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HUMAN FASCIOLIASIS

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ABSTRACT

The sources of human fascioliasis infection are analyzed for the first time in light of the evolving global context of this disease. Key infection sources include food, water, and combinations of both. The primary source is the ingestion of freshwater wild plants, particularly watercress, followed by other vegetables. Concerns regarding vegetables sold in unregulated urban markets are highlighted. A distinction is made between infection sources from freshwater-cultivated plants, terrestrial wild plants, and terrestrial-cultivated plants. Risks associated with consuming traditional local dishes made from wild plants and raw liver are also addressed. Contaminated water is increasingly implicated, including its use in drinking, preparing beverages and soups, and washing vegetables, fruits, tubers, and kitchen utensils.

Three methods for assessing infection sources are identified: detecting metacercariae on plants or in freshwater, conducting anamnesis in individual patients, and using questionnaire surveys in endemic areas. The infectivity of metacercariae is reviewed under field conditions and in experiments involving various physicochemical factors. Preventive measures, both individual and general, are found to be more complex than previously thought. The high diversity of infection sources and their variability across countries contribute to the significant epidemiological heterogeneity of human fascioliasis worldwide.

1. INTRODUCTION

The World Health Organization (WHO) recognizes fascioliasis as one of the Neglected Tropical Diseases (NTDs), specifically within the group of food-borne trematodiases (WHO, 2013). This parasitic zoonosis is caused by two species of liver flukes: *Fasciola hepatica*, which is distributed across Europe, Africa, Asia, Oceania, and the Americas, and *Fasciola gigantica*, found in parts of Africa and Asia 2009a). Historically considered a secondary concern in humans, fascioliasis gained significance after 1990 with the identification of numerous human endemic areas and a growing number of reported cases 2014a).

The disease's impact is attributed to its high pathogenicity) and its ability to suppress the immune system, not only during the migratory or acute phase al., 2013), as previously understood1990), but also during the long biliary or chronic phase), which affects nearly all individuals in endemic areas 2014a). Repeated reinfections in hyperendemic regions further exacerbate the problem). Globally, an estimated 17 million people are infected 2009a), with severe cases leading to neurological and ophthalmological complications, permanent sequelae, or even fatalities 2014b), underscoring the public health significance of this disease.

Human fascioliasis exhibits considerable variability worldwide in transmission patterns and epidemiological scenarios. This complexity, driven by a range of interconnected factors, calls for a multidisciplinary 2009b). Notably, human fascioliasis prevalence and intensity do not parallel those observed in animals, reflecting variations in behavior, habits, traditions, and dietary practices across different regions and cultures. Key factors contributing to this heterogeneity include:

1. Parasite adaptability,
2. Transmission dynamics,
3. Ecological strategies and spread of lymnaeid snail vectors,
4. Livestock and domestic animal management,
5. Climate changes,
6. Global changes,
7. Human behavioral patterns, and
8. Sources of human infection.

Fasciolids are highly sensitive to environmental conditions 1999, 2001), making fascioliasis susceptible to climate and global changes. The disease's zoonotic nature, low host specificity 2002), reliance on freshwater snail vectors, and the involvement of numerous lymnaeid species capable of transmission 2001) contribute to its responsiveness to environmental shifts. Additionally, human and animal movements and anthropogenic disruptions of ecosystems further influence the spread of fascioliasis 2009b).

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Fasciolid transmission

The two species *F. hepatica* and *F. gigantica*follow a similar two-host life cycle pattern. It takes about 14–23 weeks and comprises four phases :

