Humans can become infected with worms in numerous ways: schistosomiasis is transmitted through contact with contaminated water, soil transmitted helminthiasis through infective soil and lymphatic filariasis through mosquito bites.

But there is another transmission route which is given much less attention in the public health arena and yet puts over 10% of the world’s population at risk and currently infects over 40 million people. The transmission route is via food - and specifically food related to water, for example, fish, shellfish and water plants. And the scale of the problem is only just being investigated.

This issue of Action Against Worms looks at one of the worms in the food-borne trematode (FBT) family. “Foodborne” reflects the transmission route; “trematode” refers to the class of the worm.

Within the FBT family, there are more than 70 species that are known to infect humans. Each one has its particular impact on the body, with most of the damage inflicted on the liver, lungs and intestine. From a public health perspective, four are particularly important: clonorchiasis (Chinese liver-fluke disease), paragonimiasis (lung-fluke disease), opisthorchiasis (liver-fluke disease) and – the subject of this newsletter - fascioliasis (common liver-fluke disease) which infects at least two million people and is the most geographically widespread of the FBT.

Foodborne trematode infections are among the most neglected tropical diseases. Scarce attention is given to them by ministries of health or indeed the medical community. Their difficult names, complex life-cycles and specific geographical distribution simply add to their anonymity.
Animal infections that jump to humans

Fascioliasis is a zoonosis, in other words, primarily an animal infection that has “jumped” to humans. The life-cycle of fascioliasis is complex, involving a final host (usually a domestic ruminant) where the adult worm lives, and an intermediate host where the larval stages of the worm develop.

Typically, the process starts when infected animals – usually cattle or sheep (but also donkeys and pigs) – defecate in fresh-water sources. The worm’s eggs are passed in the faeces and hatch into larvae that find their way to a particular type of water snail – the intermediate host. In the snail, the worm reproduces and releases yet more larvae into the water. The larvae swim to nearby aquatic or semi-aquatic plants where they stick to the leaves and stems and form small cysts. The plants, with the cysts attached, are then ingested, acting as carriers of the infection. Watercress is a particularly good plant for transmitting fascioliasis, but encysted larvae may also be found on many other salad vegetables.

Transmission of fascioliasis is mainly perpetuated by animals with humans typically only becoming infected occasionally. In other words, if humans did not eat the aquatic plants, or if there was an adequate separation between the water used by the domestic animals and the community’s water sources, they would not become infected.

In some areas, however, transmission to humans is intense, and the prevalence of infection can reach extremely high levels. One of the world’s fascioliasis “hot spots” is in the South American highlands where up to 100% of the school age children are infected in some communities.
Transmissions pathways for fascioliasis

Animals and humans can both play a role as final hosts in the transmission of fascioliasis.

Four elements are needed for the successful transmission cycle to come full circle, thus completing the worms life-cycle.

1. the parasite,
2. a final host (animal or human),
3. an intermediate host (a suitable snail),
4. a carrier, i.e. a suitable aquatic or semi-aquatic plant.

The blue arrows in the figure below show the usual transmission route where animals perpetuate the infection in the environment and humans only occasionally become infected. It has been suggested that in certain endemic areas humans also play a role in the transmission route (the red arrows).
IMPACT ON HEALTH

Of all the body’s organs, fascioliasis does the most damage to the liver, hence the term “common liver-fluke infection”. Following ingestion of the larvae, a symptomless incubation phase starts, which lasts for a few days up to a few months. Then follows an acute phase and a chronic phase.

Acute phase
The acute phase, which lasts 2–4 months, begins when the immature worms burrow their way through the intestinal wall and the membrane that wraps around and protects the internal organs. From here, they puncture the liver’s surface and eat their way through the liver’s tissues until they reach the bile ducts. This journey kills the liver’s cells and causes intense bleeding.

Typical symptoms of this phase include fever, nausea, a swollen liver and extreme abdominal pain. A simple blood test is possible which can be routinely carried out at district level: if an elevated number of specific white blood cells - called eosinophils - is found, fascioliasis should be suspected.

Chronic phase
The chronic phase begins when the worms reach the bile ducts, where they develop into adults and start producing eggs. These eggs are then released into the bile and reach the intestine, where they are passed out in the faeces, completing the transmission cycle.

During this phase, intermittent pain, jaundice and anaemia are typical characteristics. The clinical picture can then be complicated by pancreatitis, gallstones and bacterial super-infections. In patients with chronic infections, the liver starts to harden – a process called fibrosis – as a result of the long-term inflammation. For infected children, one of the signs of infection is that their growth starts to falter.

