Background: Fascioliasis is an infection caused by flukes of the class Trematoda, most often characterized by fever, eosinophilia, and abdominal pain, although as many as half of these cases may be asymptomatic. Humans are incidental hosts for *Fasciola hepatica* (Fh), commonly known as the sheep liver fluke, and *Fasciola gigantica* (Fg); these flukes cause similar illnesses in those who become infected
by ingesting contaminated watercress or water. The illness occurs worldwide, particularly in regions with intensive sheep or cattle production. Incidence of human infection apparently is increasing over the past 20 years.

Pathophysiology: When pathogen eggs in mammalian stool are deposited in tepid water (22-26°C) miracidia appear, develop, and hatch in 9-14 days. These miracidia then invade many species of freshwater snails, in which they multiply as sporozoites and redia for 4-7 weeks. They leave as free-swimming cercaria that subsequently attach to watercress, water lettuce, mint, parsley, or khat. Free-swimming cercaria may remain suspended in the water and encyst over a few hours.

When humans consume contaminated plants or water, the larvae excyst in the duodenum, migrate through the bowel wall and peritoneal cavity, and penetrate the Glisson capsule, actions that initiate the acute larval, hepatic, and invasive stages of human infection. Larvae sometimes also travel to ectopic body sites. This stage may last 3-4 months, during which the larvae mature and migrate through the liver into the large hepatic and common bile ducts. Mature flukes consume hepatocytes and duct epithelium and reside for years in the hepatic and common bile ducts, also occasionally in the gall bladder, the chronic adult biliary stage of infection. Adult fluke worms produce eggs about 4 months (range: 3-18 mo) after infection; these eggs traverse the sphincter of Oddi and intestine, then continue the cycle of infection. Acute and chronic stages can overlap, particularly in a high-level infection.

Frequency:

- **In the US:** Fascioliasis is exceptionally rare in the United States, especially among children. Travelers to and immigrants from regions of high endemicity are most frequently affected.

- **Internationally:**
  - An estimated 2 million cases of fascioliasis exist worldwide, and incidence apparently has increased since 1980.
  - Fh typically occurs worldwide in temperate regions, except Oceania. Fg causes outbreaks in tropical areas of southern Asia, Southeast Asia, and Africa. Infection is most prevalent in regions with intensive sheep and cattle production. Miracidia require temperate water to develop and hatch.
  - Disease prevalence is particularly high in specific regions of Bolivia (65-92%), Ecuador (24-53%), Egypt (2-17%), and Peru (10%). As many as 68% of Bolivian children in hyperendemic areas have evidence of infection, as do 11% of Ethiopians who emigrated to Israel.
  - In a study of approximately 3000 Egyptian children, 3% were infected. Many were severely anemic. Among individuals who presented with fever of unknown origin to an Egyptian hospital, 4% had Fh. Fh-caused disease that formerly occurred in scattered endemic foci along the Nile river in Egypt now is epidemic throughout the Nile valley.
A distinct syndrome of fascioliasis, termed *halzoun* in Lebanon and *marrerra* in the Sudan can result from consuming raw livers of infected sheep, goats, or cows. The living fluke adheres to the posterior pharyngeal wall, causing severe pharyngitis and laryngeal edema.

**Mortality/Morbidity:** Because of the large numbers of people infected worldwide, fascioliasis causes considerable morbidity. In children, fascioliasis often is associated with severe anemia, although it seldom is fatal.

**Race:** Fascioliasis infection has no apparent racial predilection.

**Sex:** Approximately 60% of infections occur in males, which may reflect occupational, dietary, or recreational exposures.

**Age:** Although most reported patients are adults, fascioliasis appears to affect people of all ages equally.

**History:**

- Approximately 50% of infections are subclinical.
- The most common symptoms are fever, hepatomegaly, and abdominal pain.
- Symptoms of fascioliasis (derived from a large series, primarily involving adult patients) include the following:
  - Abdominal pain, generalized or involving the right hypochondrium or right upper quadrant - 65%
  - Intermittent fever - 60%
  - Malaise and weight loss - 35%
  - Hives - 20%
  - Cough, shortness of breath, and/or chest pain - 15%
  - Change in bowel habits, nausea, anorexia, vomiting, diarrhea, and/or jaundice - Less frequent
- Generally, patients with chronic infection are asymptomatic, with the following exceptions:
Symptoms of biliary colic may exist because of ascending cholangitis (eg, fever, jaundice, abdominal pain).