1. (A) The fluke adult stage infects the large biliary passages and gallbladder of the definitive host, both humans and animals, mainly livestock but also wild herbivores; eggs reach the external milieu by way of bile and intestine; the definitive host is infected by ingestion of metacercariae; metacercariae excyst in the small intestine within 1 h after ingestion, penetrate the host's intestine wall, and appear in the abdominal cavity by about 2 h after ingestion; most reach the liver within 6 days after excystment; in the liver they migrate for 5–6 weeks, preferentially feeding directly on liver tissue; they eventually penetrate into the bile ducts where they become sexually mature; the prepatent period (from the ingestion of metacercariae to the first appearance of the first eggs in the feces) varies according to the host and also depends on the number of the adult flukes in the liver.
2. (B) The transit between the definitive mammal host and intermediate snail host includes the long resistance phase of the egg and the short active phase of miracidium.
3. (C) At the intermediate host level, the development includes miracidium penetration into the snail, development of sporocyst and redial generations, production of cercariae and shedding of the latter into water.
4. (D) The transit between intermediate snail host and definitive mammal host includes the short swimming phase of cercaria and the long resistance phase of metacercaria until its ingestion by the definitive host; the shedding process takes place independently of light or darkness, between 9 and 26 °C in *F. hepatica* (at a somewhat higher temperature range in *F. gigantica*, whose minimum temperature threshold is 16 °C – m); cercariae swim for a short time (1 h) until contacting a solid support, mostly leaves of water plants above or below the water line; they then lose their tails and quickly encyst (Fig1A, B), changing into round metacercariae (Fig1C) attached to the vegetation (Fig1E); floating infective metacercarial cysts (Fig1D) are also originated at the level of the water surface line (Fig1F) (Vareille-Morel *et al*.,); metacercarial cysts become infective within 24–72 h.

