Dientamoeba
(protist: flagellate)

Overview

Protists are single-celled organisms with membrane-bound nuclei (eukaryotes). Flagellates are protists that swim using one or more flagella (undulipodia); each arising from a small centriole (basal body, kinetosome) and having a microtubular axoneme core (2+9 configuration). Rather than forming a monophyletic group, flagellates are divided into several disparate groups: metamonads (amitochondriate flagellates), heteroloboseans (amoeboflagellates), euglenozoans (euglenids and kinetoplastids), stramenopiles (heterokonts), alveolates (dinoflagellates) and cercozoans (biflagellates). The metamonads comprise fornicates (diplomonads), parabasalians (trichomonads, hypermastigids, retortamonads) and preaxostylans (oxymonads). Parabasalid flagellates are anaerobic amitochondriate protists which have distinctive parabasal bodies (dictyosomes) adjacent to flagellar basal bodies (kinetosomes) and an axostyle-pelta complex providing structural support. Trichomonads are a major constituent group and most have 4-6 apical flagella, one being recurrent and often forming an undulating membrane supported by a costa. Dientamoebids, however, do not have recurrent flagella or associated structures (histomonads have only one flagellum and *Dientamoeba* have none). Most are parasites of insects although a few species infect domestic animals. *Dientamoeba* are small nonflagellated binucleate amoebae that have been shown to have trichomonad affinities due to the presence of a parabasal apparatus (basal body and axostyle lacking), a paradesmosome as part of an extranuclear spindle originating from attractophores, and hydrogenosomes (modified mitochondria). The species *D. fragilis* is frequently found in humans and may cause enteritis and diarrhoea.

Classification:

Domain:	Eukaryota (membrane-bound nucleus)
Supergroup:	Excavata (with conspicuous ventral feeding groove)
Group:	Metamonad (amitochondriate flagellates with karyomastigonts)
Phylum:	Parabasalia (anaerobic flagellates with parabasal body supporting Golgi cisternae or dictyosome, trichomonads, hypermastigids, retortamonads)
Class:	Tritrichomonadea (single mastigont, comb-like structure, infrakinetosomal body)
Order:	Tritrichominadida (variable possession of undulating membrane and costa)
Family:	Dientamoebidae (0-4 flagella, undulating membrane absent, costa absent, cone-like axostyle, comb-like structure absent, infrakinetosomal body absent)
Genus:	*Dientamoeba* (symbiotic in gut of humans/rodents)
Species:	*D. fragilis* (may cause diarrhoea in humans)

Parasite biodiversity and host range: Protists are unicellular eukaryotes that move using undulipodia (flagella or cilia), pseudopodia (false-feet) or a unique gliding motion. Flagellated species have one or more flagella with an internal microtubular core (in a characteristic 2+9 configuration comprising 2 single central microtubules and 9 peripheral doublets) anchored to a submembranous protein structure (known variously as a centriole, basal body, kinetosome or blepharoplast). Many types of flagellated cells have been described and recent phylogenetic studies have classified them into several disparate groups: including the metamonads (amitochondriate flagellates), heteroloboseans (amoeboflagellates), euglenozoans (euglenids and kinetoplastids), stramenopiles (heterokonts), alveolates (dinoflagellates) and cercozoans (biflagellates). While most flagellated protists are free-living organisms swimming and feeding in aquatic environments, representatives of several groups have developed symbiotic relationships with various hosts; some being endoparasitic in vertebrates (notably anaerobic metamonads in tubular organs, and heterotrophic euglenozoans occurring in blood or tissues), and some being parasitic in invertebrates (alveolates in crustacean tissues) (representatives tabulated below).

