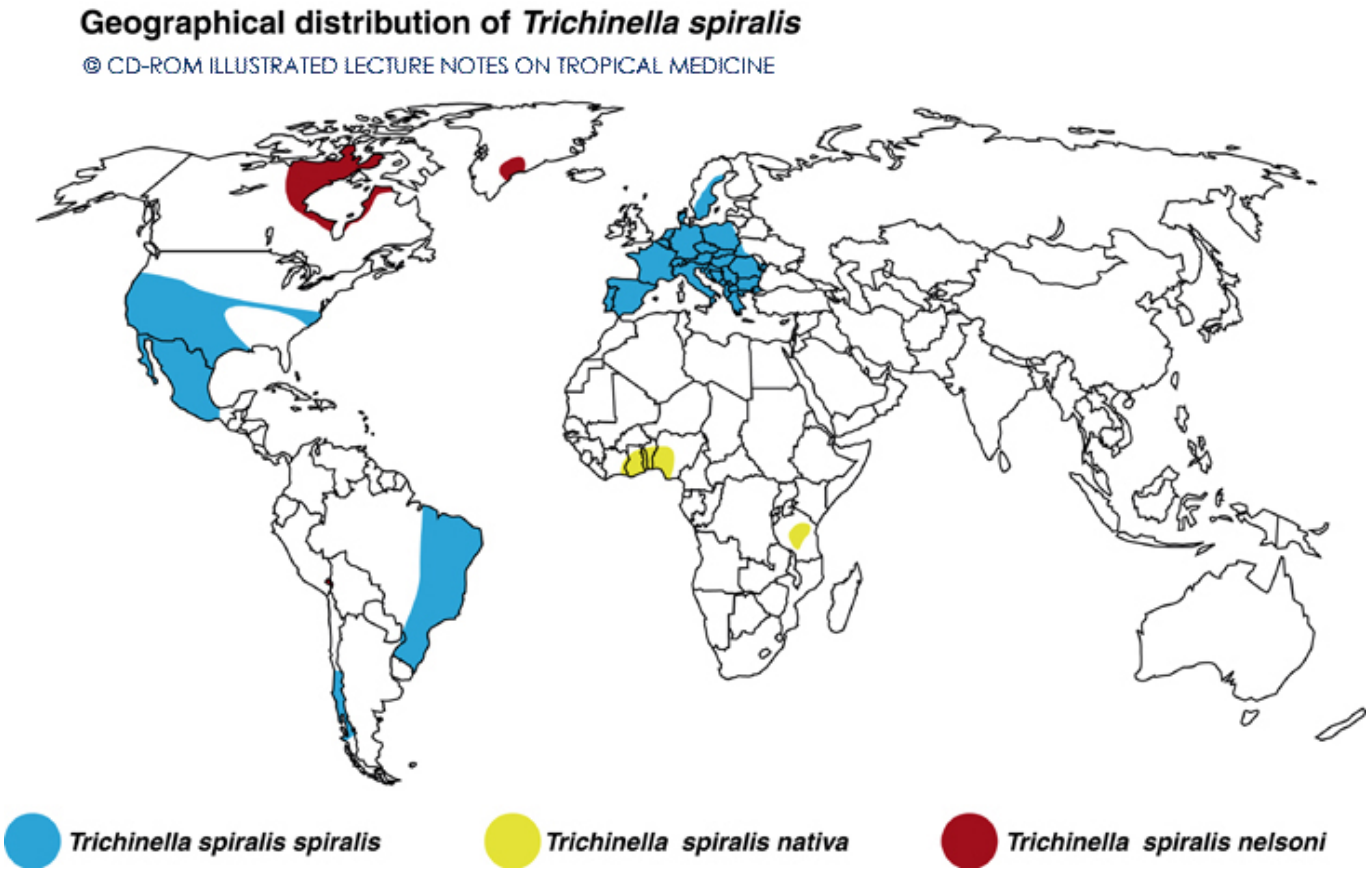
Historical note

In 1835 a 51-year-old Italian bricklayer died of tuberculosis in St Bartholomew's Hospital, London. Jim Paget, a first-year student (later of "Paget's disease" or osteitis deformans fame), was present during the autopsy and observed fine hard white inclusions in the diaphragm. Similar inclusions had been observed by doctors from time to time in the past but were attributed to commonplace muscle calcification, which quickly blunted the dissecting scalpel. Paget inspected the lesions with a hand lens and with a compound microscope in the British Museum. At the time there was only one such instrument in the entire Museum and it belonged to Robert Brown, of "Brownian motion" fame. Paget quickly recognised their worm-like structure and wrote of his discovery to his brother. After the word got out, surgeon Thomas Wormald took a second piece of the "sandy" diaphragm to Richard Owen, at that time assistant conservator of the Huntarian collection in the museum of the Royal College of Surgeons. He later become a major figure in comparative anatomy and paleontology, coining for example the name "Dinosauria". He published the discovery of the parasite ("a microscopic entozoon", but didn't give the proper credit to Jim Paget. The name "*Trichina spiralis*" was suggested. This name *Trichina* had already been given to a fly, and the name was later changed to "*Trichinella*". In 1846, the American Joseph Leidy found *Trichinella* larvae in the pork he had for dinner. He hypothesized that trichinosis is caused by consuming undercooked pork. In 1859 Rudolph Virchow carried out transmission experiments in which infected human muscle was fed to a healthy dog. After only 3 to 4 days adult *Trichinella* worms were found in the dog's duodenum and jejunum. He also discovered that heating the meat for 10 minutes was enough to stop transmission. He

started to spread the message that eating raw or lightly smoke-cured ham was dangerous. In Germany, where sausages were an important part of the daily diet, he provoked resistance from the German Veterinarian's Society. At a public meeting when denounced by a veterinarian, he showed the public an infected piece of ham and challenged his opponent to dare to eat it. In front of the crowd the veterinarian wisely declined the offer. Virchow's reputation grew quickly after this incident. When later challenged to a duel by Baron von Bismarck, he choose infected sausages as his weapon. The Baron declined to eat them after hearing what trichinosis was but the two men became friends later on. These days, Virchow is mainly remembered as the father of cell theory ("omnis cellula e cellula" or every living cell comes from another living cell).

PS. Robert Brown died in 1858, just before Charles Darwin received news from Alfred Russel Wallace's independent discovery of the role of natural selection in the evolution of animals and plants. It was Brown's death that provided the vacant slot in the Linnean Society's programme that allowed Darwin (spurred on by Wallace's findings) to describe his theory (and Wallace's) in public.

General



Map showing the areas endemic for the different subspecies of Trichinella spiralis: Trichinella spiralis spiralis, Trichinella spiralis nativa, Trichinella spiralis nelsoni. Copyright ITM

