Summary

- Infection by *T. solium* eggs followed by development of cysticerci (= larvae) in the body.
- Symptoms depending on localization of the larvae.
- Neurocysticercosis with epilepsy is a common complication.

General

At the end of the 19th century cysticercosis was still occurring frequently in Europe. At that time cysticercosis was found in 2% of the autopsies in Berlin. Nowadays the disease has virtually disappeared in the West. There are still occasional imported cases. Approximately 50 million people worldwide are estimated to have cysticercosis infection, although subclinical infection may underestimate this number. The disease occurs in regions where pigs are kept and eaten (thus not in Muslim regions). In many poor areas pigs are not kept in a pigsty, but run about in the open. This is encouraged in some areas, so that the animals function as a kind of free waste-disposal system. These are generally also places where the sanitary facilities are inadequate. The animals can become infected from human faeces via coprophagy. Insufficient meat control is an important risk factor in endemic regions. Not cooking meat through is another risk factor. Cases of cysticercosis in non-endemic regions may sometimes occur via infection from the carriers of adult worms who have come from endemic regions. If these infected migrants are employed in a household they may cause infections in their new surroundings (e.g. Mexican women who go to work in households in the USA).

Life cycle

When larval *Taenia solium* infect a human they develop into an adult tapeworm. In contrast, if the eggs of *Taenia solium* are swallowed (food or water infected with human feces) the larvae (oncospheres) which emerge from them penetrate the intestinal wall and spread throughout the whole body via the blood stream. Therefore note that cysticercosis is caused by infected human faeces and not directly by eating insufficiently cooked pork. People with cysticercosis do not necessarily have an adult tapeworm. Auto-infection in humans infected

with an adult *Taenia solium*, is a possibility, however. In approximately 40% of people with cysticercosis an adult worm is found in the intestinal tract. The larvae migrate to various tissues and within 2 months convert into what are known as bladder worms (cysticerci). The typical bladder worm is a small ellipsoidal bag measuring 5-15 mm surrounded by a white translucent membrane. This bag contains clear fluid and a single round head, the protoscolex. When the cysticerci die off they are absorbed or encapsulated and calcify. Each egg produces 1 cysticercus. Larval multiplication does not occur. In the brain, cysticerci can become extremely large (many centimeters diameter) when they develop in the ventricles (racemose form, see below).

Cysticerci which are present in pork, evaginate normally in the human intestine to then grow to full adult worms. Evagination is also possible, (but rare) in the human eye and intraventricular evagination may occur in the brain. These are sites where no inflammatory capsule is formed around the parasite. Evagination does not occur in the muscles or in the cerebral parenchyma.