Higher taxonomy	Class or order	Family	Genera	Hosts (tissues)	Trans-mission*
Supergroup: Excavata (with conspicuous ventral feeding groove)					
Group: Metamonad (amitochondriate flagellates with karyomastigonts)					
Phylum: Fornicata (diplomonads)	Order: Diplomonadida (1-2 karyomastigonts)	Hexamitidae (2 karyomastigonts with binary axial symmetry)	*Giardia*	vertebrates (gut)	direct (f-o)
			Hexamita *Spironucleus*	vertebrates (tissues)	direct (f-o, w)
Phylum: Parabasalia (with parabasal body)	Order: Trichomonadida (3-5 anterior flagella plus recurrent flagellum)	Monocercomonadidae (costa absent, most without undulating membrane)	*Histomonas*	birds (gut, liver)	direct (f-o)
			Dientamoeba	vertebrates (gut)	direct (f-o)
		Trichomonadidae (stout axostyle, costa, undulating membrane)	*Trichomonas*	vertebrates (urogenital tract, gut)	direct (f-o, v)
		Cochlosomatidae (anterior adhesive disc)	*Cochlosoma*	birds (gut)	direct (f-o)
Group: Discoba (diverse group supported robustly by molecular studies)					
Phylum: Euglenozoa (flagella inserted in anterior pocket, heterotrophs, autotrophs)	Class: Kinetoplastea (heterotrophs, with extranuclear DNA (= kinetoplast) associated with mitochondrion)	Ichthyobodonidae (flagellar pocket continues as groove)	*Ichthyobodo* (= *Costia*)	fish (gills, skin)	direct (w)
		Parabodonidae (epizoic or endozoic)	*Cryptobia*	fish (gills, skin)	direct (w)
			Trypanoplasma	fish (blood)	indirect (v-b)
		Trypanosomatidae (monogenetic forms in insects/plants, digenetic forms in vertebrates & arthropods)	*Trypanosoma*	vertebrates (blood, tissues)	indirect (v-b)
			Leishmania	vertebrates (blood, tissues)	indirect (v-b)
Supergroup: SAR (Stramenopiles + Alveolata + Rhizaria) (3 groups unified by molecular studies)					
Group: Alveolata (with cortical alveoli)					
Phylum: Dinoflagellata (with unique mesokaryotic nuclei)	Order: Blastodiniales (uninucleate trophonts with chloroplasts)	Oodiniaceae (trophont with rhizoid-like invasive organelle)	*Amyloodinium* *Crepidoodinium* *Piscinoodinium*	fish (skin)	direct (w)
	Order: Syndiniales (multinucleate plasmodial trophonts)	Syndiniaceae (without chloroplasts)	*Haematodinium* *Ichthyodinium*	crustaceans, fish (tissues)	direct (w)
Phylum: Perkinsozoa (parasitic)	Order: Perkinsorida (released trophonts form biflagellated zoospores)	Perkinsidae (incomplete conoid)	*Perkinsus*	gastropods, bivalves (tissues)	direct (w)

*f-o = faecal-oral transmission; v-b = vector-borne transmission, w = water-borne transmission; v = venereal transmission

Metamonads are a group of excavates (with ventral feeding groove) that have several subcellular elements associated with their flagella forming a unique mastigont (an ultrastructural complex of organelles and cytoskeletal fibrils (incl. dictyosomes (Golgi bodies), centrioles (basal bodies) and a microtubular axostyle)). The metamonads comprise fornicates (diplomonads), parabasalians (trichomonads, hypermastigids, retortamonads) and preaxostylans (oxymonads). Most metamonads are amitochondriate but have retained reduced organelles of mitochondrial origin (fornicates containing mitosomes while parabasalians possess hydrogenosomes). Members of the phylum Parabasalia typically possess parabasal bodies adjacent to Golgi bodies (dictyosomes), and have microtubular arrays forming a conspicuous pelta-axostyle complex (cap-like pelta and a cone- or tube-like longitudinal axostyle). Six parabasalid classes are currently recognized on the basis of morphological, biological and molecular phylogenetic studies. Cells in three classes (Trichomonadea, Tritrichomonadea, Hypotrichomonadea) bear single mastigonts (set of kinetosomes (basal bodies) and associated appendages – ancestral unit comprising 4 kinetosomes) with flagella arranged in an anterior tuft, but many have one recurrent flagellum forming an undulating membrane (lamelliform or rail-type) supported by a costa (A- or B-type) and sometimes a basal comb-like structure and/or infrakinetosomal body. Many species are symbiotic (mutualists, commensals or parasites) in animals, although some are free-living in moist habitats. Most species have simple life cycles with longitudinal binary fission of motile-flagellated or rounded tissue-phase cells (only a few species form cysts). Cells in another three classes (Cristamonadea, Trichonymphea, Spirotrichonymphea) have more complex structures, often with multiple mastigonts bearing hundreds to thousands of flagella. Most were previously assigned to the now-defunct group Hypermastigida and they are primarily found as symbionts (mutualists) in insects (mostly termites).

