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REVIEW

# Amoebic Colonization in Humans: the Role of Zoonotic Transmission in Infection Ecology

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## Abstract

**Purpose of Review** *Entamoeba histolytica* is the primary causative agent of amebiasis, with transmission occurring mainly through contaminated food and water. A possible, though secondary, zoonotic component has been identified, involving animal reservoirs, primarily non-human primates and dogs.

**Recent Findings** Recent studies indicate that various amoebae species can colonize the human gut, and specific strains may have animal reservoirs capable of maintaining their life cycle and facilitating zoonotic transmission.

**Summary** This review highlights the importance of animal-to-human transmission of pathogenic, potentially pathogenic, and non-pathogenic amoebae species, and discusses their implications from a public health perspective.

**Keywords** Entamoeba histolytica · Amoebiasis · Zoonotic transmission · Animal reservoir · Pathogenic amoebae · Non-pathogenic amoebae

## Introduction

Amebiasis is an intestinal infection caused by the protozoan parasite *Entamoeba histolytica*, which is responsible for significant morbidity and mortality worldwide, particularly in tropical and subtropical regions with poor sanitation. The infection is primarily acquired via the fecal-oral route through ingestion of water or food contaminated with *E. histolytica* cysts. Most infections are asymptomatic, but a subset of individuals develop invasive disease, as amoebic colitis or extraintestinal complications such as liver abscesses [1]. *Entamoeba histolytica* exists in two forms: the infective cyst and the invasive trophozoite. After ingestion, the excystation occurs in the terminal ileum, releasing trophozoites that colonize the colon. In some cases, the latter invade the colonic mucosa, with tissue destruction and, potentially, dissemination to the liver [1, 2].

Other species of intestinal amoebae besides *E. histolytica* can infect humans and are considered potentially pathogenic, but their clinical significance differs substantially. The most notable are *E. dispar*, *E. moshkovskii*, and *E. bangladeshi* that are morphologically indistinguishable from *E. histolytica* by light microscopy, historically leading to an overestimation of amebiasis prevalence and unnecessary treatment. Moreover, several amoebic species, regarded as non-pathogenic occur quite frequently in human stool samples, especially in certain settings [3–6]. The correct identification of intestinal amoebic species is crucial to distinguish the pathogenic species from the non-pathogenic ones in order to apply appropriate treatment [6].

Although human-to-human transmission remains the primary route of infection for *E. histolytica*, the zoonotic contribution to the global burden of amebiasis, while limited, is not negligible [3, 4]. Although humans are the main hosts, the potential involvement of animals in the transmission of *E. histolytica* is gaining recognition. Non-human primates can act as reservoirs, and zoonotic transmission may occur, especially in environments where humans and animals share water contaminated with cysts [3].

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## Potentially Pathogenic Entamoeba spp. Infecting Humans

In 1993 *E. dispar* was officially recognized as a species distinct from *E. histolytica*, based on genetic, immunological, and biochemical analyses [5]. This distinction had originally been proposed by Brumpt in 1925, who suggested that the differences between asymptomatic and symptomatic amoebic infections could be explained by the presence of two morphologically identical but biologically different species. *Entamoeba dispar* is generally regarded as a non-pathogenic commensal in humans, but there are few reports suggesting that some strains may be associated with mild gastrointestinal symptoms or, rarely, extraintestinal disease [7]. Recent molecular and epidemiological studies have detected *E. dispar* in both symptomatic and asymptomatic subjects and, some experimental work showed that South American strains can induce liver lesions in animal models, with variable pathogenicity among strains [8]. However, these findings are not widely accepted as clinically significant, moreover wide clinical studies have not established a robust association between *E. dispar* and symptomatic disease or extraintestinal manifestations in humans [9, 10]. The prevailing consensus remains that *E. dispar* cannot be considered a clinically relevant pathogen in routine practice [6–10].