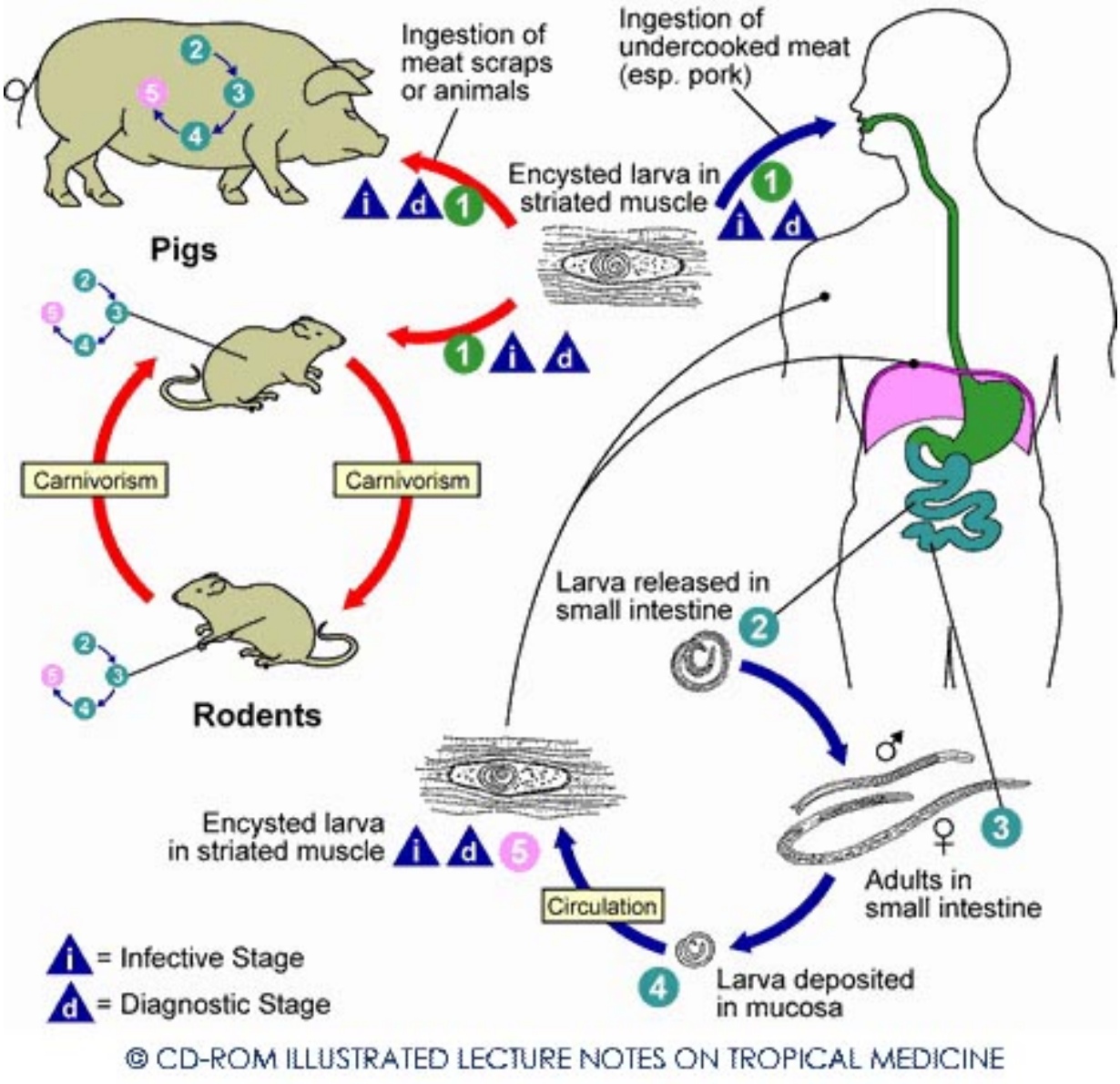
Trichinosis or trichinellosis is a zoonosis. It refers to infection with the larval and adult stages of a group of closely related nematodes which belong to the genus *Trichinella*. The infection is meat-borne.

Typically pork is implicated. Other meat sources such as horses and wild game, certain birds and even reptiles increase in significance as more study results are becoming available. Carnivores and omnivores represent the most important reservoirs.

Trichinella species

There are 9 *Trichinella* species. All species can develop in mammals and some in birds or even reptiles. The parasites are widespread on all continents except Antarctica. *T. spiralis*

occurs in temperate regions and infects mainly pigs. *T. nativa* occurs in the arctic and subarctic areas in terrestrial and marine carnivores (e.g. polar bear, walrus). These parasites are resistant to freezing which is important for meat storage. *T. britovi* occurs in temperate areas of the Palearctic region, as well as North and West Africa. *T. spiralis nelsoni* occurs in Africa and southern Europe with a reservoir in wild carnivores and wild pigs.



Trichinella spiralis life cycle. Courtesy of CDC, Division of Parasitic Diseases

More than 100 species of mammals are susceptible to the infection. By and large pigs and

horses seem to be responsible for the majority of human infections. Horses are considered herbivores, but 32% of horses tested ate meat when offered. The feeding of animal products to horses is a practice that occurs in several countries. Eating walrus meat plays a role in the arctic. On a global scale *T. spiralis* is responsible for the majority of human infections. Rats play an important part in the transmission in pig-raising areas. It is unclear if they form a true reservoir. The use of rat pesticides can actually augment transmission as poisoned rats are easy prey for pigs.

Gravid female worms embedded in the intestinal mucosa release newborn larvae. These larvae measure about 100 µm by 6 µm. These immature larvae are extracellularly exposed to the humoral immune system. The larvae migrate to the intestinal lymphatics, then enter blood vessels and subsequently penetrate striated muscle cells. Then something strange happens. After entering the muscle cell, the larvae are completely intracellular. This is unique. They will convert their host cell into a so-called nurse cell. Their metabolism is mainly anaerobic, which helps their survival after the death of the host. In the muscle cells, larvae can survive several decades. They are now called infective larvae and are visible with low magnification. Larvae do not mature or become encapsulated in heart muscle. When a new host ingests muscle tissues, the larvae are released in the stomach by digestion. In the duodenum they penetrate the villi and undergo 4 molts, developing into adults which measure about 1 mm (males) to 3 mm (females) with a thickness of about 30 µm. Males and females copulate and 6 to 7 days post-infection, the females start to produce new-born larvae. This continues for a few weeks according to the immune response of the host. Afterwards adults are expulsed. It is extremely rare to find an adult worms in a human patient.