Symptoms of pancreatitis occur, particularly in children.

- Fever of unknown origin or without an obvious source may occur, with or without eosinophilia.
- Fever and abdominal pain occur more frequently in children than in adults.
- Sweating, dizziness, and hives may occur.
- Patients may present with painful or pruritic subcutaneous nodules, although this condition is rare.
- *Halzoun/marrerra* presents with severe pharyngitis, dysphagia, foreign body sensation, and/or airway obstruction.

**Physical:**

- Physical examination typically reveals no specific signs of infection.
- Abdominal tenderness may be general or may be localized to the right hypochondrium, right upper quadrant, gall bladder, mid epigastrium, or left upper quadrant.
- Tender or nontender hepatomegaly may occur.
- Patients often have fever, pallor, and/or evidence of weight loss.
- Less often, patients present with urticaria, wheezing, subcutaneous nodules as large as 6 cm in diameter, or other manifestations of ectopic larval migration to the skin, lungs, heart, brain, eye, intestine, and genitourinary tract.
- Patients with *halzoun/marrerra* may have severe pharyngitis and/or laryngeal edema.

**Causes:**

- The major risk factor is consumption of contaminated water plants or water. Almost all patients report consuming watercress.
- Consumption of raw liver from infected sheep, goats, or cows also is a reported cause.
- Consumption of raw, infected sheep, goat, or cow liver is reported.
Amebiasis
Ancylostoma Infection
Anemia, Chronic
Ascariasis
Bancroftian Filariasis
Biliary Atresia
Catscratch Disease
Cholecystitis
Cholelithiasis
Cholestasis
Cutaneous Larva Migrans
Cysticercosis
Dirofilariasis
Dracunculiasis
Echinococcosis
Fever Without a Focus
Filariasis
Giardiasis
Gnathostomiasis
Hepatitis A
Hepatitis B
Hepatitis C
Hookworm Infection
Hymenolepiasis
Hyperciosphilic Syndrome
Intestinal Protozoal Diseases
Leptospirosis
Schistosomiasis
Taenia Infection

Other Problems to be Considered:

Ascending cholangitis
Familial Mediterranean fever
Fever of unknown origin

Lab Studies:

- Complete blood count
Leukocytosis may occur.

Severe anemia may occur, especially in children.

Eosinophilia occurs in 95% of acute stage infections.

Eosinophilia may wax and wane during the chronic stage of infection.

Among Egyptian children with acute fascioliasis, 14-82% had peripheral eosinophilia.

About half of affected patients have an elevated erythrocyte sedimentation rate.

Serology

Serologic modalities include complement fixation, immunofluorescence, indirect hemagglutination, counterimmunoelectrophoresis, and enzyme-linked immunosorbent assay (ELISA).

The Falcon screening test-ELISA is the most reliable diagnostic study and is the test of choice because of its routine availability, cost, sensitivity, and specificity.

A serum ELISA test result may become positive months before stool examination for ova because flukes do not produce eggs until the chronic stage (ie, 4 mo after infection, 3-18 mo).

Immunoglobulin levels may be elevated, particularly immunoglobulins G and E.

Liver function tests

Elevated levels of gamma-glutamyl transpeptidase, alkaline phosphatase, and bilirubin suggest cholestatic liver injury.

Although rare, elevated transaminase levels suggest hepatocellular injury.

Stool examination for ova and parasites

The small number of eggs in stool requires multiple specimens. The eggs measure 30 X 15 mm, X 60-90 micrometers and can be confused with *Fasciolopsis buski* eggs.

ELISA may be performed on stool specimens.

The 30 X 15 mm flukes almost never appear in stool; the rare exceptions follow a successful treatment.

Imaging Studies:

Chest radiography

In patients with pulmonary symptoms, parenchymal infiltrates rarely are visible.
A right-sided pleural effusion also is rare.

**Ultrasonography**

- Ultrasonography (US) may show hypodense/hypoechoic lesions in the liver that correspond to the burrow tracks of the larvae.
- US may reveal the adult fluke in a bile duct or the gallbladder.
- US rarely identifies scant ascites.

**CT scanning**

- CT scanning may show multiple 1-10 mm lesions or tunnels in the liver parenchyma.
- A radiating pattern of tunnels is diagnostic.
- CT scanning may also identify an adult fluke in a bile duct or the gallbladder.

