



# AMOEBAE

## Part 2

LECTURE NO. 6

Course Name: PARASITOLOGY

Course Code: 0520442

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# **PATHOGENESIS AND CLINICAL FEATURES**

# Introduction

- *E. histolytica* causes **intestinal** and **extraintestinal** amoebiasis.
- Incubation period is highly variable. On an average, it ranges from 4 days to 4 months.
- Amoebiasis can present in different forms and degree of severity, depending on the organ affected and the extent of damage caused.

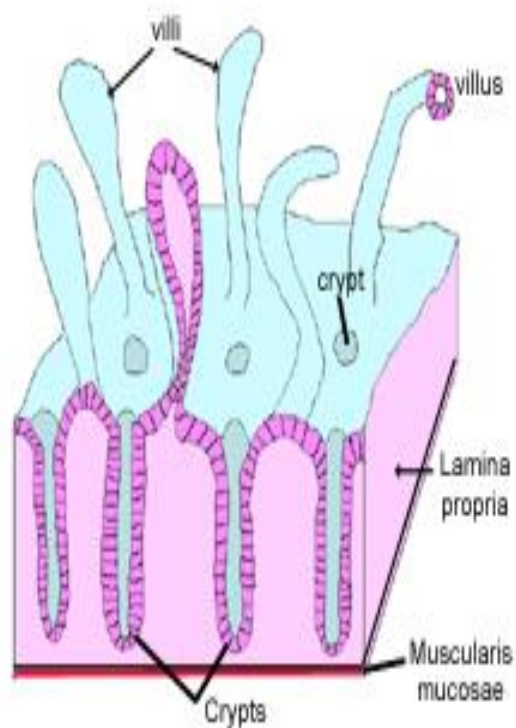
# ***1-Intestinal Amoebiasis***

- **The lumen-dwelling amoebae do not cause any illness.**
- **They cause disease only when they invade the intestinal tissues.**
- **This happens only in about 10% of cases of infection, the remaining 90% being asymptomatic.**

## ***1-Intestinal Amoebiasis (continued)***

- The metacystic trophozoites penetrate the columnar epithelial cells in the crypts of Liberkühn in the colon.
- Penetration of the amoeba is facilitated by the motility of the trophozoites and the tissue lytic enzyme, histolysin, which damages the mucosal epithelium. Amoebic lectin another virulence factor mediates adherence.

# Crypts



- The crypts additionally contain
- **Paneth cells** (at the base of the crypts) - they have a defensive function, and stain intensely eosinophilic, due to secretory granules of antimicrobial peptides called defensins, as well as lysozyme and phospholipase A. These cells last for several weeks.
- **Endocrine cells**, (also eosinophilic) which produce secretin, somatostatin, enteroglucagon and serotonin. One type of endocrine cell for each type of hormone.
- **Stem cells**, found at the base of the crypts, which divide continuously to replace enterocytes (every 2-3 days), goblet cells, paneth cells and neuroendocrine cells. Intraepithelial lymphocytes (mostly T-cells).

## 1-Intestinal Amoebiasis (continued)

- Mucosal penetration by the amoeba produces **discrete ulcers with pinhead center and raised edges**.
- Sometimes, the invasion remains superficial and heals spontaneously.
- More often, the amoeba penetrates to submucosal layer and multiplies rapidly, causing lytic necrosis and thus forming an abscess. The abscess breaks down to form an ulcer.



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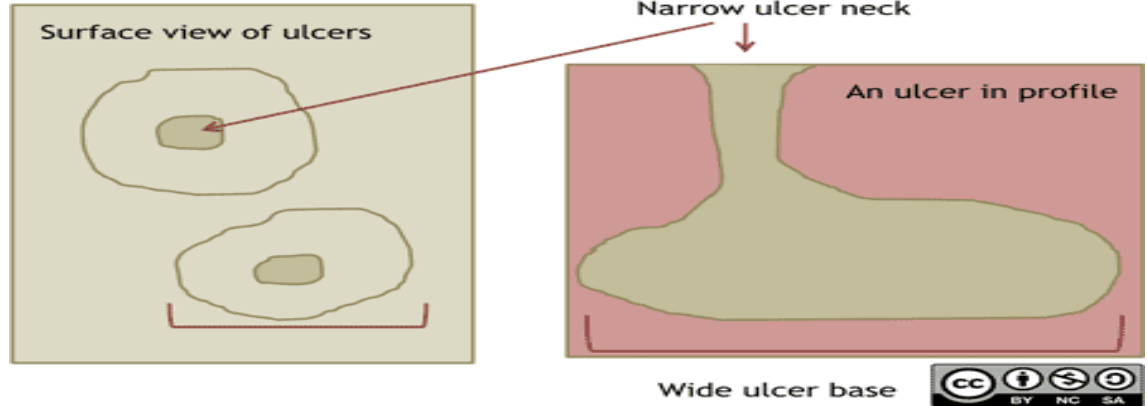
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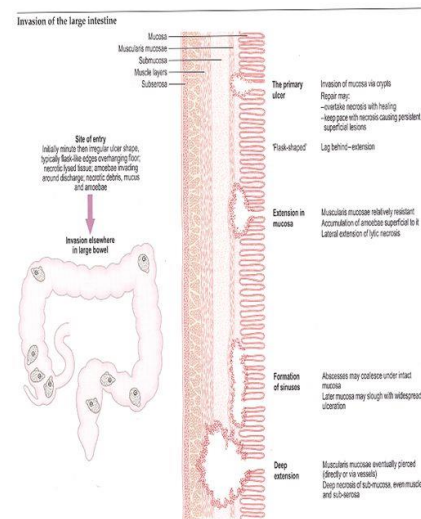
# Flask-shaped amoebic ulcers



**Figure 1.** Invasion of submucosa by trophozoites. The lesion spreads out laterally, creating the flask-shaped amoebic ulcer. (Histopathology, UFPA, Araújo R.).