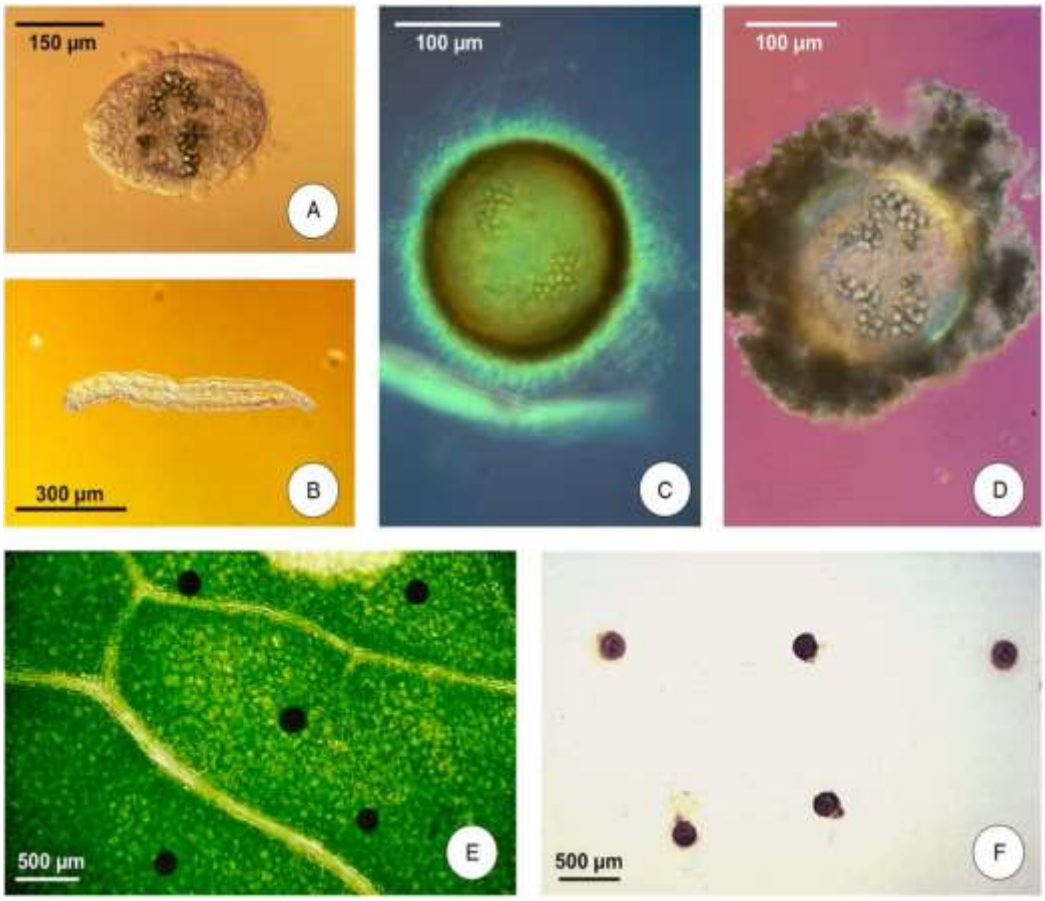

Fig. 1. Life cycle stages of Fasciola hepatica involved in the infection of humans: (A) cercarial body beginning the encystment process; (B) cercarial tail after detachment from cercarial body; (C) metacercarial attached cyst; (D) metacercarial floating cyst; (E) metacercariae attached to a green plant leaf; (F) metacercariae floating in water. (Photographs S. Mas-Coma).

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The cercarial shedding process seems to follow an infradaily shedding pattern of 7 days in the daily production during the whole emergence and a circadial rhythm with maximum production between midnight and 1.00 h a.m., as seen in the lymnaeid vector Galba truncatula infected by F. hepatica(Audousset e). Higher cercarial productions following different shedding chronobiologies have been seen in the same lymnaeid at very high altitude and by other Galba/Fossaria species in the lowland.

Human Infection Risk: Epidemiological Scenarios and Transmission Patterns

The risk of human fascioliasis infection is influenced by the transmission rate in a specific area and its intra- and interannual variability, which is closely tied to climatic factors. The significant diversity in epidemiological scenarios and transmission patterns across the globe highlights that established patterns of fascioliasis may not always explain the disease's characteristics in a particular region.

Transmission rates can be inferred from local prevalence and infection intensity in humans and livestock. Various epidemiological scenarios for human fascioliasis have been identified, with the classification (1999a, 2009a) remaining highly relevant and practical. These scenarios include:

1. **Imported cases**
2. **Autochthonous, isolated, non-constant cases**
3. **Three types of human endemic situations**:
   - **Hypoendemic**: Prevalence <1%; mean egg intensity <50 eggs per gram (epg) of feces.
   - **Mesoendemic**: Prevalence between 1–10%; children aged 5–15 may show higher prevalence; mean intensity ranges from 50 to 300 epg.
   - **Hyperendemic**: Prevalence >10%; children aged 5–15 usually exhibit higher prevalence; mean intensity often exceeds 300 epg.
4. **Two types of human epidemic situations**:
   - Epidemics in areas where animals, but not humans, are endemic.
   - Epidemics in areas where both humans and animals are endemic.

Climatic Factors and Transmission Variability

The intra- and interannual variability of transmission rates is due to the environmental sensitivity of fasciolid larval stages (phases B and D) and intramolluscan larval stages (phase C) (. Key environmental factors include:

- **Surface water availability**: Derived from rainfall or freshwater sources like rivers, streams, lakes, irrigation canals, and fountains, which support the lymnaeid snail vectors
- **Temperature**: Air and water temperature are critical, with specific minimum and maximum thresholds for larval development varying between *F. hepatica* and *F. gigantica* (**Transmission Patterns in Human Endemic Areas**

Distinct transmission patterns have been identified in human endemic regions

1. **High-altitude pattern** (*F. hepatica* only): Found in Andean countries, with two sub-patterns:
   - **Altiplanic pattern**: Transmission occurs year-round.
   - **Valley pattern**: Seasonal transmission with prevalence and intensity varying by altitude.
2. **Caribbean insular pattern**: Characterized by reduced but repeated outbreaks in hypoendemic areas.
3. **Afro-Mediterranean lowland pattern**: Overlapping of *F. hepatica* and *F. gigantica*, with seasonal transmission.
4. **Caspian regional pattern**: Hypoendemic areas with large epidemics occasionally affecting up to 10,000 people; both *F. hepatica* and *F. gigantica* are present.
5. **Vietnam lowland pattern** (*F. gigantica* only/mainly): Large human epidemics linked to lowland regions
6. **Argentinian arid pattern**: Recently identified in desert and semi-arid regions; transmission depends on overlapping temperature and water availability during specific seasons