**MRI** may suggest granulomata of the liver parenchyma and provide findings similar to CT scanning.

- Cholangiography may show a fluke in the biliary tree.
- US-guided gallbladder aspiration can demonstrate eggs in the bile, even when stool exam results are negative.
- Technetium-99 scan demonstrates multiple intrahepatic defects in approximately 50% of cases.

**Other Tests:**

- Bone marrow aspiration, performed only as part of the diagnostic evaluation for other conditions, can reveal increased bone marrow eosinophils.

**Procedures:**

- Duodenal aspiration may reveal eggs.
- Liver biopsy
  - Liver biopsy can demonstrate microabscesses and tunnels of parenchymal necrosis surrounded by inflammatory infiltrates containing abundant eosinophils.
  - Older lesions may be fibrotic.
- Laparoscopy often shows multiple gray-white and yellow nodules, 2-20 mm in diameter, as vermiform cords on the liver surface. In rare cases, these nodules may occur throughout the peritoneal cavity and intestine wall.
• Exploratory laparotomy may reveal identical findings as laparoscopy; flukes often present in bile duct or gallbladder.

• Upper GI endoscopy
  o Endoscopy can demonstrate a filling defect in the bile duct.
  o Endoscopic removal of the fluke is possible.
  o Administration of intravenous cholecystokinin can promote egg release, which can be sampled endoscopically for diagnosis.

• Thoracentesis for pleural effusion may demonstrate increased eosinophils in pleural fluid.

Histologic Findings: Flukes can be found during autopsy or in surgical specimens. Multiple subcavities (5-10 mm in diameter) may exist, filled with necrotic material from which necrotic tracks radiate and surrounded by inflammatory infiltrates that contain large numbers of eosinophils. Fibrosis may characterize older lesions. Tissues taken from ectopic sites of larval migration may demonstrate granulomatous nodules or small abscesses.

Medical Care:

• Bithionol continues to be the DOC, although it is available in the United States only under investigational protocol from the Centers for Disease Control and Prevention (CDC).

• A new fasciocide, triclabendazole, cured 31 of 40 infected Egyptian children with 1 day of therapy. A second day of treatment cured the remaining 9 children. Further studies of the safety and efficacy of triclabendazole are pending. This agent is not now available in the US.

• Praziquantel is safe, although it may not be effective against Fh. Praziquantel administration is recommended only if bithionol or triclabendazole is unavailable.

• Among the medications previously used but no longer recommended because of toxicity or unproven efficacy are emetine, dehydroemetine, chloroquine, albendazole, and mebendazole.

• Fascioliasis complicated by ascending cholangitis requires treatment with appropriate antibiotics.

Surgical Care:

• Patients with ascending cholangitis may require surgery.

• Although 1 study promoted endoscopic flushing of the gallbladder with povidone-iodine for patients in whom oral fasciolicides proved ineffective, this technique has had no further validation.

Consultations:
An infectious disease specialist and gastroenterologist for patients with suspected fascioliasis.

Surgeon

Patients with an ectopic infection, a visceral larva migrans–like illness, may require additional consultations for specific manifestations of the condition.

Consult with the CDC Drug Service (404-639-3670) to obtain bithionol.

- See Drugs Available Through the CDC Drug Service.
- See CDC Drug Service: Bithionol.

New fasciolicides are being used in small numbers of children with encouraging results and minimal toxicities. The best studied, bithionol, is available from the CDC Drug Service (see CDC Drug Service: Bithionol). Despite limited data on their use and safety in United States children, these new fasciolicides are the DOC because of the poorer efficacy and greater toxicities of older, more familiar agents. The Medical Letter (2000 Edition) recommends triclabendazole as the DOC, a veterinary drug not approved for human use in the United States.