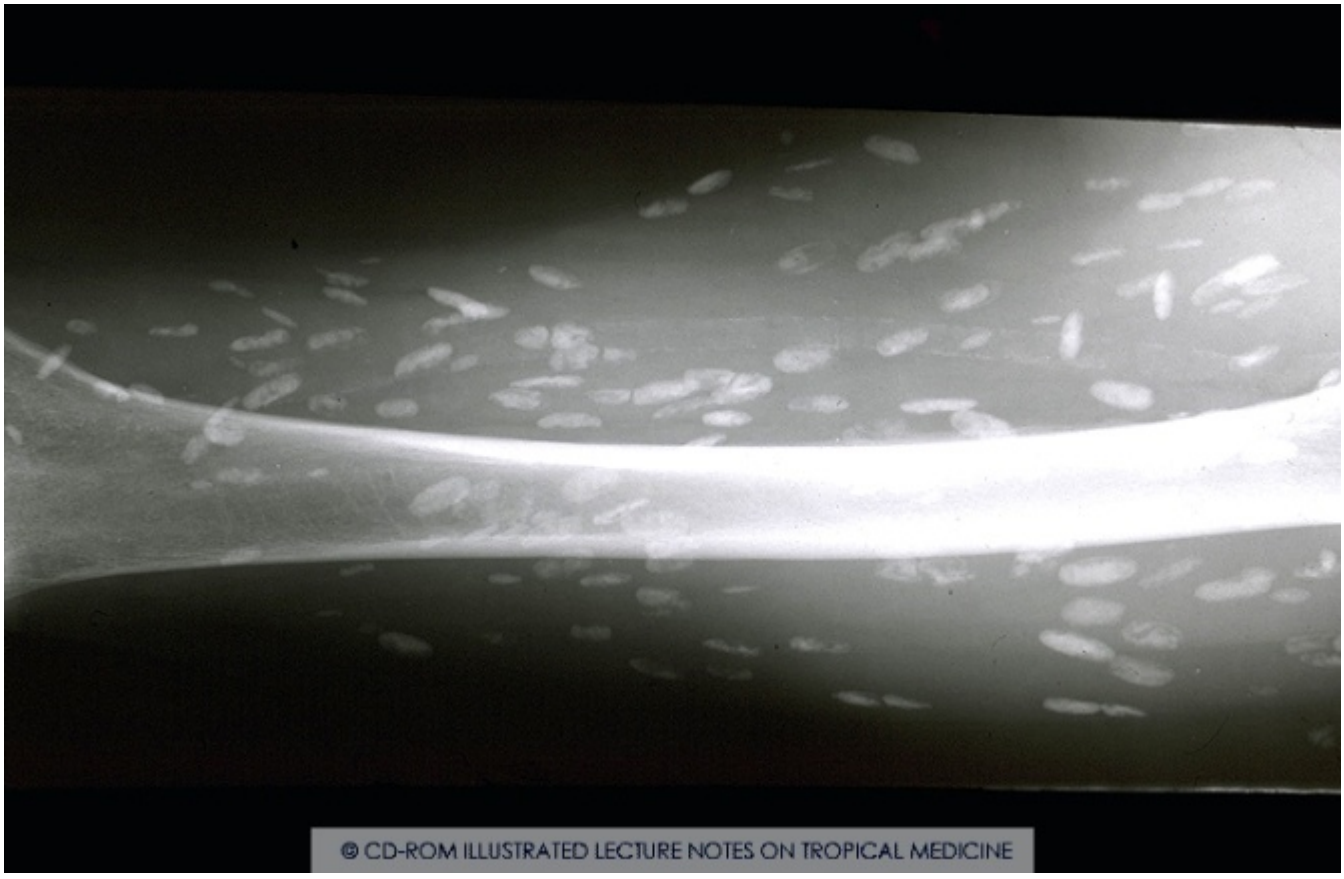
Clinical aspects

Symptoms vary greatly, depending on the location of the cysticerci and the immune response of the individual. Small cysts may be found in the muscles, subcutis, eyes and in other tissues, where they are usually asymptomatic but may cause discomfort when inflamed. They appear as small nodules (5-10 mm). Sometimes they are much larger (e.g. 30 mm or even larger). In neurocysticercosis (NCC) there are parenchymal, subarachnoidal, intraventricular, spinal and ocular forms. Racemose cysticercosis is an aberrant development form of the parasite similar to a bunch of grapes. Live cysticerci in the central nervous system often cause remarkably few symptoms. When the parasites degenerate there may be focal encephalitis and oedema. Sometimes they may trigger a severe inflammatory response within a few days, which can be fatal.

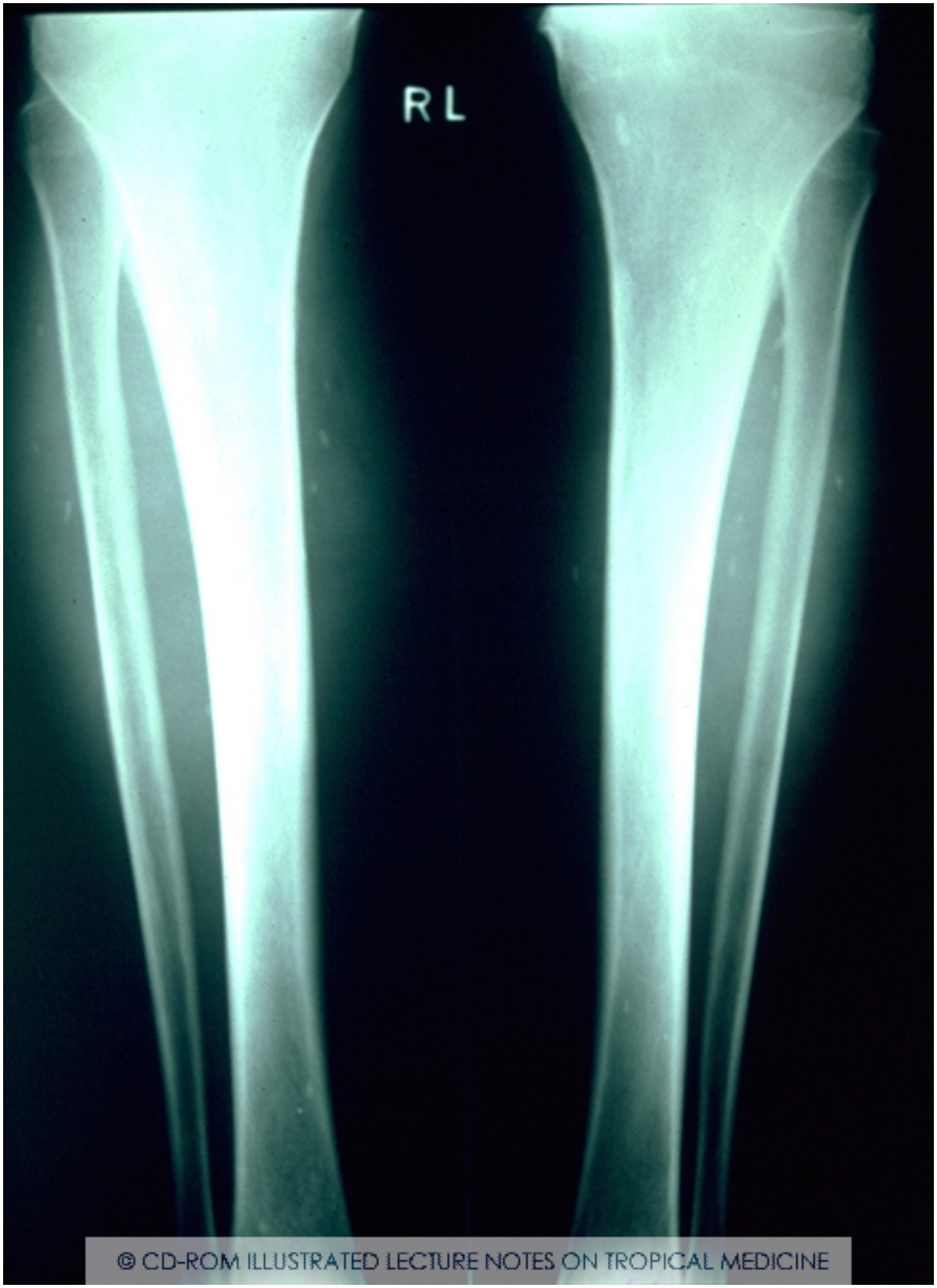
In the brain they often cause late-onset epilepsy (common in Mexico and South America). Adult-onset seizures in endemic regions are therefore highly suggestive of neurocysticercosis. This can manifest itself as focal seizures (Jacksonian epilepsy). This is often followed by postictal confusion or transient paralysis (Todd’s paralysis) and/or speech ± vision problems. Todd’s paralysis usually disappears within 48 hours. Intraventricular cysts