Community, familial and social factors in infection risk

Fascioliasis is predominantly a rural disease because human infection risk is in the field where the disease transmission occurs in freshwater bodies inhabited by the lymnaeid vectors. A thorough epidemiological study in the highest human hyperendemic area known, the Northern Bolivian Altiplano, proved that prevalence and intensity of infection in the communities show a direct correlation with, and are therefore dependent on, the distance of the village from the closest water collection inhabited by lymnaeid snail vectors (.,). In a developed country as France, human infection in 10 000 reports, happened during the 1956–1982 period, correlated well with the zones for cattle and sheep husbandry

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Human infection in urban settlements occurs only sporadically due to consumption, mainly at home but also very rarely at restaurants and hotels, of metacercariae-carrying vegetables acquired in an uncontrolled market to where they were transported from the field. This does however not exclude the possibility of urban inhabitants to become infected in field trips.

The infection distribution by sex appears to be very similar in several areas, as in Europe, although in human hyperendemic areas the females show higher infection rates, whether prevalences as in Egypt , or intensities as in Bolivia). Regarding age relationships, all age groups can be affected, although in human hyperendemic areas children appear to be the most).

The incidence of infection is significantly aggregated within family groups because the family shares the same contaminated food and/or water, as it has been observed in for instance Spain. Familial clustering has been also found in patients from the French island of Corsica (Gil-Benito *et al*., m) and in community-based surveys in the Northern Bolivian Altiplano). In a community-based survey in Egypt, among 25 families with at least one infected person, 20% had two members infected and another 20% had three members infected

Human infection sources

Over the past three decades, studies conducted in various countries have revealed a greater diversity of human infection sources for fascioliasis than previously recognized in traditional textbooks 2004). Notably, fascioliasis is one of the few diseases capable of infecting humans through both food and drinking water. Consequently, dietary and drinking habits play a critical role in the disease's transmission.

Ingestion of Freshwater Wild Plants

Plant Markers of Transmission Foci

Research conducted in the field and laboratory experiments indicate that fasciolid cercariae do not exhibit a preference for specific types of aquatic plants. Instead, their selection of plants for attachment and encystment as metacercariae depends on the ecological characteristics of the lymnaeid snail vectors in each endemic area. Because lymnaeid snails prefer stagnant or slow-moving waters and cercariae have limited swimming capabilities, the plants chosen for encystment are typically those found in the same water bodies inhabited by the snails.

Two key factors significantly influence the presence of lymnaeid vectors:

1. **Salt Concentration**: Lymnaeids cannot survive in brackish or saline waters, as they are intolerant to even low salt levels.
2. **Shade**: Permanent shade that blocks sunlight prevents the growth of freshwater algae, the primary food source for lymnaeids, thereby limiting their presence.

These ecological dependencies highlight the role of specific freshwater wild plants as markers of transmission foci, closely linked to the habitat of lymnaeid vectors.

In summary, the role of freshwater wild plants in the transmission of fascioliasis to humans depends largely on the dietary habits and cultural traditions of the local population. These plants serve as significant sources of infection in areas where animals are endemic carriers, as well as in specific human endemic regions. The freshwater plant species implicated in human infection vary according to geographical location and dietary practices. Additionally, the plant species responsible for infection may differ between individuals infected through regular dietary consumption ("at the table") and those infected in the field by consuming, sucking, chewing, or biting plants directly from nature that may not typically be part of the local diet.

Watercress as a Key Source of Infection

In most cases of human fascioliasis, patient anamnesis often points to watercress as the likely source of infection. However, the term "watercress" encompasses several aquatic plant species, including Nasturtium officinale (common watercress), Nasturtium or Roripa silvestris, and Roripa amphibia (wild watercress). Wild watercress is frequently identified as the primary source of infection in areas with high endemicity of fascioliasis among domestic animals.

Watercress, a leafy green vegetable, thrives in many temperate and tropical regions worldwide and is one of the most commonly implicated vegetables in human fascioliasis cases, including in the United States. In Latin America, wild watercress has been associated with infections in several countries, including:

- Mexico: Reported in cases
- Cuba: Linked to human infection
- Dominican Republic: Identified as a significant infection source
- Venezuela: Documented in various studies

- Peru: Reported as a major contributor to human infection.