Family	Key characters to 'trichomonad' families in vertebrates*						Representative genera
	Number of flagella	Undulating membrane	Costa	Axostyle	Comb-like structure	Infra-kinetosomal body	
Class Trichomonadea (single karyomastigont)							
Order Trichomonadida (with costa) (endobiotic in vertebrates (mammals, birds, reptiles, amphibia) and invertebrates)							
Trichomonadidae	5-6	lamelliform	B-type	cone-like	absent	absent	*Cochlosoma, Trichomonas, Trichomitopsis, Tetratrichomonas, Pentatrichomonas*
Order Honigbergiellida (without costa) (endobiotic in vertebrates (mammals, reptiles, amphibia))							
Hexamastigidae	5-6	absent	absent	cone-like	absent	absent	*Hexamastix*
Class Tritrichomonadea (uninucleate to binucleate)							
Order Tritrichomonadida (endobiotic in vertebrates (mammals, birds, reptiles, amphibia, fish))							
Tritrichomonadidae	4-5	rail-type	A-type	tube-like	present	present	*Tritrichomonas*
Simplicimonidae	4	absent	absent	tube-like	present	present	*Simplicimonas*
Monocercomonidae	4	absent	absent	cone-like	present	present	*Monocercomonas*
Dientamoebidae	0-4	absent	absent	cone-like	absent	absent	*Dientamoeba, Histomonas*
Class Hypotrichomonadea (single karyomastigont)							
Order Hypotrichomonadida (endobiotic in vertebrates (reptiles, amphibia, mammals) and invertebrates)							
Hypotrichomonidae	4	lamelliform	A-type	cone-like	present	absent	*Trichomitus, Hypotrichomonas*

*Taxa found only in invertebrate hosts (such as termites and cockroaches) are not listed

The genus *Tritrichomonas* was separated from other trichomonads initially on the basis of ultrastructural studies, notably involving the possession of different undulating membranes (rail-type), costae (A-type), axostyles (tube-like) and the presence of comb-like structures and infrakinetosomal bodies. Molecular characterization studies, however, revealed that many of these characters were not apomorphic but plesiomorphic, with many related taxa varying considerably in their structural complexity, and often demonstrating reductive evolution by lacking (or having lost) various features. The novel class Tritrichomonadea was erected to accommodate a diverse range of cells with 1-2 nuclei and 0-5 flagella but otherwise varying in their possession of various cytoskeletal, membranous and cytoplasmic elements. The order Tritrichomonadida contains 4 families: one family with 'trichomonad' features (Tritrichomonadidae (genus *Tritrichomonas*) with uninucleate cells, 4-5 flagella, rail-type undulating membranes, A-type costae, tube-like axostyles); and 3 families with greatly simplified structures (Dientamoebidae syn. Protrichomonadinae (4 genera: *Dientamoeba, Histomonas, Parahistomonas, Protrichomonas*) with uni- to bi-nucleate cells, 0-4 flagella, cone-like axostyles if present, but lacking undulating membranes, costae, comb-like structures and infrakinetosomal bodies; Monocercomonadidae (one genus *Monocercomonas*) with uninucleate cells, 4 flagella, marginal plates, cone-like axostyles, but lacking undulating membranes and costae; and Simplicimonadidae (one genus *Simplicimonas*) with uninucleate cells, 4 flagella, marginal plates, tube-like axostyles, but lacking undulating membranes and costae). Most cognate species have been recorded as symbiotes (mutualists, commensals or parasites) of insects, but a few species infect vertebrate hosts, including humans and domestic animals.

The genus *Dientamoeba* contains one species (*D. fragilis*) which forms uni- or bi-nucleate non-flagellated stages in the lower alimentary tracts of humans and pigs, although experimental infections have been established in sheep and monkeys. There is ongoing debate as to the clinical significance of the organism, with some regarding it to be a nonpathogenic endocommensal while others consider it to be a sporadic cause of chronic diarrhoea and fatigue in humans.