Clinical aspects

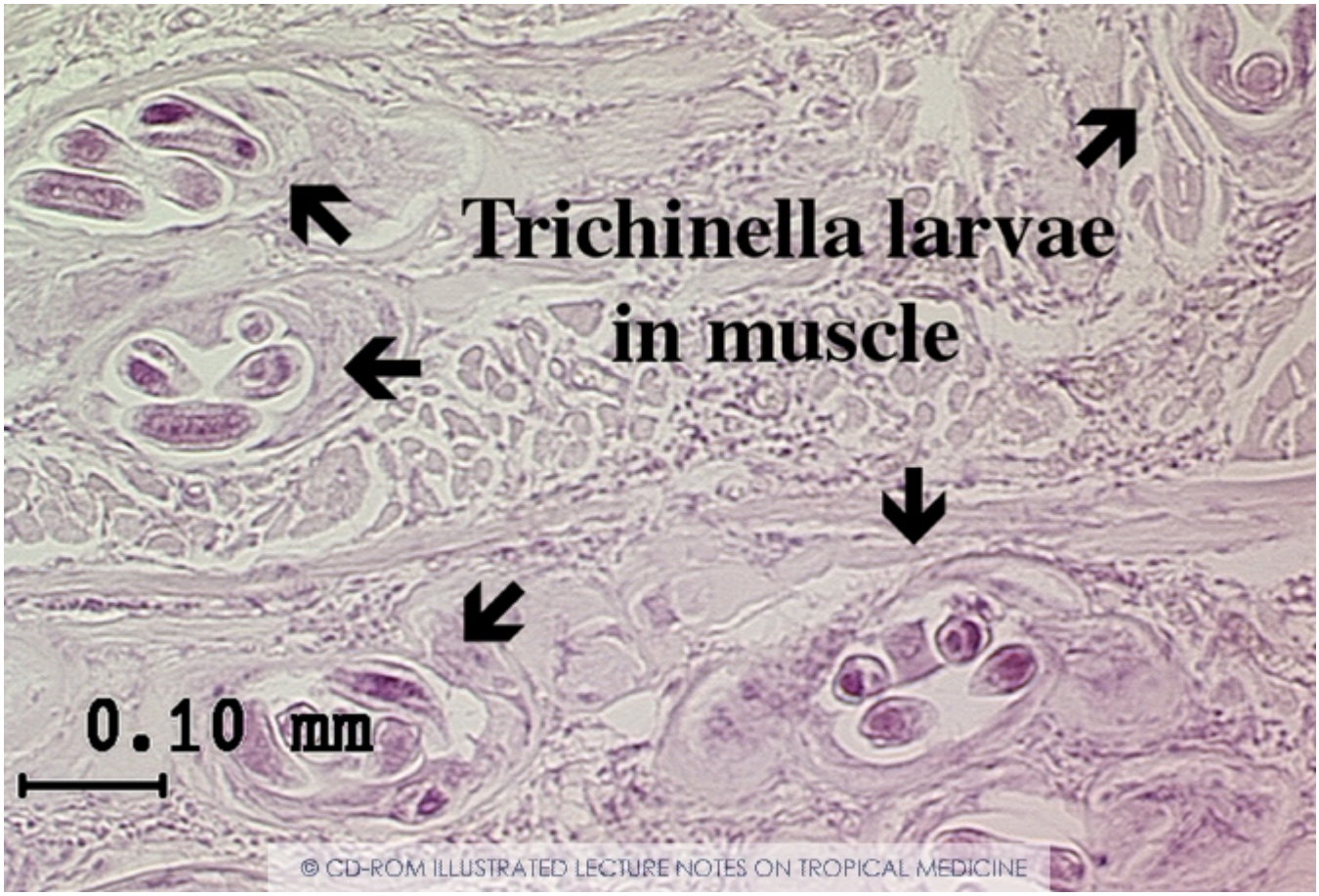
Light infections may be asymptomatic. About 70 live larvae are sufficient to provoke clinical disease. In more typical cases there is nausea, non-bloody diarrhoea, abdominal pain, vomiting and fever; a few days after eating infected meat. After 10 days the fever tends to increase. The patient is very ill, asthenic and debilitated, there are muscle pains and a typical peri-orbital oedema (differential diagnosis acute trypanosomiasis, angioedema, gnathostomiasis and nephrotic syndrome). This oedema is caused by invasion of the small muscles around the eye. In severe cases, oedema extends to arms and legs. Conjunctival and