*Entamoeba moshkovskii* was first described by Tshalaia (1941) from sewage in Moscow [11] and has since been described in several countries [12, 13]. Although initially considered as a free-living organism, its potential clinical significance was recognized in 1961, when *E. histolytica*-like strain (syn Laredo strain) was isolated from a symptomatic patient in Texas [14]. This strain shared key biological features with *E. moshkovskii*, setting it apart from *E. histolytica* and *E. dispar*. Subsequent molecular studies confirmed that the Laredo strain is indeed a variant of *E. moshkovskii* [13]. This species has been detected in both symptomatic and asymptomatic individuals [9, 15, 16]. Several studies, including prospective pediatric cohorts and large cross-sectional surveys, have reported an association between *E. moshkovskii* infection and diarrhea, particularly in children [15]; mice models also demonstrate that *E. moshkovskii* is able to cause colitis and diarrhea [15]. However, the evidence in humans is inconsistent: while some studies show a temporal association with diarrheal episodes, others find high rates of asymptomatic carriage, and there is no convincing evidence of invasive or extraintestinal disease [15, 16]. The current consensus is that *E. moshkovskii* may be associated with diarrhea in some settings, but its pathogenicity in humans is not definitively established [6, 9, 15, 16].

*Entamoeba bangladeshi*, morphologically similar to *E. histolytica*, is a recently described species found in both symptomatic and asymptomatic individuals in several regions, including South Asia (notably Bangladesh and India) [9] and, more recently, South Africa, but without a clear association with clinical disease or diarrhea [17]. In these studies, *E. bangladeshi* was found at a lower prevalence than *E. histolytica* and *E. dispar* and, its detection did not correlate with gastrointestinal symptoms or changes in the host microbiome. The Infectious Diseases Society of America classify this species as non-pathogenic and not causally linked to diarrheal illness in humans [18].

As fare as animals are concerned, *E. dispar* and *E. moshkovskii* are both found in a variety of animal hosts: the former is commonly detected in non-human primates, with molecular studies confirming its presence in both captive and wild populations, with evidence of the presence of both zoonotic and zooanthroponotic transmission between humans and non-human primates [19, 20]. For instance, in Kathmandu, a survey of schoolchildren and macaques [20] showed high prevalence and genetic diversity of *Entamoeba* spp. in macaques but no evidence of transmission to humans, suggesting instead possible human-to-macaque transmission and complex host–parasite dynamics. *Entamoeba moshkovskii* has been identified in non-human primates and is also frequently found in swine and dogs, indicating a wider host range and possible zoonotic potential [21, 22]. In contrast, *E. bangladeshi* has so far only been reported in humans [9, 17, 18], with no evidence in the current medical literature supporting its presence in animal host, suggesting that its host range may be restricted to humans at this time.

## Human non-pathogenic Amoebae: Diagnostic implications, Animal Infection and Sentinel Role of Fecal Contamination

Several *Entamoeba* species while detectable in stool samples are considered non-pathogenic; these include *E. hartmanni*, *E. coli*, *E. polecki*, *Iodamoeba buetschlii*, and *Endolimax nana* [6, 9]. While these species can be distinguished microscopically from *E. histolytica*-like species due to their distinct morphological traits, accurate identification depends on skilled and experienced laboratory personnel. Although non-pathogenic *Entamoeba* species do not cause clinical disease, a correct identification is crucial to differentiate them from the pathogenic *E. histolytica* [6].

*Entamoeba hartmanni*, a small, tetra-nucleated cyst producing *Entamoeba* species, is generally regarded as a non-pathogenic commensal organism that inhabits the human intestinal lumen. Epidemiological and molecular studies have identified *E. hartmanni* in both symptomatic and asymptomatic patients, but there is no evidence supporting a causal relationship between its presence and clinical disease

[23]. This species has been identified in animal hosts beyond humans. Molecular analyses have confirmed its presence in non-human primates (NHP), including both wild chimpanzees [24] and different species of captive NHP, suggesting a broader host range [19], and recently it has been detected in mandrills (*Mandrillus sphinx*) and chimpanzees (*Pan troglodytes*) in a zoological garden in Madrid [25]. These findings underscore the potential zoonotic significance and ecological importance of *E. hartmanni* in both human and NHP populations.