## PATHOLOGY: Intestinal amoebiasis :



**Formation of flask-shaped ulcers.**

## ***Clinical Features of Intestinal Amoebiasis***

- **The clinical picture covers a wide spectrum from noninvasive carrier state to fulminant colitis.**
- **The incubation period is highly variable from 1–4 months.**
- **The clinical course is characterized by prolonged latency, relapses and intermissions.**

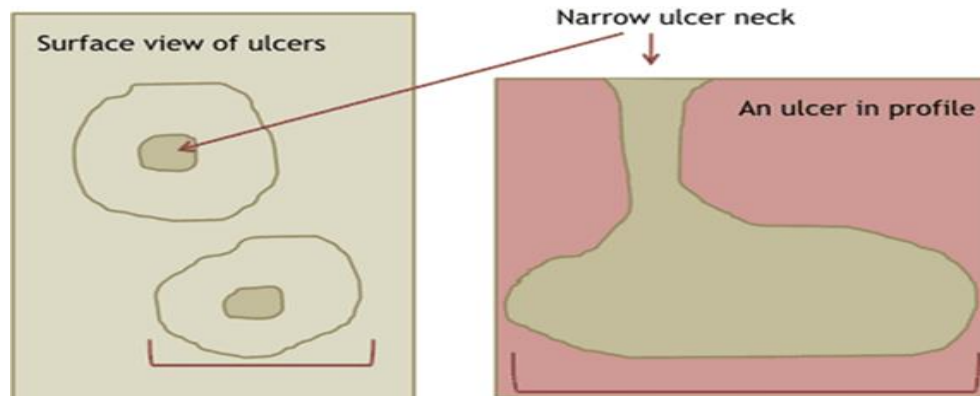
## ***Clinical Features of Intestinal Amoebiasis (continued)***

- The patient is usually afebrile and nontoxic.
- In fulminant colitis, there is confluent ulceration and necrosis of colon.
- Intestinal amoebiasis does not always result in dysentery. Quite often, there may be only diarrhea or vague abdominal symptoms popularly called 'uncomfortable belly' or 'growling abdomen.'

# Lesions in chronic intestinal amoebiasis

- Small superficial ulcers involving only the mucosa.
- Round or oval-shaped with ragged and undermined margin and flask-shaped in cross-section.
- Marked scarring of intestinal wall with thinning, dilatation, and sacculation.

## Flask-shaped amoebic ulcers



## Lesions in chronic intestinal amoebiasis

- Extensive adhesions with the neighboring viscera.
- Formation of tumor-like masses of granulation tissue (amoeboma).
- Chronic involvement of the caecum causes a condition simulating *appendicitis*.

## ***Clinical Features of Intestinal Amoebiasis (Stool examination)***

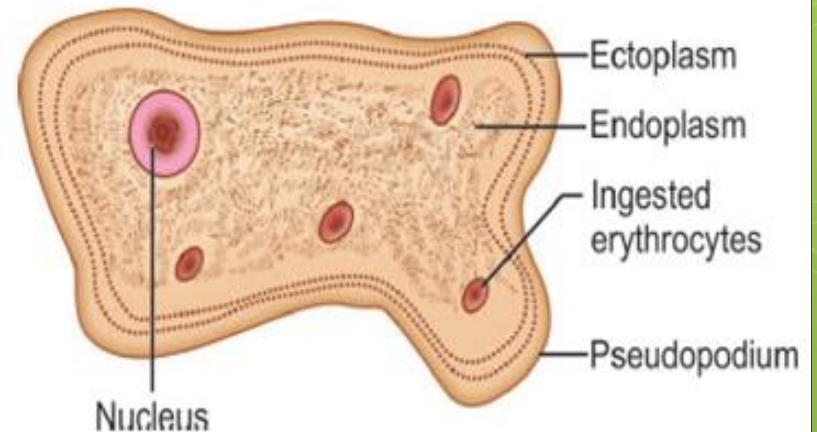
- **The stools are large, foul-smelling, and brownish black, often with blood streaked mucus intermingled with feces.**
- **The RBCs in stools are clumped and reddish-brown in color.**
- **Cellular exudate is scanty.**

## Clinical Features of Intestinal Amoebiasis (continued)

- Charcot-Leyden crystals are often present.



- E. histolytica* trophozoites can be seen containing ingested erythrocytes.