subungual haemorrhages may occur (due to vasculitis, not endocarditis). There may be signs of myocarditis, encephalitis, urticaria and asthma. A small number of persons may develop a maculopapular rash after the onset on muscular pain. There is often very significant eosinophilia. This lasts from several weeks to three months.

A massive decrease in eosinophils in persons with severe trichinellosis predicts a severe outcome. Myositis causes an increase in the muscle enzymes (creatine phosphokinase, CK). Wandering newborn larvae can become trapped in small blood vessels leading to vasculitis and peri-vasculitis with diffuse or focal lesions in the central nervous system. Aspecific cortical and subcortical lesions (ischemia) can be identified on MRI, and much more rarely, white matter lesions (granulomatous reaction). Severe myalgia generally lasts for two to three weeks.

Dyspnoea is relatively common and is primarily caused by invasion and inflammation of the diaphragm. After a few months the symptoms are reduced or disappear, although asthenia and chronic muscle pain can persist for up to 6 months. Mild infections are self-limiting but live larvae will persist in muscles for years.

Diagnosis



Trichinella spiralis in a muscle biopsy. Copyright ITM

The clinical picture is of a patient with acute fever and myalgia, pronounced asthenia, possibly diarrhoea and a swollen face. Cardiopulmonary, neurological or renal complications may be fatal. The consumption of insufficiently cooked or raw meat can often be found in the patient's history, and this is often game that the patient has hunted (e.g. wild boar) or raw meat eaten in Asian cuisine or the Arctic.

Here it is important to consider the incubation period; one week for severe disease, two weeks for moderate disease, and three to four weeks for benign forms. Sometimes the infection can be traced to infected horsemeat. There is leukocytosis with eosinophilia, although eosinophilia can be absent in immunocompromised persons (renal graft, HIV, chronic myeloid leukaemia). Muscle biopsy should be performed (deltoid muscle or other). An infection is clinically patent in humans when the number of larvae per gram of muscle biopsy

is around ten and severe when above hundred. In early stages of infection, histology is more sensitive than trichinelloscopy. The larvae can be seen coiled inside myocytes. There are various serological techniques (e.g. ELISA, Western blotting) for identifying antibodies against Trichinella species. Serology is negative during the first days of the febrile phase (seroconversion during second to fifth week of infection). PCR can be performed in the International Trichinella Reference Centre (Instituto Superiore di Sanita, Rome, Italy). Remember that there will be no eggs in the faeces.

Treatment

For mild infection symptomatic treatment is often sufficient. In the early stage albendazole (800 mg/day) or mebendazole at high doses can eradicate adult worms in the intestine. Mebendazole is poorly absorbed. Albendazole 800 mg daily for 7-14 days may be used, in combination with high-dose prednisolone. With treatment the duration of the disease may be reduced to one or two weeks. Pyrantel is sometimes used during pregnancy, but its efficacy is disputed.

Prevention

- Meat should be well boiled or roasted through.
- Importance of meat inspection. The identification of *Trichinella* larvae in muscle samples is limited to post-mortem inspection of carcasses. Selection of muscles for sampling in meat inspection requires identification of predilection sites in a particular animal, but in low grade infection, distribution of the larvae is not homogeneous. In pigs infected with *T. spiralis*, predilection sites are the diaphragm crus, the tongue and the masseter. The diaphragm of a slaughtered animal is inspected (the piece of muscle of a certain minimum weight is flattened between two glass slides and examined using transillumination). This technique (trichinoscopy) is not so good for *Trichinella pseudospiralis* because it is not surrounded by a capsule and is easily missed. Pooled muscle samples can be inspected with a method which employs artificial enzymatic digestion to free and to look for the larvae.
- Pig food (which may include infected rats) should be boiled for 30 minutes.
- To store pork for 10 days at -25°C is generally impractical in developing countries. In the West meat is sometimes irradiated with high doses of gamma rays, which will kill any

larvae.