*Entamoeba coli*, *End. nana*, and *I. bütschlii* are commonly reported in both humans and non-human primates, as well as in other mammalian species. In contrast, *E. polecki* appears to be more frequently found in pigs than in humans [3]. Additionally, their presence can serve as a useful indicator of environmental sanitation and may hold epidemiological and public health significance, particularly when detected in animal hosts [26].

For instance, *E. nana* has been identified in a variety of primate hosts worldwide, and there is experimental evidence suggesting that it can be transmitted between non-human primates and humans (from *Macaca sinica* to humans and from humans to *M. rhesus*). This indicates a potential for cross-species transmission and supports the view that *E. nana* is not strictly host-specific [27]. However, within *E. nana* there is considerable genetic variability, suggesting the existence of at least two distinct clades, which Hocke et al. [28] designated as *E. nana* RL1 (Ribosomal Lineage) and RL2, with the former encompassing isolates from both humans and swine.

*Iodamoeba bütschlii*, a sister taxon of *Endolimax*, is morphologically different in its cyst stage by a prominent iodophilic glycogen mass, facilitating its identification during coprological examinations. This amoeba has been documented not only in humans but also in a range of non-human primates and other mammals, including suids, ruminants, and camelids. Molecular analyses reveal a degree of host specificity associated with ribosomal lineages and in particular due to the presence of sublineages: RL1 sublineages are predominantly identified in humans and some primates, whereas RL2 sublineages are primarily found in other mammals such as goats, fallow deer, dromedaries, and pigs. Notably, pigs harbor a unique sublineage (RL2a) that also occurs in humans, suggesting a potential overlap and possible zoonotic exchange [29]. Importantly, studies reporting the presence of *Iodamoeba* in mammalian samples without molecular confirmation may overestimate its occurrence in hosts other than humans. This is because early cyst stages of other amoebae, such as *Entamoeba* spp., can exhibit iodophilic glycogen masses, potentially leading to misidentification [6].

In humans, *E. polecki* is considered a rare intestinal parasite, and although regarded as non-pathogenic species, there are documented cases where it has been associated with symptomatic infection, including diarrhea, abdominal cramps and, malaise with resolution of symptoms following anti-amoebic therapy [30]. However, most human infections are asymptomatic, and the pathogenic potential is generally considered low compared to *E. histolytica* [6]. In pigs, *E. polecki* is frequently detected and has been implicated in cases of diarrhea and colitis, particularly in coinfections with other enteric pathogens such as *Lawsonia intracellularis* [31], *Salmonella typhimurium* [32] or *Brachyspira hyodysenteriae* [33]. Histopathological studies have demonstrated *E. polecki* trophozoites invading ulcerative lesions in the colon of diarrheic pigs, supporting its role as a contributor to enteric disease [34]. *Entamoeba polecki* represent a zoonotic risk at the human-pig interface, particularly in situations where pigs are reared in close proximity to human settlements. Multiple molecular epidemiological studies have demonstrated that *E. polecki* is prevalent in pigs, with subtypes 1 (ST1) and 3 (ST3) identified as zoonotic and capable of infecting both pigs and humans [35]. The detection of identical subtypes in both hosts as well as in environmental samples from pig farms supports the potential for cross-species transmission, especially where hygiene and biosecurity are suboptimal [35]. High prevalence rates in pigs and wild boars as well as the identification of *E. polecki* in human cases further underscore the zoonotic potential [36, 37]. While the clinical impact in humans is generally limited, the risk of transmission exists, and surveillance in high-prevalence areas is needed to clarify the public health concerns.

Figure 1 provides a schematic overview of the main host species and the corresponding *Entamoeba* spp. reported in the literature, along with their potential routes of transmission.