# Complications And Sequelae Of Intestinal Amoebiasis

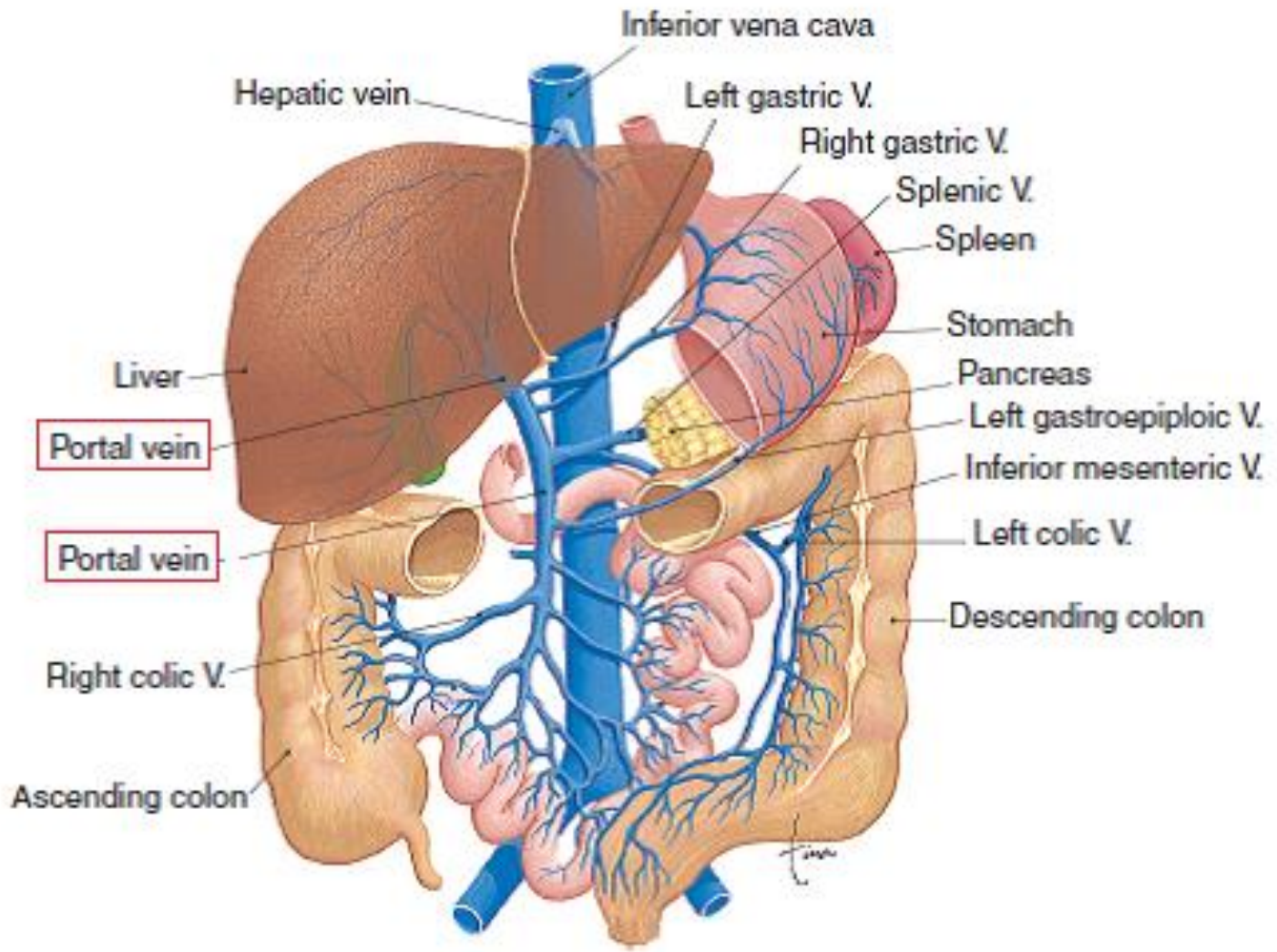
## Fulminant amoebic colitis

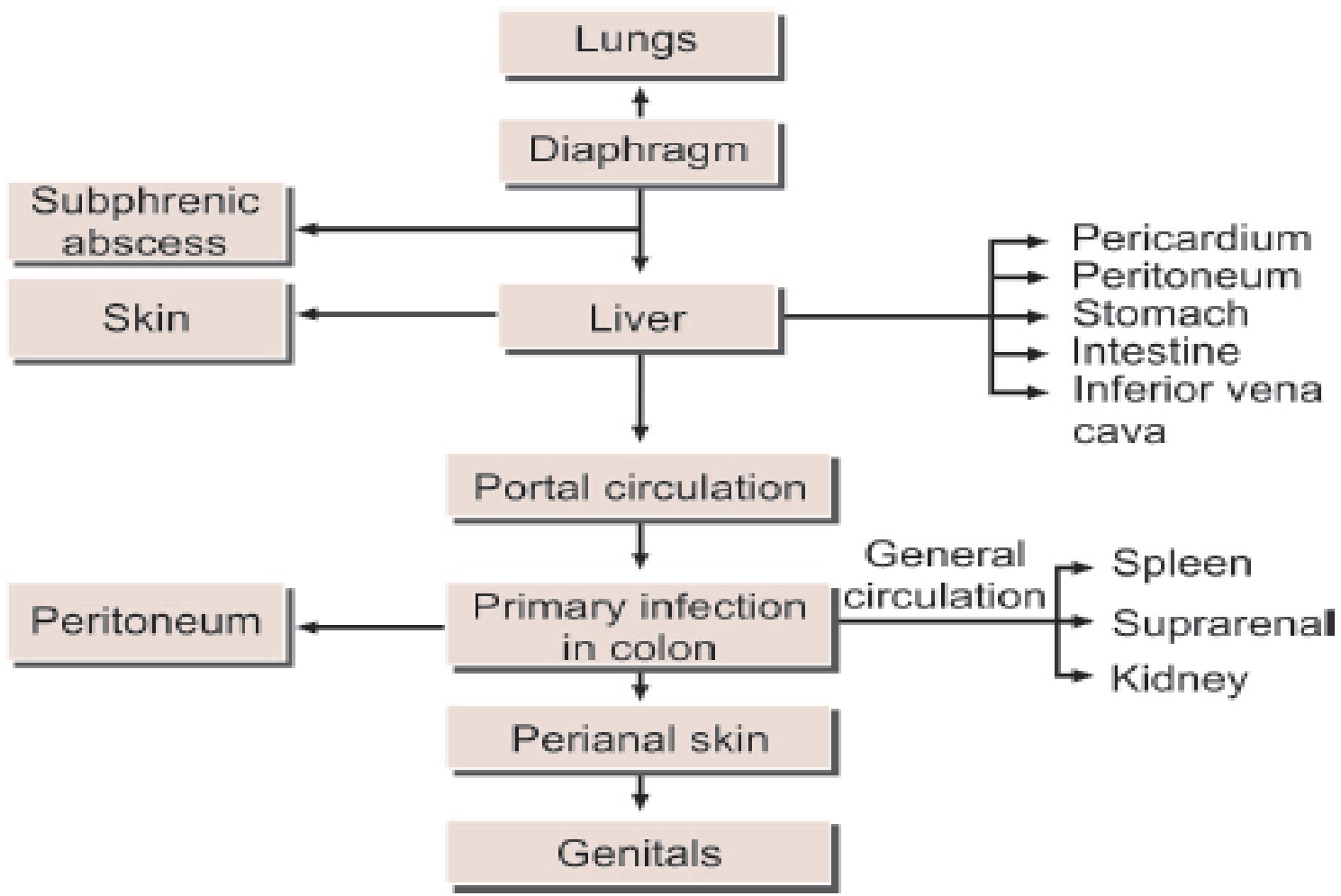
- Toxic megacolon
- Perianal ulceration
- Amoeboma