may cause obstructive hydrocephalus. According to a recent meta-analysis, the main syndromes caused by NCC by order of frequency are epilepsy (80%), focal deficits (15%), intracranial hypertension (10%) and cognitive declines (5%). Mixed locations (parenchymal + meningeal) are common, but spinal localization is rare. Chronic meningitis, paralysis of cranial nerves, spinal cord lesions and mass effects may occur.

Psychiatric symptoms, encephalitis-like, are possible in case of severe infection. All these neurological problems may be acute or delayed forms. Focal calcifications are detectable 8 months to 10 years after infection. Larvae cannot be regarded as dead, unless the lesion is **completely** calcified.



Radiograph of an arm, showing elongated oval calcifications, typical of cysticercosis (calcified cysts in muscle).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Taenia solium, calcified cysticerci in the muscles of the legs. Such lesions are typically oval and elongated when localised in a muscle.

Table: Symptoms of neurocysticercosis

Headache	(23-98%)
Meningism	(29-33%)
Papilloedema	(48-84%)
Convulsions	(37-92%)
Abnormal mental state	(74-80%)
Focal deficits (motor and/or sensory)	(3-36%)
Ataxia	(5-24%)
Myelopathy	(<1%)
Cerebral nerve defect	(1-36%)
Visual disturbances	(5-34%)

Diagnosis

Diagnosis is made by means of excision of skin nodules or by using serological techniques, including antigen detection. Antibody and antigen detection may be carried out on cerebrospinal fluid as well as serum, but are often negative if only one or two lesions are present. Lesions can be demonstrated by radiology, such as radiography targeting the soft tissues (shoulder and thigh muscles) and X-ray of the skull. In muscles, the calcified cysts tend to be elongated ovals.

MRI scanning of the brain is clearly superior to CT from a diagnostic point of view and scolices can sometimes be visualized through MRI. Living cysticerci are seen on a CT scan as hypodense lesions which are not enhanced by IV contrast. Degenerating cysticerci are

sometimes isodense or hyperdense with an edematous ring-shaped zone which can be enhanced by IV contrast. They may disappear within 3 months. Sometimes the diagnosis can only be made by stereotactic brain biopsy.

The parasite is often surrounded by an inflammatory infiltrate with plasma cells. Immunoglobulins may accumulate in the cytoplasm of reactive plasma cells, and form prominent eosinophilic inclusions (Russell bodies). They are however not specific for cysticercosis.

Serology is available and EITB (enzyme-linked immunoelectrotransfer blot assay) uses affinity-purified glycoprotein antigens fractionated by electrophoresis which performs better than ELISA. Antigenic tests have been also developed, reflecting the presence of viable cysts (if their numbers is sufficient however), in contrast to antibody detection tests reflecting only (past) exposure. Field-adapted lateral flow antigen-based diagnostics are being evaluated.