Parasite species	Length (µm)	Vertebrate Hosts	Location	Clinical signs	Distribution
Class: **Tritrichomonadea** (uninucleate to binucleate) [0-5F±RUM+AC+CLS+IKB+CA/TA]†					
Order: Tritrichomonadida (as for class)					
Family: Dientamoebidae (syn. Protrichomonadidae) (uninucleate to binucleate, marginal plate present [0-4F-UM-C±CA-CLS-IKB]					
Dientamoeba (aflagellar lumen forms, binucleate or uninucleate)					
Dientamoeba fragilis [0F]	3.5-12	Primates: hominid (human, gorilla); Artiodactyla: suid (pig); experimentally in Artiodactyla: bovid (sheep), Rodentia: murid (mice, rats); Primates: cercopithecid (baboon, macaques)	colon	diarrhoea	worldwide

†Coding: + = present; - = absent; #F = total number of flagella; UM = undulating membrane; RUM = rail-type undulating membrane; C = costa; AC = A-type costa; CA = cone-like axostyle (*Trichomonas*-type); TA = tube-like axostyle (*Tritrichomonas*-type); CLS = comb-like structure; IKB = infrakinetosomal body.

Parasite morphology: *Dientamoeba fragilis* forms motile vegetative stages known as trophozoites, which are variable in size (ranging from 3.5-12 µm in length but sometimes being as large as 20-40 µm). They are usually rounded in shape, but motile forms may appear fan-shaped due to the possession of small hyaline irregularly-lobed pseudopodia. These parasites lack flagella, undulating membranes, costae, and axostyles, but are nonetheless classified with the tritrichomonads on the basis of ultrastructural and molecular studies. Trophozoites often have a highly vacuolated cytoplasm with large food vacuoles, inclusion bodies and granules. They also contain multiple osmiophilic membrane-bound bodies known as hydrogenosomes, which are energy-producing organelles that generate molecular hydrogen (by metabolizing pyruvate to acetate and carbon dioxide producing ATP by substrate-level phosphorylation with release of hydrogen ions). The majority of the trophozoites are binucleate with 2 eccentric nuclei measuring 1-3 µm in diameter, although some mononucleate stages may be recently divided cells. The nuclei contain 3-8 granules imparting a fragmented appearance without peripheral chromatin. An extracellular spindle lies between the nuclei, and numerous dictyosomes (Golgi complexes) cover the filaments. The parasites have not been observed to form true cysts in humans, but cyst formation has been reported in laboratory mice. The cysts were rounded and encapsulated by a filamentous cyst wall with a peritrophic space between the enclosed parasite and the dense outer shell.

Site of infection: Infections in humans are confined to the large intestines, ranging from the caecum to the rectum, but most frequently in the proximal colon and appendix where trophozoites infect mucosal crypts beneath the epithelium. Infections in other primates, pigs, sheep and rodents are localized in the lower digestive tract.

Pathogenesis: *Dientamoeba fragilis* was initially considered to be a harmless commensal as the majority of infections (up to 90%) were found in people that did not have any clinical symptoms. Nonetheless, the organism was sometimes found as the only putative aetiological agent present in patients with mild gastrointestinal complaints. Trophozoites feed on bacteria within the gut by phagocytosis but they do not invade host tissues. They digest material in food vacuoles and eliminate wastes by exocytosis. The presence of motile feeding stages may cause local irritation with eosinophilic inflammatory responses. Clinical symptoms and signs include loose stools or diarrhoea (often mucoid, sometimes watery, sometimes with blood), abdominal pain, tenderness, cramping, nausea, vomiting, low grade fever, fatigue, anorexia, weight loss and failure to thrive in children. Persistent infections have also been associated with malnutrition, dehydration, appendicitis and rarely pruritic skin rashes. Dientamoebiasis may be acute (over 2 weeks) or chronic (up to 2 years) and a common misdiagnosis is irritable bowel syndrome or colitis (similar symptoms). Clinical infections are more prevalent in children (< 10 years of age), in males, during spring and summer, and in populations living in crowded conditions with poor hygiene (e.g. developing countries). Epidemiological observations have indicated that many infections are coincident with enterobiasis, caused by the pinworm (*Enterobius vermicularis*).