## Extraintestinal amoebiasis

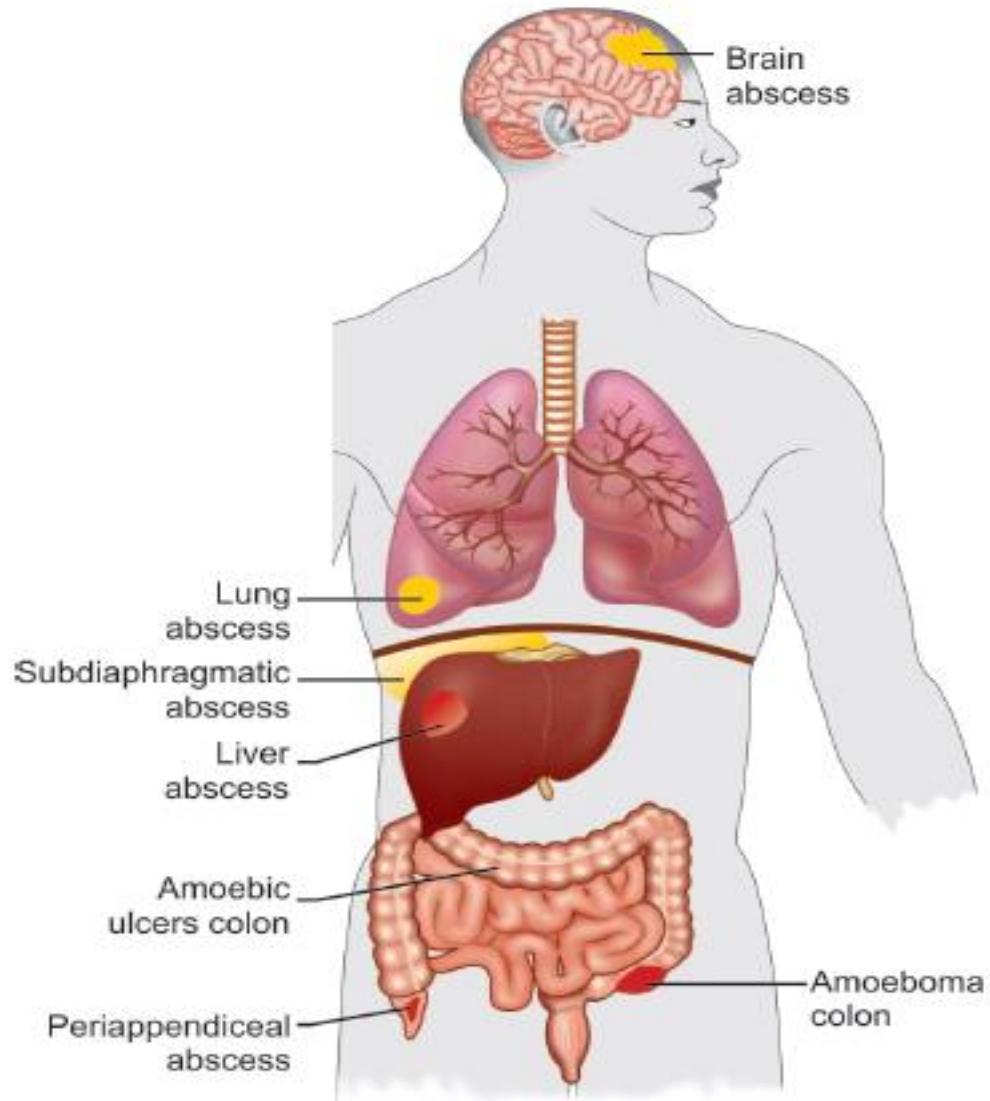
- Amoebic hepatitis
- Amoebic liver abscess
- Amoebic appendicitis and peritonitis
- Pulmonary amoebiasis
- Cerebral amoebiasis
- Splenic abscess
- Cutaneous amoebiasis
- Genitourinary amoebiasis







