Summary

- Small liver flukes: eating infected fish leads to cholangitis, icterus, eosinophilia, cancer of the bile duct
- Large liver flukes: eating contaminated plants leads to cholangitis, icterus, eosinophilia

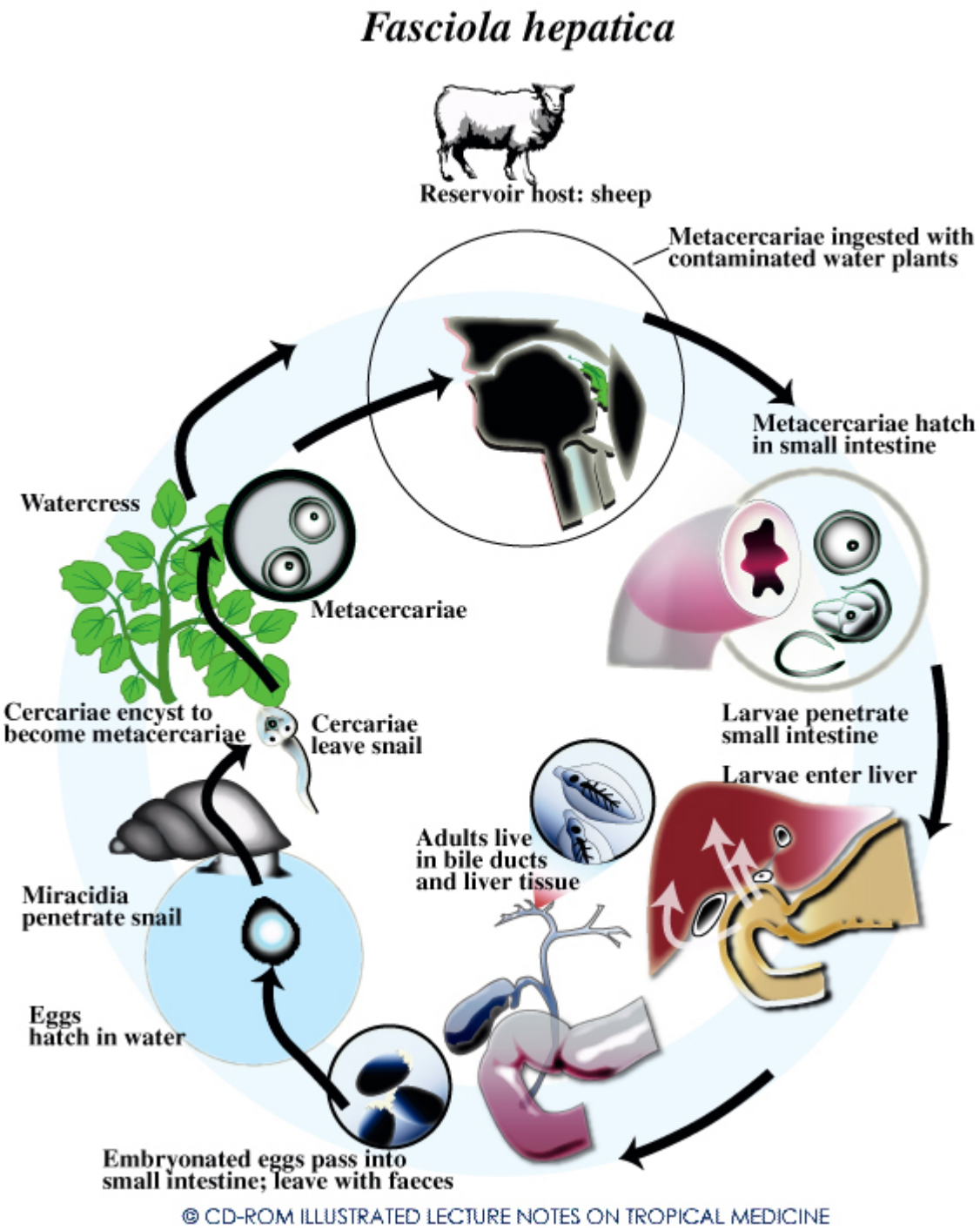
Small liver flukes: Clonorchis, Opisthorchis and Metorchis

Opisthorchis viverrini and *Clonorchis sinensis* (= *Opisthorchis sinensis*) occur in Asia. Eggs eliminated in the bile and faeces are taken up by snails. After further development in these animals, they leave the mollusk and penetrate freshwater fish (metacercariae). Humans become infected by eating raw fish such as carp. After the larvae are released in the duodenum, they migrate directly via the main bile duct to the intrahepatic bile ducts. Thus, there is no tissue passage. The parasites are approximately 1 to 2 cm long and can live for 20 years. Dogs and cats form a reservoir.