Who is most at risk?
Where humans are only sporadically infected, there is no specific risk group. Whereas where the infection is highly endemic, the prevalence and intensity of infection often peaks in school-age children - which make the school system a particularly useful treatment channel.

Which drug should be used and what dosage should be administered?
Triclabendazole is the drug of choice to treat fascioliasis and is on the WHO list of essential medicines. The correct dosage is calculated based on the person’s weight (10 mg/kg) and the tablets are given at one time. To ease administration, body-weight groupings can be used (Table 1).

Table 1: Triclabendazole dosage using weight

<table>
<thead>
<tr>
<th>Number of triclabendazole tablets (250mg)</th>
<th>Dosage (mg)</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>½</td>
<td>125</td>
<td>&lt;12.5</td>
</tr>
<tr>
<td>1</td>
<td>250</td>
<td>&gt;12.5 – &lt;25</td>
</tr>
<tr>
<td>1½</td>
<td>375</td>
<td>&gt;25 – &lt;37.5</td>
</tr>
<tr>
<td>2</td>
<td>500</td>
<td>&gt;37.5 – &lt;50</td>
</tr>
<tr>
<td>2½</td>
<td>625</td>
<td>&gt;50 – &lt;62.5</td>
</tr>
<tr>
<td>3</td>
<td>750</td>
<td>&gt;62.5 – &lt;75</td>
</tr>
<tr>
<td>3½</td>
<td>875</td>
<td>&gt;75 – &lt;87.5</td>
</tr>
<tr>
<td>4</td>
<td>1000</td>
<td>&gt;87.5 – &lt;100</td>
</tr>
</tbody>
</table>

A school child in Ecuador
**THE VISIBLE WORM**

The worms that cause fascioliasis are leaf-shaped and large enough to be visible to the naked eye.

There are two main species, *Fasciola hepatica* and *F. gigantica* – the disease they cause however is similar. Adaptation is a key concept in the transmission of fascioliasis. The size of the fasciola worm is related to the fact that it has adapted itself over the centuries to live in animals. With the jump to humans – a much smaller host – these large worms can cause serious damage and disease, especially in children.

**“IN THE FEET OF CATTLE” – HOW FASCIOLA SNAILS MOVED AROUND THE WORLD**

**European origins**

*Fasciola hepatica* originated in Europe, and cases are still periodically reported from countries in this region. However, given the routine separation between husbandry and humans and generally good levels of sanitation, the number of human infections has gradually dwindled. Unfortunately, this has not been the case elsewhere. From Europe, *F. hepatica* spread through the trade of cattle that carried both the worms (in their bodies) and the snails (presumably trapped in the mud in their hooves) to the entire world. *F. hepatica* is now found on every continent in varying degrees of severity.

The second species, *F. gigantica*, is currently only transmitted on the African and Asian continents and on some Pacific islands. This is probably because the specific snails needed for the transmission cycle of *F. gigantica* only exist in these areas.

**Global distribution**

Current well-known hot spots for fascioliasis are found on the extremities of the world’s continents. South and East Asia are affected, as are the mountainous areas on the western edges of South America and two outlying areas: a region around the Caspian basin and the Nile valley. While it is true that no continent is free from fascioliasis, the current lack of detailed data means that the geographical extent and burden of the disease are likely to be significantly greater than current estimates indicate.
CONTROLLING FASCIO LIASIS

Case management or blanket treatment?

In areas where cases of fascioliasis occur sporadically, clinical case management of individuals reporting to their local hospital is sufficient to tackle the disease. However, in communities where the prevalence of infection is high, a public health approach is needed. Different countries across the world have adopted different interventions:

Viet Nam: passive case-finding

Viet Nam began fascioliasis control activities in 2006 following an increasing number of reported cases from certain hospitals. The Ministry of Health (MoH) opted for a decentralized and simple passive case-finding approach because most of the cases were highly symptomatic and the affected individuals spontaneously reported to their nearest health centre for treatment. Viet Nam does not actively distribute the drugs, but instead ensures that triclabendazole is available in its district hospitals so that people can easily access treatment. To simplify diagnosis for the less well equipped rural hospitals, the diagnostic procedures were also simplified so that people could be treated as easily and effectively as possible. The government is now planning to start treating infected cattle to reduce the environmental contamination.

Egypt: selective treatment

The Egyptian MoH started fascioliasis control activities in 1998 and uses a strategy of selective treatment whereby triclabendazole is distributed free-of-charge to all school-age children who test positive during mass screenings in the villages. To date, over 60 000 children have been screened, approximately 2000 have tested positive and been treated. Using this strategy the Egyptian MoH has successfully lowered the prevalence of infection in school-age children from 6% in 1998 to around 1% in 2007 in the endemic areas.