These findings underscore the critical role of watercress, particularly wild species, in the epidemiology of human fascioliasis in endemic regions.

Pathogenetic Mechanism

Fasciolosis pathogenesis occurs in two distinct stages: the parenchymal phase and the biliary phase.

Parenchymal Phase

This phase begins when newly excysted juveniles (NEJs) penetrate the liver capsule (Glisson's capsule) and migrate through the liver parenchyma. During migration, the juvenile parasites cause mechanical damage through the abrasive action of their tegument spines, which help them anchor within the liver tissue. Additionally, the parasites secrete by-products that may contribute to tissue damage. The migration of these juveniles results in simultaneous pathological processes, including necrotic and hemorrhagic lesions in the liver parenchyma. These lesions trigger inflammatory reactions and activate the immune system. The tortuous migration path of the parasites leaves excretory and secretory products in the tissue, further attracting immune cells and amplifying inflammation.

Biliary Phase

The biliary phase begins when the parasites reach the bile ducts, where they inflict mechanical and chemical damage. Adult parasites use their oral suckers to feed on blood and adjacent liver tissue, causing trauma and erosion of the bile duct epithelium. Macerated hepatocytes have been observed within the parasite's oral sucker and pharynx. This feeding activity can lead to focal ruptures of the bile ducts and puncturing of small blood vessels. Enlargement of the bile ducts may occur, potentially induced by the release of proline, an amino acid essential for collagen synthesis by fibroblasts. The combined mechanical and chemical actions of the parasites result in severe eosinophilic and granulomatous inflammation, particularly when parasite eggs reach the hepatic parenchyma, and marked hyperplasia of the bile ducts where the parasites reside.

Liver Lesions and Dose Dependency

The damage caused during these two phases results in a range of liver lesions, with severity closely linked to the infective dose. Higher doses of metacercariae lead to more acute and potentially fatal lesions. However, studies in sheep and goats have shown that small, repeated infections (trickle infections) can cause more severe liver damage than a single large infection with the same total number of metacercariae.

These findings suggest that liver damage initially stems from the mechanical and enzymatic activities of the parasites. The immune response, healing processes, simultaneous infections at different developmental stages, and the host's immune reaction to prior infections also play critical roles in the pathogenesis of fasciolosis.

Fasciolosis in Ruminants: Regional Overview and Economic Impact

Africa

Fasciolosis is a re-emerging disease in many regions of the world, particularly in Africa, caused by Fasciola hepatica (in temperate areas) and Fasciola gigantica (in tropical zones) [14]. Its incidence among farm animals tends to rise following periods of heavy rainfall [15]. In southeastern Lake Chad, the disease is a common health issue for mobile pastoralist livestock [16]. In Kenya's coastal region, F. hepatica is a significant concern for ruminants, posing a major limitation to livestock productivity.

Americas

Fasciolosis has been reported in several countries across the Americas, including the United States, Mexico, Cuba, Peru, Chile, Uruguay, Argentina, Jamaica, and Brazil [10]. Prevalence data from five countries indicates varying levels of infection, with goats showing the highest range (24.5–100%) and cattle the lowest (3.0–66.7%). Data on prevalence rates from 2000 to 2015 are summarized in Table 3, while Table 1 and Fig. 1 provide additional insights.

Asia

Fasciolosis is widespread across Asia, affecting countries in the Middle East (Iran, Iraq, and Saudi Arabia) as well as Russia, Thailand, Turkey, China, Vietnam, Nepal, Japan, Korea, the Philippines, Pakistan, Bangladesh, and Cambodia [10]. Prevalence has been reported in 13 countries across 41 studies, with the highest range observed in cattle (0.71–69.2%) and the lowest in goats (0.0–47.0%). Prevalence rates in Asian production animals between 2000 and 2015 are detailed in Table 4.