There may or may not be symptoms, depending on the worm load and location of the worms. Intermittent pain may occur around the liver which is sometimes enlarged. If bacterial superinfection occurs, febrile suppurating cholangitis results. If impaction with obstruction of the main bile duct occurs, there will be progressive icterus. In long-existing cases of infestation with *Clonorchis sinensis*, secondary biliary cirrhosis and carcinoma of the bile duct (cholangiocarcinoma) may develop. The diagnosis is made by detecting eggs in the faeces. A concentration technique is necessary. However, if bile duct is obstructed, no eggs can be detected. Sometimes duodenal intubation is necessary (aspiration of bile containing eggs). Serology may be helpful. The treatment consists of **praziquantel.** A new drug, tribendimidine, appeared very promising for both *Opistorchis* and *Clonorchis* in recent phase 2 trial.

Large liver flukes: Fasciola hepatica and F. gigantica

General



Fasciola hepatica, life cycle. Copyright ITM

Infection with these large liver flukes is quite wide-spread among animals. For example, *Fasciola hepatica* causes liver rot in sheep. The encapsulated larvae (metacercariae) are

found on all kinds of plants such as **water cress** (*Nasturtium officinale*), etc. After infected plants have been consumed the larvae are released in the small intestine, migrate within the hour through the intestinal wall to the peritoneal cavity and then bore through the liver capsule about 5 days later. After further migration in the liver, they reach the bile duct after approximately 7 weeks and remain there, laying their eggs.

These are transferred via the bile to the intestine, and then excreted with the faeces. A single liver fluke can lay up to 20,000 eggs a day but usually produces smaller numbers. It should be noted that fertilized eggs can be produced by a single liver fluke (they are hermaphroditic).

Eggs often remain viable for months and can overwinter. Survival for more than 2 years has been demonstrated at a temperature of 2°C. Fierce heat and drying out kills the eggs. At a temperature of approximately 25° C (the optimum temperature) eggs develop in about three weeks. There is much variation in the rate at which eggs are released, which is an advantage to the parasite, since a particular habitat will remain infectious over longer periods. Under the influence of specific stimuli a 130 µm long larva (miracidium) emerges from the egg. This is covered with cilia and is immediately mobile in water. It can easily swim for hours. The larva has eye spots and is highly phototropic (it swims towards the light). This prevents the larva from wasting time and energy exploring the bottom of the pond, where the intermediate host (usually *Lymnaea trunculata*) is not to be found. This is unlike *F. gigantica* where the miracidium actively swims away from light to find *L. natalensis*, which lives deeper down. If the larva does not find the correct snail within 24 hours its glycogen reserves are exhausted and the larva dies. If a miracidium arrives some 15 cm from a snail, there is pronounced chemotaxis and the larva swims directly to the host and penetrates it. The next development takes place within the snail. These snails can survive long periods of drought (via aestivation) and long-term cold (via hibernation). Inside the snail, the miracidium develops into a sporocyst and then into rediae, a stage named after the Italian physician Francesco Redi (1688). The rediae measure approximately 1-3 mm, are mobile and may cause significant damage in the snail (if the infection is severe the snail dies). After 4-7 weeks the first cercariae emerge from the rediae; they measure 250-350 µm and leave the snail. The cercariae swim around in the water, to encyst within 2 hours on particular plants. Each cercaria then changes into a metacercaria (plural metacercariae). Due to the amplification phase in the snail, a single egg can produce 4000 metacercariae. Metacercariae can survive

for more than a year on pasture. They are destroyed by heat and drought (the effect of long hot summers).

Clinical aspects

Symptoms are present mainly during the migration period: fever, pain in the liver region, hepatomegaly, urticarial, eosinophilia. After this period symptoms are generally mild or absent.

Sometimes there is cholangitis and obstructive jaundice. If raw goat's or sheep's liver is eaten, adult worms can sometimes attach to the throat, resulting in local irritation (halzoun).

Diagnosis

The diagnosis is made by detecting the eggs in faeces or duodenal aspirate (eggs appear approximately 12 weeks after infection). Repeated specimens are often necessary in view of the small number of eggs which are produced daily. If an individual has eaten infected sheep's liver, he/she can have eggs in the faeces, although no real infection occurs (spurious infection). Ultrasound or CT scan of the liver may show a clustering of hypo reflective or hypo dense tunnels in the liver parenchyma (these are inflamed bile ducts). Sometimes it is possible to actually visualize the moving worms. Via laparoscopy, one can sometimes find slowly migrating worm tracts. The specificity of serology is lowered by cross-reactivity with other helminths.

Treatment

The therapy is problematical at present.

- Praziquantel is not sufficiently active.
- **Triclabendazole (Fasinex®, Egaten®) 10 mg/kg taken in one dose** together with a fatty meal is becoming the treatment of choice. Triclabendazole-resistant F. hepatica strains are already known in cattle.
- Nitazoxanide is an alternative drug. The dose is 500 mg BD for 1 week.
- Artemisinine may become an alternative. Worm burden reductions of 99-100% were

observed with a single dose of the drug.