The most important **differential diagnoses of cerebral ring-shaped lesions:**

- Cerebral toxoplasmosis
- Hydatid cyst
- Ectopic worms (Paragonimus, Schistosoma)
- Amoebiasis
- Tuberculosis and cryptococcosis
- Bacterial abcesses, septic emboli, nocardiosis
- Glioma, lymphoma, metastasis
- Haemangioma

Treatment

Therapy of neurocysticercosis is extremely complex and depends on the cysticerci stages (viable, degenerating, calcified) and localizations (intra- or extra-parenchymal). It remains a rather controversial area. Expert advice and a multidisciplinary approach are often required. The most important is to treat the symptoms first, mainly the seizures with anti-epileptic

drugs (up to 2 years after the last seizure, like for other epilepsy). Medical treatment, when indicated, is based on administration of praziquantel (50 mg/kg/day) or albendazole (15 mg/kg/day) for 2 weeks, but in case of multiple cysticerci (>3), association of both drugs was found superior in seizure reduction.

In adequately selected patients (see below), antihelminthic therapy may reduce the risk of generalized seizures by 67% as well as of the number of seizures, and lead to complete resolution of the lesions at CT/MRI in a substantial proportion of patients. But in real life, the outcome is rarely this favourable. It is important to note that when the bladder worms die off they cause a local tissue reaction. Neurological symptoms may therefore exacerbate (generally on the 2nd to 4th day of treatment)and can be very difficult to manage where there are no neurosurgical facilities or neuro-imaging. This effect can be mitigated by starting dexamethasone 1 day before the other drugs, maintained up to one month (a dose of 8 mg/day seems optimal), before it's slowly tapered down. Albendazole does not interfere with carbamazepine (Tegretol®) or phenytoin (Diphantoine®). Corticosteroids reduce the blood level of praziquantel and increase albendazole levels, but this is probably of no clinical importance.

Recently the benefit of medical therapy has been questioned. Probably many patients with infections recover spontaneously. When treating neurocysticercosis, it is important to know beforehand whether there are intra-ocular lesions. Degeneration of a cysticercus in the retina, together with accompanying inflammation, may lead to acute blindness. Surgical removal via vitrectomy should be considered, but such a procedure is not without risk.

Today, experts recommend antihelminthic drugs only in case of viable (symptomatic) cysts without inflammation and degenerating cysts with inflammation (to accelerate involution). Granulomatous cysts and those already calcified, for which symptomatic treatment and steroids are sufficient, do not benefit from antihelminics. More and more a segregation is made between intra-parenchymal NCC, where medical therapy may be carefully proposed, except when there are too many lesions (**contra-indicated** because of the high risk of diffuse cerebral oedema), and extra-parenchymal (intraventricular, meningeal, spinal, ocular,…) NCC where neurosurgery is almost always required (due to risk of intracerebral obstruction and hydrocephalus) in combination with longer antihelminthic treatment at higher dose (extraparenchymal cystcicerci are usually less susceptible to medication).

Sometimes a ventriculoperitoneal shunt must be inserted in obstructive hydrocephalus. Shunt blockage is common if the cerebrospinal fluid contains large amounts of protein. Appropriate treatment of NCC is nearly unfeasible without adequate diagnostic/surgical facilities, and impossible without an initial careful neuro-imaging assessment. In remote, low-resource settings, it is often preferable to just treat the complications (epilepsy) with a symptomatic antiepileptic therapy, rather than using an etiologic treatment without possibility of monitoring or neurosurgical intervention.

Prevention

Since humans are the only reservoir for adult *T. solium* the disease can be controlled by improved sanitation and hygiene, in particular by controlling pollution with human faeces. Human carriers should be treated. To reduce the number of carriers of *Taenia solium*, proper statutory meat inspection should be carried out. Furthermore, meat should be heated to above 56°C or stored for at least 10 days at -10°C (requiring a freezer). Eating raw or insufficiently cooked pork should be discouraged. If there is a patient with cysticercosis, it is best to investigate whether the patient, close family members, domestic staff and friends are carriers of adult *T. solium* and constitute a possible source. A faecal examination and an antigen-capture ELISA test are used for screening. If positive, a CT scan of the brain is carried out (detection of cysts in the brain).

Pigs can be treated with a single administration of oxfendazole, a benzimidazole. Vaccination of pigs is under study, and appears to be efficacious under controlled environments. There should be a strong recommendation that pigs not be allowed to run free. They are coprophagic. If humans do not compost their faeces, but use them directly as pig fodder or on the fields, the animals will become infected.

Composting kills the eggs. Washing hands with soap after using the toilet should be encouraged. Parasitic infections in which faeces play a part, are a taboo subject in some communities. A control program needs to take account of this.

There is no vaccine for human protection against T. solium. However, vaccines are available to prevent T. saginata infection in cattle and T. ovis in sheep.