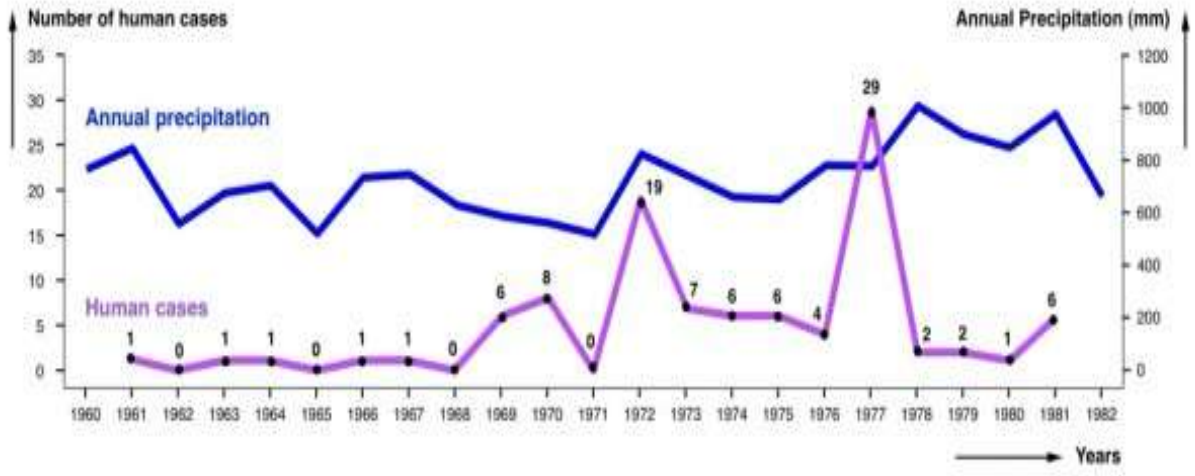
Australia/Oceania

In the Australia/Oceania region, only three studies have examined fasciolosis prevalence, focusing on two countries. The highest prevalence was reported in cattle (26.5–81.0%), while sheep showed a range of 5.5–52.2%. Data on goats

and buffalo are either unavailable or limited to single studies. Detailed prevalence data for this region are presented in Table 5 and Fig. 1.

Europe

In Europe, fasciolosis has been reported in countries including the UK, Ireland, France, Portugal, Spain, Switzerland, Italy, the Netherlands, Germany, and Poland [10]. It is a major helminthic infection across much of the continent. Prevalence data from 11 countries and 23 studies reveal a wide range, with cattle showing the highest prevalence (0.12–86.0%) and goats the lowest (0.0–0.8%). No studies have been conducted on buffalo in this region.



Host immune response

Innate Immune Response

The initial recognition of newly excysted juveniles (NEJs) occurs in the intestinal epithelial mucosa, triggering an extensive immune activation. This response involves recognizing glycosylated proteins and carbohydrate residues, which act as tegumental antigens. These antigens stimulate T-cell proliferation through dendritic cell activation. Additionally, excretory-secretory products (FhESP) released by Fasciola hepatica can activate bovine macrophages in a partially TLR4-dependent manner

The role of mast cells in fasciolosis remains unclear, and evidence of their protective effect is lacking. These tissue-resident cells respond to activation by releasing inflammatory mediators such as prostaglandins, leukotrienes, and cytokines, including TNF-α and IL-4. They may also release substances against parasites by binding IgE-parasite antigen complexes via high-affinity IgE receptors. Their role seems more significant during the early stages of infection. However, in F. hepatica-infected cattle, there is minimal evidence of increased basophils or mast cells , whereas F. gigantica infection in buffaloes shows a rise in mast cells within hepatic inflammatory infiltrates .

Macrophages and neutrophils also play a role in the innate response. Macrophages exhibit phagocytic activity and release reactive substances like nitric oxide and oxygen radicals that target the parasite. Infections provoke a Th2-type immune response with IgE production and eosinophil and mast cell infiltration in the liver. Neutrophils from patients with acute fasciolosis show heightened phagocytic activity compared to those in chronic stage). Similar trends are observed in goats, where chronic infection correlates with reduced neutrophil phagocytic function and higher fluke burdens.