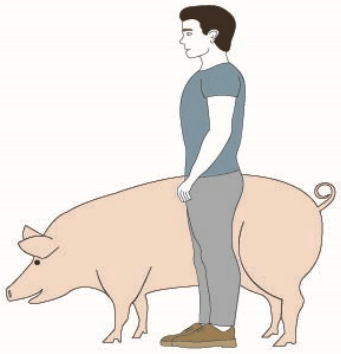
Developmental cycle and mode of transmission: The transmission cycle has yet to be established. Trophozoites occur in the lumen of the large intestine, where they multiply via binary fission, and are shed in faeces. This suggests faecal-oral transmission may occur, but trophozoites do not survive for long in faeces and cyst formation has not been demonstrated in natural infections in humans (only sometimes in experimentally-infected laboratory mice). Transmission may involve contact with contaminated fomites or the ingestion of contaminated food or water, but such routes remain to be confirmed. It has also been postulated that intermediate or paratenic invertebrates may act as alternate hosts or vectors for transmission, notably pinworms (*Enterobius vermicularis*) which show high co-infection rates, or possibly roundworms (*Ascaris lumbricoides*). However, these conjectures remain speculative as no definitive studies have yet been conducted (anecdotal evidence at best).

Differential diagnosis: Infections cannot be diagnosed on clinical grounds as most are asymptomatic and any evident clinical signs mimic those of irritable bowel syndrome or colitis. Differential diagnosis is afforded by the direct microscopic detection of fractile rounded parasites in faecal samples or gut content. Trophozoites are able to survive and move in fresh faeces, but they are sensitive to aerobic exposure and dissociate when placed in saline, tap water or distilled water. Conventional coprological techniques are ineffective as trophozoites are destroyed by formol-ether concentration and do not survive prolonged sedimentation/floatation techniques. Microscopy is usually conducted on fresh wet mounts or on permanently stained smears of unformed or formed stools. It is recommended that multiple (preferably sequential) stool samples be examined as the parasite shedding is highly variable. Trophozoites vary greatly in size and their nuclear structures cannot be seen in saline preparations. Wet mounts can be counter-stained with crystal violet haematoxylin, while fixed smears may be stained with Giemsa or Field's stain. Alternatively, faecal samples can be fixed prior to microscopy using polyvinyl alcohol (PVA), modified Schaudinn's, phenol-alcohol-formalin, or sodium acetate-acetic acid-formalin (SAF) fixatives (but not merthiolate-iodine-formalin as it is not very stable and does not stain nuclei) followed by staining with Mayer's haemalum, iron-haematoxylin, celestine blue, Wheatley's trichrome or Lawless' stain. Trophozoites may also be cultured *in vitro* in rice starch media or in xenic culture using very dilute samples. An indirect fluorescent-antibody test was developed to detect parasites in preserved faecal samples but exhibited low sensitivity. More recently, molecular biological techniques have been used to detect and characterize parasites in clinical samples following conventional and real-time (RT) polymerase chain reaction (PCR) amplification of nuclear gene sequences (small subunit ribosomal RNA).

Treatment and control: A range of drugs have been used in attempts to treat clinical infections, including organoarsenics (carbarsone, diphetarsone), tetracycline antibiotics (tetracycline, doxycycline), aminoglycoside antibiotics (paromomycin), macrolide antibiotics (erythromycin), quinolines (nitroxoline, iodoquinol) and nitroimidazoles (metronidazole, secnidazole, tinidazole and ornidazole). The most effective were metronidazole, iodoquinol, tetracycline, and paromomycin, but their application frequently caused side-effects such as abdominal cramping, nausea and rash. There are also a growing number of treatment failures using metronidazole due to the emergence of drug-resistance parasite strains. It is recommended that treated individuals be re-tested several weeks after therapy, and that other family members in close contact be tested and treated if required. It is also suggested that patients be examined for pinworm infections (*Enterobius vermicularis*) and treated with anthelmintics if required. Various common-sense preventive measures may be used to reduce the risks of transmission: including strict personal hygiene (frequently washing hands, especially before eating or handling foods), proper sanitation (clean toilets, hygienic disposal or disinfection of nappies), water treatment (filtration/chlorination, or boil water from untreated sources), and food hygiene (avoid foods fertilized with nightsoil (human waste), wash foods in clean water, and cook thoroughly).