**Flowchart 3.2: Sites affected in amoebiasis**

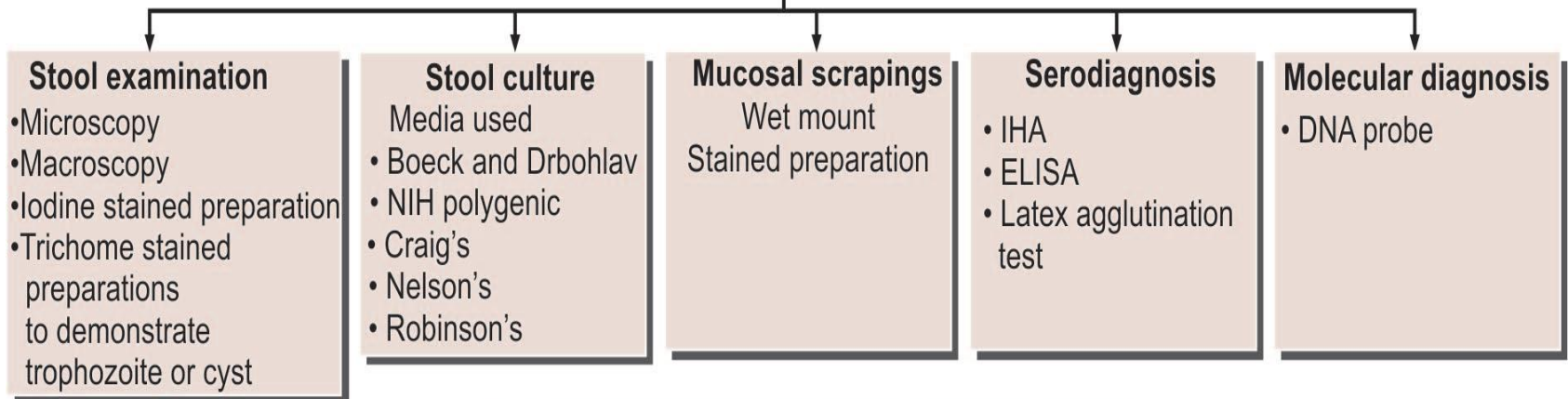


**Fig. 3.5: Lesions of Amoebiasis**

# Laboratory Diagnosis

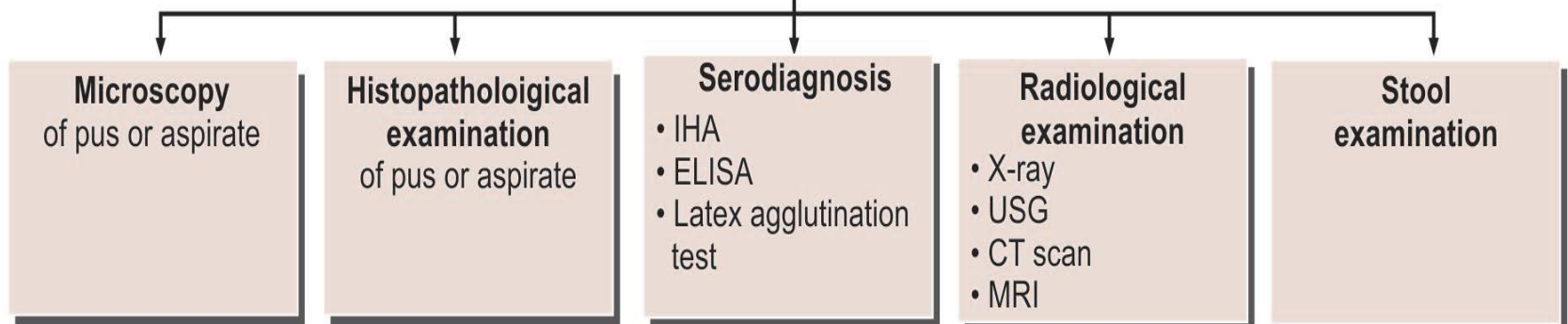
## A. Laboratory diagnosis of *Entamoeba histolytica*

### Intestinal amoebiasis

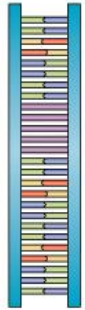


## B. Laboratory diagnosis of amoebic liver abscess

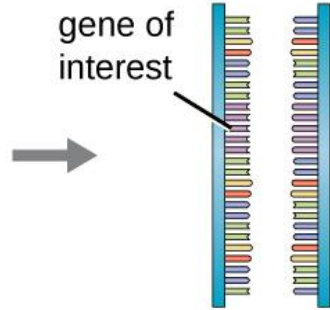
### Amoebic liver abscess



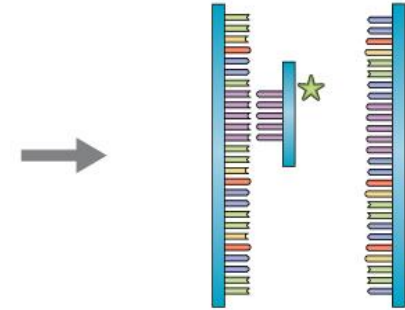
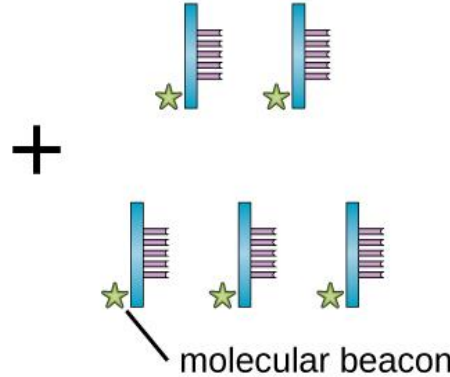
DNA sample



Denatured ssDNA



DNA probes



1 Isolate DNA from body fluid sample.

2 Denature DNA sample and combine with DNA probes. Probes are complementary to the gene of interest and labeled with a molecular beacon.

3 DNA probes will bind to the gene of interest if it is present in the DNA sample.

Abbreviations

- IHA test: Indirect hemagglutination
- ELISA: Enzyme-linked immunosorbent assay

## ***Clinical Features of Intestinal Amoebiasis (continued)***

- The typical manifestation of intestinal amoebiasis is amoebic dysentery.
- This may resemble bacillary dysentery, but can be differentiated on clinical and laboratory grounds.
- Compared to bacillary dysentery, it is usually insidious in onset and the abdominal tenderness is less and localized (Table 3.2).

## Table 3.2: Differential Features of Amoebic and Bacillary Dysentery

Features	AMOEBCIC DYSENTERY	BACILLARY DYSENTERY
<b>CLINICAL</b>		
<b>Onset</b>	Slow	Acute
<b>Fever</b>	Absent	Present
<b>Toxicity</b>	Absent	Present
<b>Abdominal tenderness</b>	Localised	Generalised
<b>Tenesmus</b>	Absent	Present

## Table 3.2: Differential Features of Amoebic and Bacillary Dysentery (continued)

Features	AMOEBCIC DYSENTERY	BACILLARY DYSENTERY
<b>STOOL</b>		
<b>Frequency</b>	6–8 per day	Over 10 per day
<b>Odor</b>	Offensive	Nil
<b>Color</b>	Dark red	Bright red
<b>Nature</b>	Feces mixed with blood and mucus	Blood and mucus with little or no feces
<b>Consistency</b>	Not adherent	Adherent to container
<b>Reaction</b>	Acid	Alkaline