In ruminants, F. hepatica induces liver and blood eosinophilia, a response also seen in sheep infected with F. gigantica. Vaccinated animals with partial protection tend to show reduced eosinophil counts, possibly due to lower fluke burdens and hepatic damage). Eosinophils mediate antibody-dependent cell cytotoxicity (ADCC) in rat and Indonesian thin-tailed (ITT) sheep, which exhibit resistance to F. gigantica but not F. hepatica. ITT sheep show effective eosinophil-mediated ADCC within the gut or peritoneal cavity but not in the liver.

Macrophages also participate in ADCC, with those targeting F. gigantica producing higher superoxide radical levels than those ineffective against F. hepatica. This suggests oxygen radicals play a critical role in killing F. gigantica NEJs . In vaccinated calves, macrophage-mediated ADCC relies on nitric oxide and induces a protective Th1 cytokine response associated with IgG2a). However, F.

hepatica NEJs can counteract this by secreting TGF-like molecules (FhTLM) that reduce ADCC effectiveness. These molecules also drive alternative (M2) macrophage activation, characterized by IL-10 and TGF-β production, which supports tissue repair but diminishes the ability to kill NEJs.

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Adaptive Immune Response

B cells play a key role in fasciolosis, as indicated by increased CD19+ B-cell recruitment to hepatic lymph nodes in infected or vaccinated animals. In ruminants, IgG1 is the dominant antibody, peaking at 12–15 weeks post-infection, whereas specific IgG2 correlates with vaccine-induced protection IgA specific to fluke antigens has been found in the bile and liver of infected cattle, where it may contribute to eosinophil activation and NEJ killing through ADCC.

The immune response during early infection is a mixed Th1/Th2 response, marked by increased levels of IFN-γ, IL-4, IL-10, and TGF-β. As the infection progresses, a dominant Th2 response develops alongside Th1 suppression, promoting chronic infection, likely mediated by IL-4 In the early stages of F. hepatica infection in sheep and cattle, IFN-γ and IL-10 levels rise, indicating a mixed immune response However, as the infection progresses, Th1 responses diminish while Th2 responses amplify, as evidenced by reduced IFN-γ and elevated IL-4 levels

In buffaloes infected with F. gigantica, both primary and secondary infections show a mixed Th1/Th2 response during early stages, with elevated serum levels of IFN-γ, IL-4, IL-5, and TGF-β. As the infection advances, Th2 responses dominate). The immune response varies across compartments; for example, IFN-γ levels in sheep liver remain high during acute and chronic F. hepatica infections but are reduced in hepatic lymph nodes and peripheral blood mononuclear cells (PBMCs). This localized IFN-γ elevation may be a reaction to hepatic necrosis caused by migrating or adult flukes and granuloma formation.

In summary, fasciolosis elicits complex immune responses, with an initial mixed Th1/Th2 reaction shifting to a predominantly Th2 response during chronic infection. These responses vary by host species, parasite species, and infection stage, influencing the pathogenesis and progression of the disease.

Treatment and Control of Fascioliasis

Treatment

Fascioliasis treatment is necessary in both acute and chronic stages to alleviate symptoms and prevent complications. Asymptomatic or mildly symptomatic individuals, particularly children, should also receive treatment to avoid potential long-term effects.

Triclabendazole is the drug of choice for treating acute and chronic fascioliasis in humans. This benzimidazole disrupts the parasite's tegument and inhibits protein synthesis, though its precise mechanism of action remains unclear. Its efficacy is limited to Fasciola and Paragonimus infections. The World Health Organization (WHO) recommends a dosage of 10 mg/kg, administered in one or two doses 12–24 hours apart. The U.S. Food and Drug Administration approved this regimen for individuals aged 6 years and older in 2019. Triclabendazole is most effective when taken with food, which increases plasma concentration by 2–3 times. Decades of use suggest it is a safe drug, though high doses in animal studies have indicated a potential for QTc interval prolongation. Caution is advised in patients with known QTc interval prolongation or those taking medications that affect QTc .