The detection of non-pathogenic amoebae in human stool samples serves as a valuable indicator in public health surveillance, reflecting faecal contamination and inadequate sanitation conditions. Their presence signals exposure to contaminated water or food sources, underscoring the need for targeted public health interventions aimed at improving hygiene and sanitation infrastructure [38]. In many cases this contamination is linked to human faecal matter; however, for species such as *E. poleki* environmental contamination of water or soil with animal faeces must also be considered. This is particularly relevant in contexts involving close human-animal contact, intensive animal farming, or inadequate animal sewage management. Such findings may therefore provide important diagnostic insights and inform public health risk assessments.

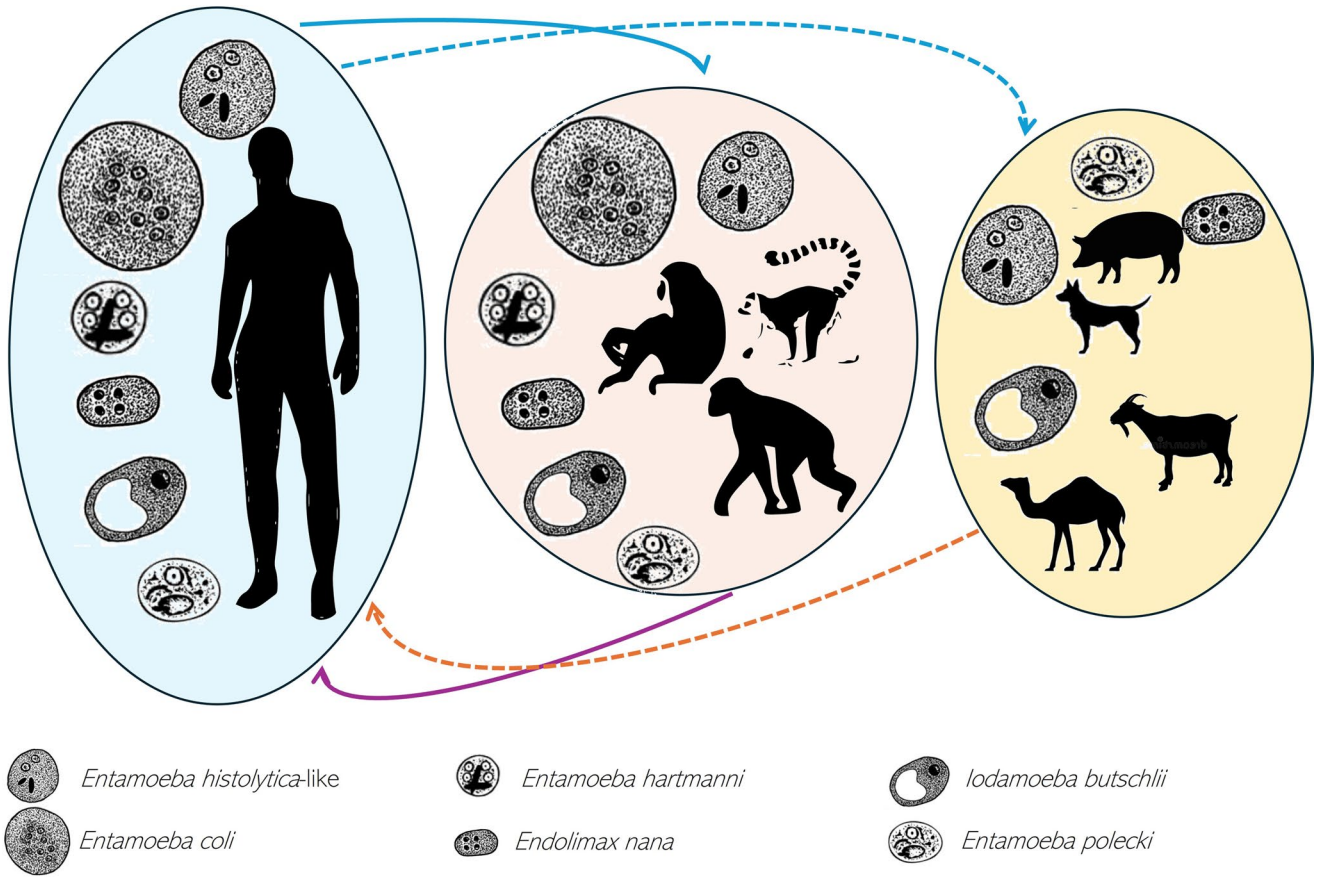


**Fig. 1** Representation of the main hosts of amoebic species colonizing the human intestine and their potential routes of transmission. Solid arrows indicate confirmed transmission pathways, whereas the dotted arrow represents a putative route, as evidence for transmission between non-primate mammals and humans remains lacking. The term *Entamoeba histolytica*-like refers to *E. histolytica*, *E. dispar*, and *E. moshkovskii*, which are morphologically indistinguishable. In primates and dogs, all three species have been reported, whereas in swine only *E. moshkovskii* has been identified

## Entamoeba histolytica and the Zoonotic Interface: Global Burden, Transmission Dynamics, and Biosecurity Challenges

*Entamoeba histolytica* is the causative agent of human amoebiasis, a parasitic infection whose invasive forms commonly manifest as amoebic dysentery and amoebic liver abscess, both associated with high mortality rates and significant healthcare costs. The disease affects up to 50 million people globally, resulting in an estimated 2.5 million disability-adjusted life years (DALYs) and over 100,000 deaths annually (most of which occur in children under five years old). Geographically, Eastern Sub-Saharan Africa had the highest age-standardized DALY rates by 2019 [39].