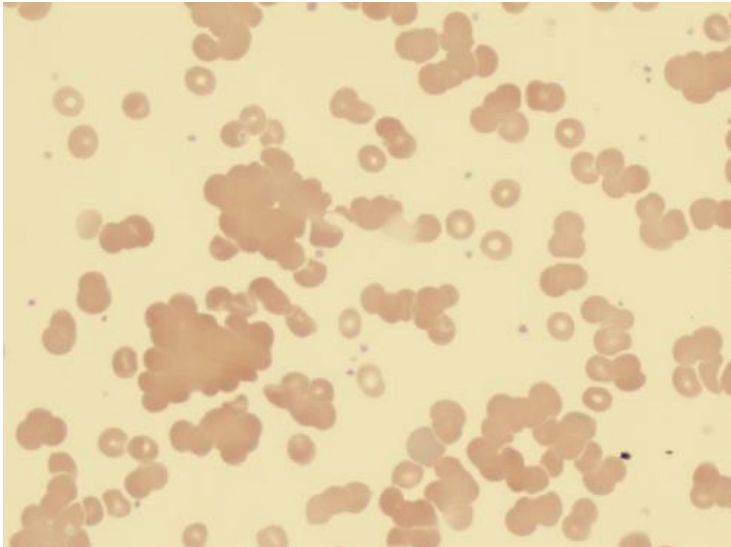


**Table 3.2: Differential Features of Amoebic and Bacillary Dysentery (continued)**

	AMOEBCIC DYSENTERY	BACILLARY DYSENTERY
<b>MICROSCOPY</b>		
<b>Cellular exudates</b>	Scanty	Abundant
<b>Red blood cells</b>	Clumped yellowish brown	Discrete or in rouleaux, bright red
<b>Macrophages</b>	Few	Several, some with ingested red blood cells
<b>Eosinophils</b>	Present	Absent
<b>Charcot-Leyden crystals</b>	Present	Absent
<b>Motile bacteria</b>	Present	Absent
<b>Amoeba</b>	Motile trophozoites with ingested red blood cells	Absent

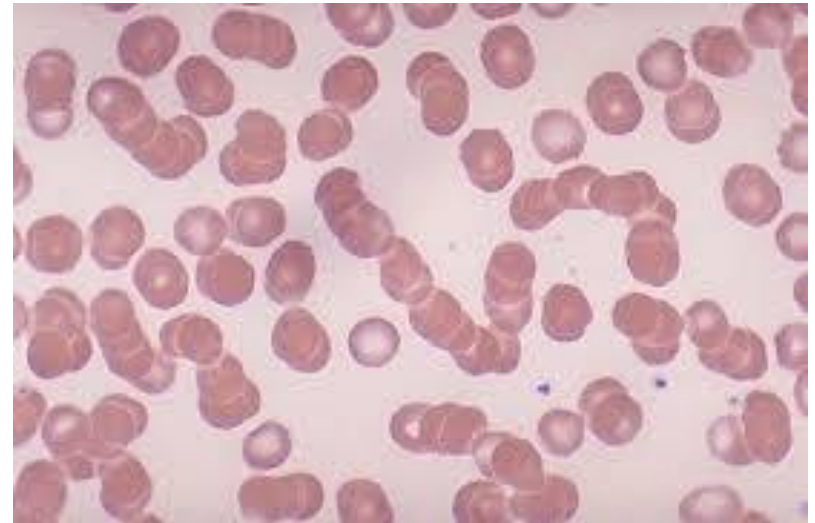
## **AMOEBIC DYSENTERY**

**RBCs are Clumped  
yellowish brown**



## **BACILLARY DYSENTERY**

**RBCs are Discrete  
or in rouleaux  
bright red**



# Treatment

*Three classes of drug are used in the treatment of amoebiasis.*

## **Luminal amoebicides:**

Diloxanide furoate, iodoquinol, paromomycin, and tetracycline act in the intestinal lumen but not in tissues.

## **Tissue amoebicides:**

Emetine, chloroquine, etc. are effective in systemic infection, but less effective in the intestine. Dosage of chloroquine in amoebic liver abscess is 1 g for 2 days followed by 5 g daily for 3 weeks.

## **Both luminal and tissue amoebicides:**

Metronidazole and related compounds like tinidazole and ornidazole act on both sites and are the drug of choice for treating amoebic colitis and amoebic liver abscess.

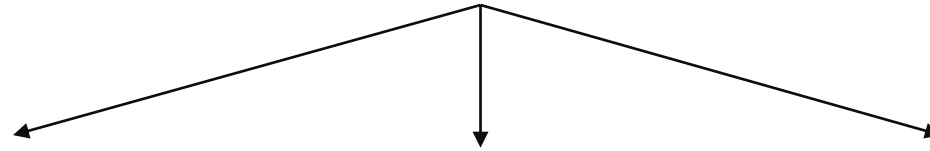
# Notes

- Although metronidazole and tinidazole act on both the sites but **NEITHER** of them **reach high levels in the gut lumen**; therefore, patients with amoebic colitis or amoebic liver abscess **should also receive treatment with a luminal agent** (paromomycin or iodoquinol) to ensure eradication of infection (Table 3.3).
- Paromomycin is the preferred agent.

## Notes (continued)

- **Asymptomatic individuals** with documented *E. histolytica* infection should also be **treated** because of the risks of developing amoebic colitis or amoebic liver abscess in the future and risk of transmitting the infection to others.
- Paromomycin or iodoquinol in the doses listed in the Table 3.3 should be used in these cases.
- Oral rehydration and electrolyte replacement should be done wherever necessary.