Nitazoxanide has been proposed as an alternative treatment, but its efficacy is inconsistent. Clinical trials report success rates between 40% and 60%, while observational studies range widely, from 36% efficacy in Egypt) to 94% in Mexico.

Some studies, including those in Cusco, Peru, found nitazoxanide ineffective in cases where triclabendazole failed. Due to conflicting evidence, nitazoxanide cannot be recommended as a standard treatment. Other antiparasitic drugs, like praziquantel, are ineffective against Fasciola.

Patients should undergo follow-up testing to confirm the success of treatment. In acute fascioliasis, symptoms and eosinophilia typically improve within days, though eosinophil levels may take weeks to normalize. Stool microscopy for Fasciola eggs is recommended 1–2 months post-treatment to confirm the cure. In chronic cases, multiple stool samples with egg concentration methods are needed for accurate assessment. Serological testing may be useful, though its role in clinical follow-up is unclear due to variability in antibody titer reduction and the time needed to revert to negative results. Family members of infected individuals in endemic areas should also be screened using stool microscopy, as fascioliasis often clusters within households.

Control

Control efforts focus on disrupting the Fasciola lifecycle, particularly by targeting intermediate snail hosts. However, snail control methods, such as molluscicides or draining water bodies, are often temporary and can harm other species.

Treatment of livestock is a key strategy in both developed and developing countries. Drugs like triclabendazole, albendazole, clorsulon, and closantel are used, but triclabendazole remains the most effective due to its efficacy against both immature and adult flukes. Acute fascioliasis in sheep, which causes significant morbidity and mortality, can be managed with triclabendazole to prevent losses. However, the widespread use of this drug has led to reduced effectiveness, necessitating the implementation of stewardship programs to better target infected and vulnerable animals.

The WHO supports mass drug administration (MDA) programs in high-burden countries to reduce human fascioliasis prevalence. Countries like Bolivia, Egypt, Peru, and Vietnam have implemented various strategies, including school-based treatment and community-wide MDA. In Egypt, a screen-and-treat program reduced prevalence from 6% to 1% over seven years. In Bolivia, a long-term MDA program near Lake Titicaca reduced prevalence to less than 1% from historical rates of 12–27% . However, these programs are often discontinued, and their sustainability requires further evaluation.

Challenges and Future Directions

Reliance on triclabendazole for treatment and control poses challenges due to the emergence of drug resistance. Resistance in livestock has been reported in over 17 endemic countries, linked to inconsistent farming practices, poor-quality veterinary products, and underdosing . Triclabendazole resistance in humans is also emerging, likely associated with resistant livestock infections. Treatment failures have been documented in Chile , the Netherlands (Peru Portugal , and Turkey). For example, a Peruvian study reported that only 38% of children with chronic fascioliasis responded to a second round of triclabendazole after failing the first round.

Efforts are underway to develop effective vaccines for livestock. Promising candidates include antigens like FhCL1, FhCL2, FhPrx, FhLAP, and FhHDM. Among these, FhLAP has shown 83–90% protection in livestock. However, no vaccines are currently available, and further research is needed to enhance their efficacy and durability.

In summary, effective treatment and control of fascioliasis require a multifaceted approach, combining improved drug stewardship, targeted livestock treatment, and the development of vaccines to reduce reliance on triclabendazole and address the growing issue of drug resistance.

2. CONCLUSION

Fascioliasis is a neglected zoonotic disease with a worldwide presence, but the true extent of its infection and disease burden remains unclear. The disease, in its asymptomatic, acute, and chronic forms, has both short-term and long-term health implications for humans. The complex pathophysiology of *Fasciola* infection presents challenges for its diagnosis and management. However, once diagnosed, treatment is necessary for all forms of the infection. Triclabendazole is the only drug currently recommended for the treatment and control of human fascioliasis. The emergence of *Fasciola*resistance to triclabendazole in both livestock and humans poses a significant threat to effective treatment and control strategies. Further research is essential to better understand the interactions between susceptible and resistant parasites and their intermediate, livestock, and human hosts. Additionally, there is an urgent need for research into alternative drugs to treat human infections and address triclabendazole resistance.

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