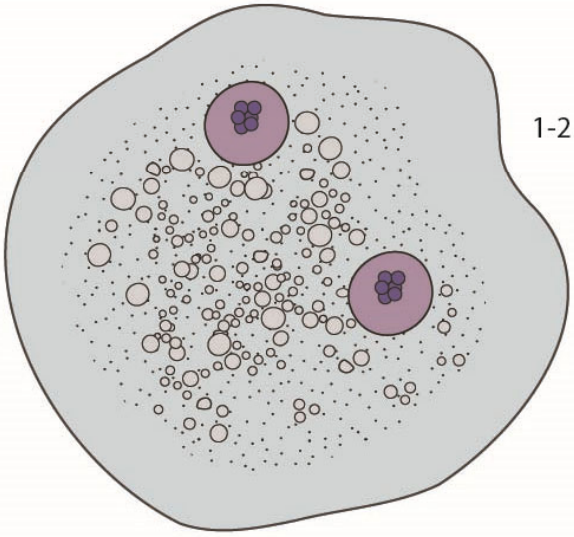
Dientamoeba

intestines
(enteritis, diarrhoea)



Vertebrate Hosts
(mammals)

division by
longitudinal
binary fission



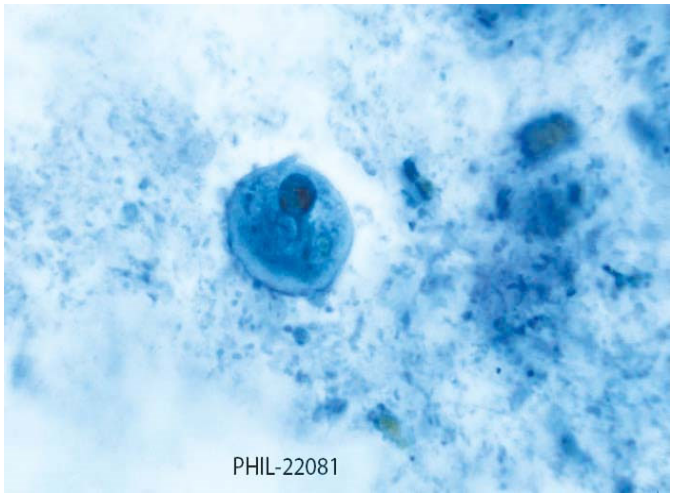
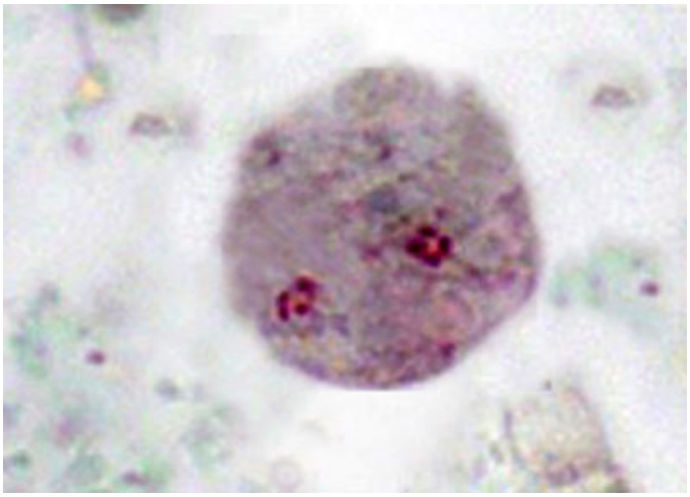
1-2 nuclei

amoeboid
nonflagellated
stage

trophozoites
(4-40 µm)

no cyst formation

transmission unknown
(speculated to involve close contact
or contaminated fomites)

	
Dientamoeba trophozoite	*Dientamoeba* trophozoite