# Treatment of amoebiasis



## Luminal amoebicides

- Diloxanide furoate
- Iodoquinol
- Paromomycin
- Tetracycline

## Tissue amoebicides

- Emetine
- Chloroquine

## Both luminal and tissue amoebicides

- Metronidazole
- Tinidazole
- Ornidazole



Tinidazole



Metronidazole



Clinical syndrome	Drug of choice
<ul style="list-style-type: none"> <li>Asymptomatic (Carrier)</li> </ul>	Iodoquinol <u>OR</u> Paromomycin
<ul style="list-style-type: none"> <li>Mild to severe colitis</li> <li>Extraintestinal like amoebic liver abscess</li> </ul>	Metronidazole <u>OR</u> Tinidazole <b>PLUS</b> Iodoquinol <u>OR</u> Paromomycin*

\* Paromomycin is preferred

# Recommended Dosages of Antiamoebic Drugs

Drug	Dosage	Duration (in days)
<b>Amoebic colitis or Amoebic liver abscess</b>		
Tinidazole	2 g/day orally	3
Metronidazole	750 mg three times a day, orally or IV	5 - 10
Chloroquine (For amoebic liver abscess)	1 g daily	for 2 days
	followed by 5 g daily	For 3 weeks
<b>Intestinal amoebiasis</b>		
Paromomycin	30 mg/kg 4 times a day, orally in 3 divided doses	5 - 10
Iodoquinol	650 mg orally, three times day	20



# Prophylaxis

- **General prophylaxis is as for all fecal-oral infections. Food and water have to be protected from contamination with human excreta.**
- **Detection and treatment of carriers and their exclusion from food handling occupations will help in limiting the spread of infection.**
- **Health education and inclusion of healthy personal habits helps in control.**

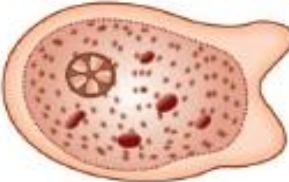






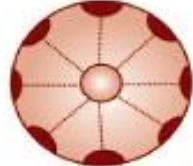
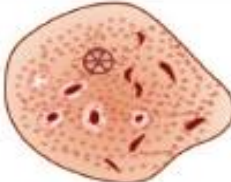


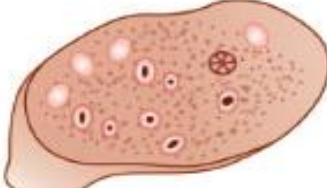

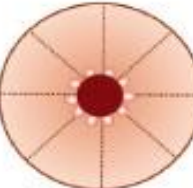


# Immunity

- Infection with invasive strains includes both humoral and cellular Immune responses.
- Local and systemic antibodies can be demonstrated within a week of invasive infection.
- Infection confers some degree of protection as evidenced by the very low frequency of recurrence of invasive colitis and liver abscess in endemic areas.
- The course and severity of amoebiasis does not seem to be affected by human immunodeficiency virus (HIV) infection.
- Serological response is hardly ever seen in infection with non-invasive zymodemes.

## Table 3.1: Classification of Amoebae

Intestinal amoebae	Free-living amoebae
<i>Entamoeba histolytica</i> <i>Entamoeba dispar</i> <i>Entamoeba coli</i> <i>Entamoeba polecki</i> <i>Entamoeba hartmanni</i> <i>Entamoeba gingivalis</i> <i>Endolimax nana</i> <i>Iodamoeba butschlii</i>	<i>Naegleria fowleri</i> <i>Acanthamoeba</i> spp. <i>Balamuthia mandrillaris</i>
<b>Note:</b> All intestinal amoebae are nonpathogenic, except <i>Entamoeba histolytica</i>	<b>Note:</b> All free-living amoebae are opportunistic pathogens

# Comparative morphology of intestinal amoebae infecting humans (nonpathogenic)

	Trophozoite	Cyst	Nucleus
<i>Entamoeba histolytica</i>			
<i>Entamoeba coli</i>			
<i>Entamoeba gingivalis</i>			
<i>Endolimax nana</i>			
<i>Iodamoeba butschlii</i>			
<i>Dientamoeba fragilis</i>			