Bolivia and Peru: targeted treatment

In the highlands of Bolivia and Peru, fascioliasis transmission is so intense that tens of thousands of people are estimated to be infected, particularly children. The MoHs in La Paz and Lima have therefore decided that individual diagnosis does not make practical sense and would be more costly. Instead they have decided to treat all school-age children living in the endemic areas once a year and free-of-charge. This, incidentally, is the same strategy advocated by WHO to control schistosomiasis and common intestinal worms in high transmission areas. Both countries are now planning pilot interventions for the end of 2007, which will be followed up with their first large-scale campaigns in 2008.

The way forward for effective control

In order to interrupt transmission of fascioliasis to humans, two parallel measures are needed. The first is to establish effective veterinary public health measures that contain the animal sources of infection. The second is to educate people living in endemic areas about the risks of eating uncooked freshwater plants and why the safe disposal of human waste is important. Since both measures take time, the key interim measure is to treat infected individuals who either test positive or on a presumptive basis. This is the fastest, and cheapest way of alleviating the suffering caused by fascioliasis which at the same time controls the morbidity associated with the disease.
WHO’S NEW POLICY – AND A GROUND BREAKING DRUG DONATION

Of massive significance for fascioliasis control is WHO’s recent shift in its policy for neglected tropical diseases which has triggered a global interest in diseases that have until recently been on the edges of the public health agenda. For fascioliasis after decades of anonymity, this means there are now new and exciting opportunities for control. WHO has embarked on the first step which is to document and learn from ongoing country experiences. This will pave the way for fascioliasis to be added to the preventive chemotherapy concept (see Action Against Worms Issue 9).

In 2007, another ground breaking turning point was announced. WHO’s Department of Control of Neglected Tropical Diseases and Novartis Pharma AG joined forces to make triclabendazole available free-of-charge for the treatment of fascioliasis-infected individuals in endemic countries. In practical terms this means that for the first time, infected people living in underprivileged countries will have access to the drugs they need.

HOW TO APPLY FOR TRICLABENDAZOLE

WHO invites ministries of health in affected developing countries to take advantage of this landmark donation programme.

No continent is free from fascioliasis, and it is likely that where animal cases are reported, human cases also exist.

Only with a reasonable triclabendazole stockpile, will ministries of health be in a position to (1) supply their hospitals with enough drugs to allow their health staff to treat self-reported cases and (2) plan and implement large scale drug distributions if fascioliasis is found to be a large-scale public health problem.

How to apply for donated triclabendazole

- Make a rough estimate of how many people you aim to treat in a year. If you do not have data on the epidemiology and distribution of fascioliasis in your country, you can make a reasonable estimate by contacting the major hospitals and asking them how many cases they see per year.


- Fill out the form, sign it and officially stamp it.

- Submit the application to the WHO Country Office with a covering letter, or, fax it to +41.22.79.14777, or, e-mail it to: fasciola@who.int

If you need more information on the application please visit the NTD web site: http://www.who.int/neglected_diseases/en/ or send an e-mail to fasciola@who.int
**FACT SHEET ON FASCIOILIASIS**

**What causes fascioliasis?**
*Fasciola hepatica* and *F. gigantica*, both trematode worms.

**Where is fascioliasis transmitted?**
In each of the five continents.

**Which countries are known to have a serious problem?**
- Bolivia
- Ecuador
- Egypt
- Islamic Republic of Iran
- Peru
- Viet Nam

**How is fascioliasis transmitted?**
By ingesting raw plants to which the worm larvae have attached themselves.

**What are the symptoms and signs of fascioliasis?**
Fever, abdominal pain, biliary cholic, jaundice, anaemia, a high eosinophils count.

**How is fascioliasis diagnosed?**
By examining a stool sample for the parasite’s eggs. The Kato-Katz technique is the preferred method for mass screenings. Immunological techniques based on the detection of circulating antibodies (e.g. ELISA) are also commonly used.

**How is fascioliasis treated?**
Triclabendazole, a benzimidazole compound, is the drug of choice recommended by WHO for the treatment of fascioliasis. It is active against the adult parasites in the bile ducts and the immature flukes migrating through the liver. A single-dose of 10 mg/kg body weight is the recommended treatment. The dose can be doubled in the case of treatment failure and given in two divided doses 12–24 hours apart.

**Who must not be treated?**
Children below four years of age and pregnant or lactating women should be excluded from large-scale interventions. In clinical settings, medical staff can administer triclabendazole to treat these groups as they can better monitor any possible risks which may need follow-up.