Drug Category: Anthelmintics -- Parasite biochemical pathways are different from the human host, thus toxicity is directed to the parasite, egg, or larvae. Mechanism of action varies within the drug classes. Antiparasitic actions may include the following:

- Inhibition of microtubules causes irreversible block of glucose uptake
- Tubulin polymerization inhibition
- Depolarizing neuromuscular blockade
- Cholinesterase inhibition
- Increased cell membrane permeability, resulting in intracellular calcium loss
- Vacuolization of the schistosome tegument
- Increased cell membrane permeability to chloride ions via chloride channels alteration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Bithionol (Lorothidol, Bitin) -- Inhibits oxidative phosphorylation in the parasite, leading to blockade of adenosine triphosphate (ATP) synthesis. DOC because of its safety and effectiveness for Fh and Fg. Most supporting data are from developing countries. It is a phenolic compound structurally related to hexachlorophene.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>30-50 mg/kg on alternate days PO divided tid for 5-15 treatment days; some patients may require repeat treatment courses</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Triclabendazole (Fasinex) -- Recent reports suggest this veterinary drug is safe, well tolerated, and effective in adults and children. It remains the second DOC until further data accumulate, supporting its preferential use. Binds selectively to fluke tubulin, disrupting microtubule formation and function. As of 2002, is unavailable in the United States.</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>Adult Dose</td>
<td>10-12 mg/kg/d PO pc divided q12-24h for 1 dose</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Administer as in adults</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>May cause anorexia, nausea, vomiting, diarrhea, abdominal pain, hypotension, dizziness, headache, photosensitivity, or pruritus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Praziquantel (Biltricide) -- Although generally safe and effective for other trematode infections, praziquantel appears much less efficacious against Fh and Fg. Because it is readily available and more familiar than triclabendazole (Fasinex), it is the third DOC. Reserve use for situations in which the first and second DOC are unobtainable. Praziquantel increases permeability of the trematode tegument to calcium, causing contraction of the parasite muscle.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>25 mg/kg/dose PO q8h for 1 d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Administer as in adults</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; ocular cysticercosis</td>
</tr>
<tr>
<td>Interactions</td>
<td>Hydantoins may reduce serum praziquantel concentrations, possibly leading to treatment failures</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>B - Usually safe but benefits must outweigh the risks.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Destruction of parasite within eyes can cause irreparable lesions (ocular cysticercosis should not be treated with praziquantel); caution while driving or performing other tasks requiring alertness on day of and day following treatment; minimal increases in liver enzyme levels reported; when fluke infection</td>
</tr>
</tbody>
</table>
Drug Category: Corticosteroids -- May ameliorate the treatment course in children with severe acute phase infection.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Prednisolone (Pediapred, Delta-Cortef, Econopred) -- A short course that is given for 2 d preceding fasciolicidal therapy in children with severe acute phase infection is reported anecdotally to ameliorate the course of the illness and to decrease fever, pain, pruritus, and toxicity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>2 mg/kg/d PO divided q12-24h; not to exceed 60 mg/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Administer as in adults</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; viral, fungal or tubercular skin lesions</td>
</tr>
<tr>
<td>Interactions</td>
<td>Decreases effects of salicylates and toxoids (for immunizations); phenytoin, carbamazepine, barbiturates, and rifampin decrease effects</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Caution in hyperthyroidism, osteoporosis, cirrhosis, nonspecific ulcerative colitis, peptic ulcer, diabetes, and myasthenia gravis; mood changes, seizures, hyperglycemia, diarrhea, nausea, abdominal distension, and GI bleeding are unusual with short courses of therapy</td>
</tr>
</tbody>
</table>

Further Inpatient Care:

- Patient condition dictates the decision on inpatient vs outpatient care.

Further Outpatient Care:

- No particular outpatient care is required once treatment is successfully completed.

Transfer:

- Transfer is necessary only when specialized services or care (see Consultations) are unavailable.

Deterrence/Prevention:

- Fascioliasis can be prevented through public education about avoiding consumption of contaminated water plants, water, or raw liver.
Complications:

- Severe anemia and, less commonly, pancreatitis, occur in children more frequently than in adults.
- Rare complications include ectopic foci of infection, hemoperitoneum, subcapsular hematoma, hepatic mass, cholecystitis, ascending cholangitis, hemobilia from ulceration of the biliary epithelium, gallstones, and sclerosing cholangitis.

Prognosis:

- Prognosis is excellent with adequate therapy.

Patient Education:

- Advise patients to avoid high-risk behaviors (ie, consumption of contaminated water plants, raw liver).

Medical/Legal Pitfalls:

- Failure to consider the diagnosis for patients who may have had exposure to the fluke worm.

Special Concerns:

- For information on selected cases seen by 2002 course participants in the Gorgas Course in Clinical Tropical Medicine, please see http://info.dom.uab.edu/gorgas/030802d.html.

Caption: Picture 1. Fascioliasis. Life cycle of Fasciola hepatica

Picture Type: Graph

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Fascioliasis excerpt

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