The burden of amoebiasis is closely linked to socioeconomic and environmental factors. A systematic review and meta-analysis by Atabati et al. (2020) [38] highlighted a strong correlation between the prevalence of *Entamoeba* spp. infections and socioeconomic deprivation, including inadequate sanitation infrastructure and poor access to healthcare. Marginalized populations (particularly in rural and peri-urban areas where humans and domestic animals often live in close proximity) are especially vulnerable. These environments facilitate the zoonotic transmission of gastrointestinal protozoa and increase the risk of infection through poor hygiene, untreated water, and lack of proper waste disposal systems.

While developed countries benefit from advanced water purification, higher education levels, and robust sanitation systems, amoebiasis remains a persistent threat due to factors such as globalization, international travel to endemic regions, immigration, and even sexual transmission, especially among certain populations [39, 40]. Today, amoebiasis is the third most common gastrointestinal disease among returning international travellers, after giardiasis and campylobacteriosis [41]. Despite modern infrastructure, outbreaks can still occur as demonstrated by a significant waterborne outbreak in Georgia (USA) from July to September 1998, caused by contaminated municipal water [42]. Several outbreaks have been reported worldwide, underscoring the

fact that amoebiasis remains a global public health concern that requires continuous monitoring and intervention from health authorities [3].

The most important documented examples of zoonotic transmission scenarios for *E. histolytica* involve close contact between humans and non-human primates, particularly in regions where their habitats overlap or in captive settings. Studies have demonstrated that *E. histolytica* infects both humans and non-human primates such as chimpanzees, baboons, and lemurs, with molecular evidence supporting the potential for cross-species transmission. In the Greater Gombe Ecosystem in Tanzania, *E. histolytica* was detected in humans, chimpanzees and, baboons living in proximity, with similar genotypes found across species, suggesting possible zoonotic transmission routes via shared environmental contamination [43]. Similarly, in Madagascar, wild lemurs living near human settlements were found to be infected with *E. histolytica*. Infection rates increased with proximity to humans, indicating that lemurs closer to villages are more likely to carry the parasite, further supporting the risk of pathogen exchange at human–wildlife interfaces [44].

In developed countries these scenarios are related to captive settings, such as zoos. In the Singapore Zoo, outbreaks of *E. histolytica* among non-human primates have been documented, with the maintenance of infection reservoirs in both captive and free-roaming wildlife complicating eradication efforts and raising concerns about potential transmission to humans working in or visiting these environments [45]. From 2004 to 2020, 27 confirmed cases by histopathology and immunohistochemistry of *E. histolytica* clinical infection in different species of non-human primates have been documented in different zoological gardens from UK [46], even if its frequency in European zoos remain low [25, 47, 48].

Beyond primates, *E. histolytica* infection has also been documented in companion animals, particularly dogs. Although relatively rare, molecular and epidemiological investigations from Pakistan and Malaysia have demonstrated that dogs can harbor *E. histolytica* as well as other related *Entamoeba* species, raising important zoonotic concerns [22, 49]. These studies further reported significantly higher prevalence rates in dogs exhibiting gastrointestinal signs compared with asymptomatic animals, suggesting that symptomatic household dogs may be more prone to infection due to their close association with humans. Infection was most frequently detected in younger dogs and in those with access to untreated water sources or frequent human contact, underscoring the influence of environmental and behavioural risk factors [22, 49]. In regions where human *E. histolytica* infection is endemic, dogs may therefore act as mechanical carriers or potential reservoirs, contributing to the epidemiology of human amoebiasis, although their exact role in direct transmission remains to be fully elucidated [22].

Overall, the most important scenarios involve shared environments and close contact between humans and non-human primates, with transmission likely occurring via the fecal-oral route through contaminated water, food, or surfaces [43, 44]. These findings underscore the need for improved sanitation and biosecurity measures in both wild and captive settings to reduce zoonotic risk. Equally important is the education and training of personnel working in these settings to ensure they maintain high standards of biosecurity.

## Conclusions

The diverse range of *Entamoeba* species colonizing humans and animals, including both pathogenic and non-pathogenic forms, reflects a complex ecological and epidemiological scenario. While *Entamoeba histolytica* is the most clinically significant species, responsible for considerable global morbidity and mortality, its natural host range appears largely restricted to humans and non-human primates, with occasional reports in dogs likely linked to their close contact with human-associated environments. Other species, namely *E. dispar*, *E. moshkovskii*, and *E. polecki*, exhibit varying degrees of pathogenic potential and zoonotic relevance. The identification of these species not only in non-human primates, but also in swine and other animals, highlight the importance of a One Health approach that integrates human, animal and environmental health perspectives. Accurate species identification is critical not only for effective clinical management but also for understanding the transmission dynamics, particularly at the human-animal interface. Moreover, the detection of non-pathogenic amoebae in both humans and animals can serve as a valuable indicator of fecal contamination and hygiene standards. These findings emphasize the urgent need for improved sanitation, enhanced diagnostic capacity, targeted surveillance, and strengthened biosecurity protocols, especially in environments where humans and animals interact closely, such as zoos, wildlife sanctuaries, and agricultural settings. Ongoing research and cross-sector collaboration are essential to fully elucidate the zoonotic potential of *Entamoeba* spp. and to inform public health strategies aimed at reducing transmission and safeguarding both human and animal health.

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This study reveals high prevalence and genetic diversity of *Entamoeba* spp. in macaques in Nepal but no evidence of macaque-to-human transmission among schoolchildren, instead suggesting possible human-to-macaque transmission and highlighting complex host–parasite dynamics

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This study provides the first DNA-based evidence of *Iodamoeba* in goats, dromedaries, fallow deer, and donkeys, revealing host-specific genetic diversity and broad geographic distribution

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This meta-analysis demonstrates that inadequate access to safe drinking water and sanitation facilities significantly increases the risk of intestinal *Entamoeba* spp. infection, highlighting the critical need for improved public health infrastructure to reduce disease burden.

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**Data Availability** No datasets were generated or analysed during the current study.

## Declarations

**Human and Animal Rights and Informed Consent** All reported studies/experiments with human or animal subjects have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

**Competing interests** The authors declare no competing interests.

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