# PATHOGENIC FREE-LIVING AMOEBAE

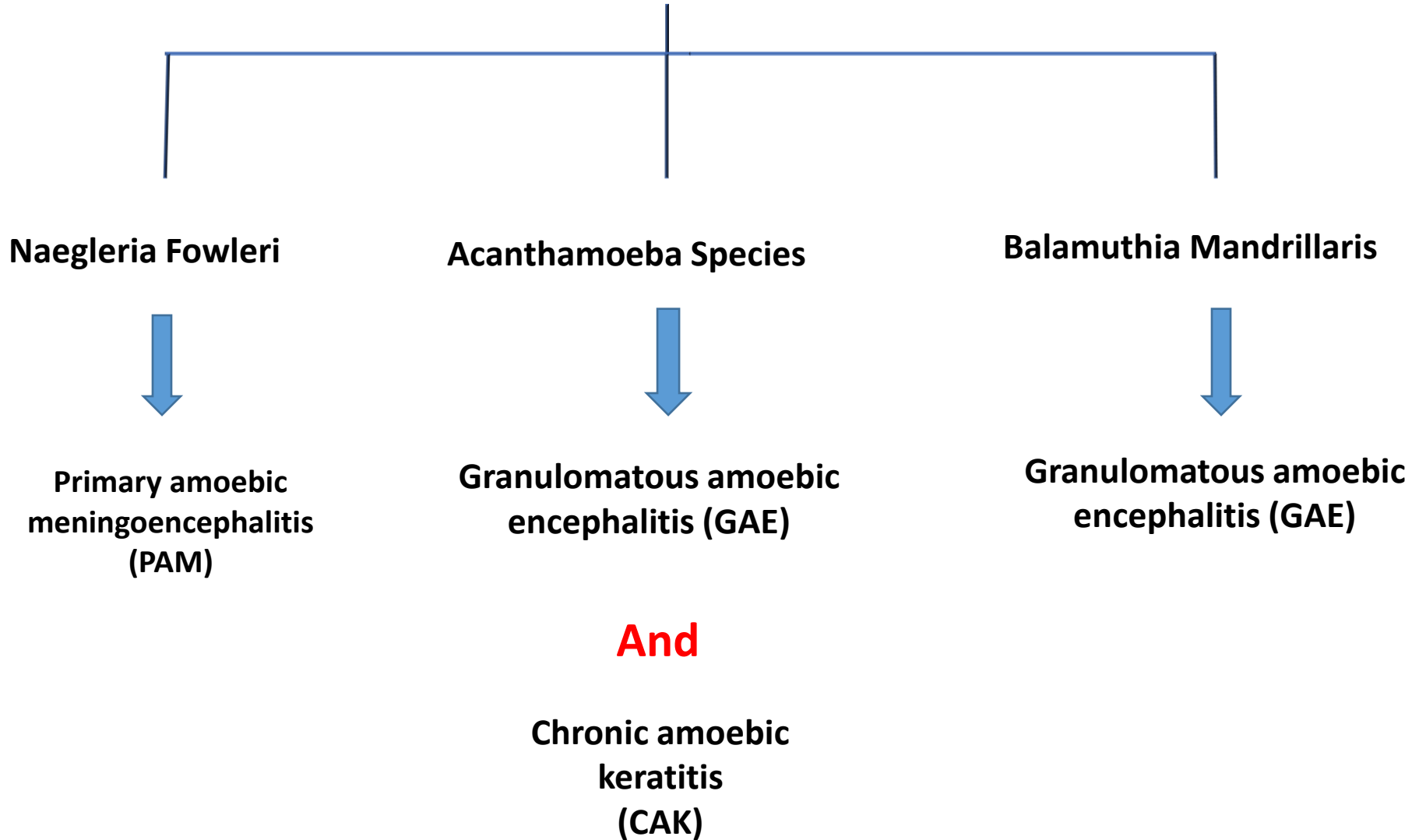
## Introduction

- Among the numerous types of free-living amoebae found in water and soil, a few are potentially pathogenic and can cause human infections.
- **Primary amoebic meningoencephalitis (PAM)** caused by amoeboflagellate *Naegleria* (**the brain eating amoeba**).

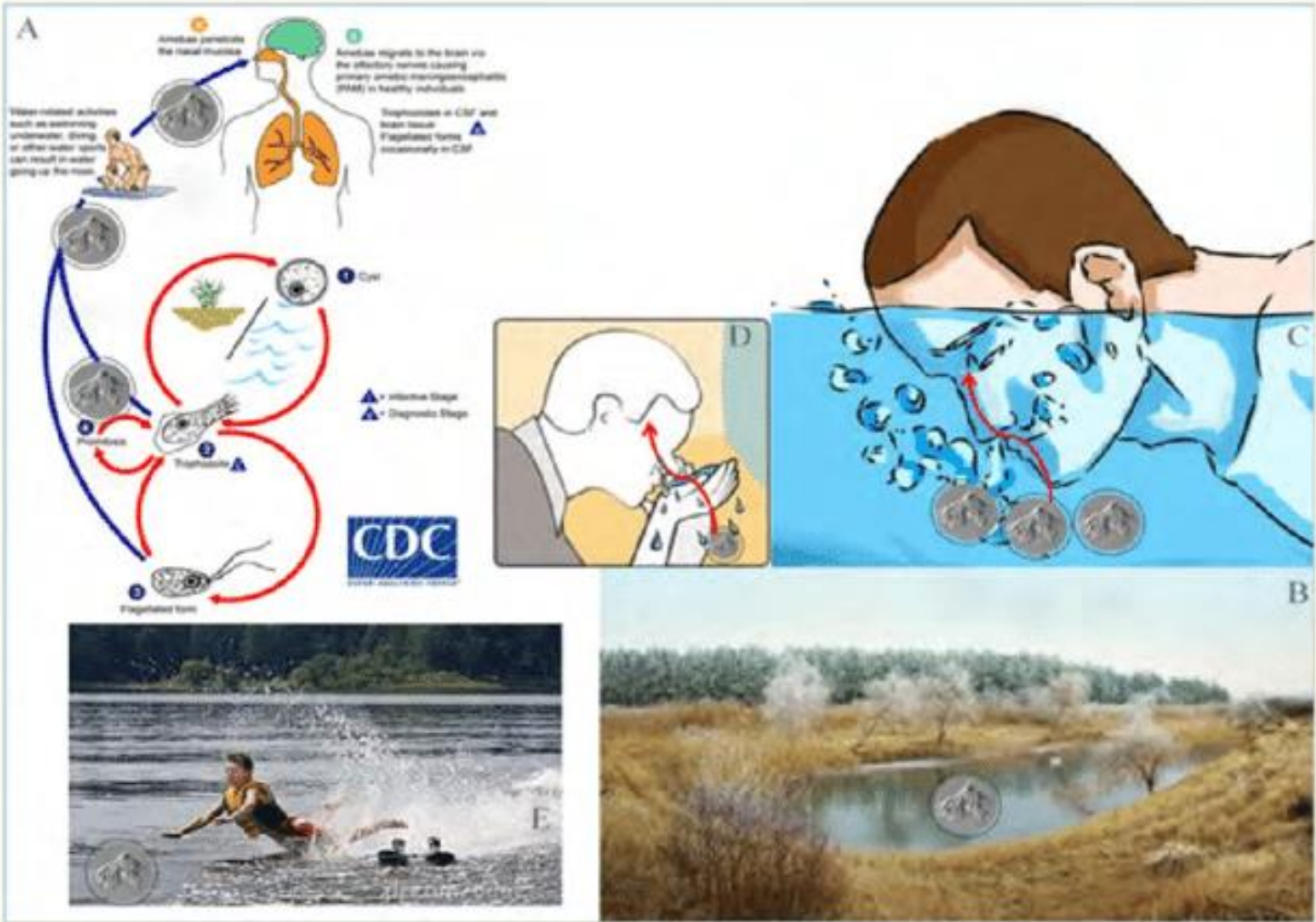
# Introduction (continued)

- **Granulomatous amoebic encephalitis (GAE)** and **chronic amoebic keratitis (CAK)** – caused by *Acanthamoeba*.
- A few instances of GAE caused by lyptomyxid amoeba like *Balamuthia* have also been reported. While PAM and CAK occur in previously healthy individual, GAE has been associated with immunodeficient patients.
- The term **amphizoic** has been used for organisms such as these, which can multiply both in the body of a host (**endozoic**) and in free-living (**exozoic**) conditions.

# PATHOGENIC FREE-LIVING AMOEBAE



# Naegleria Fowleri

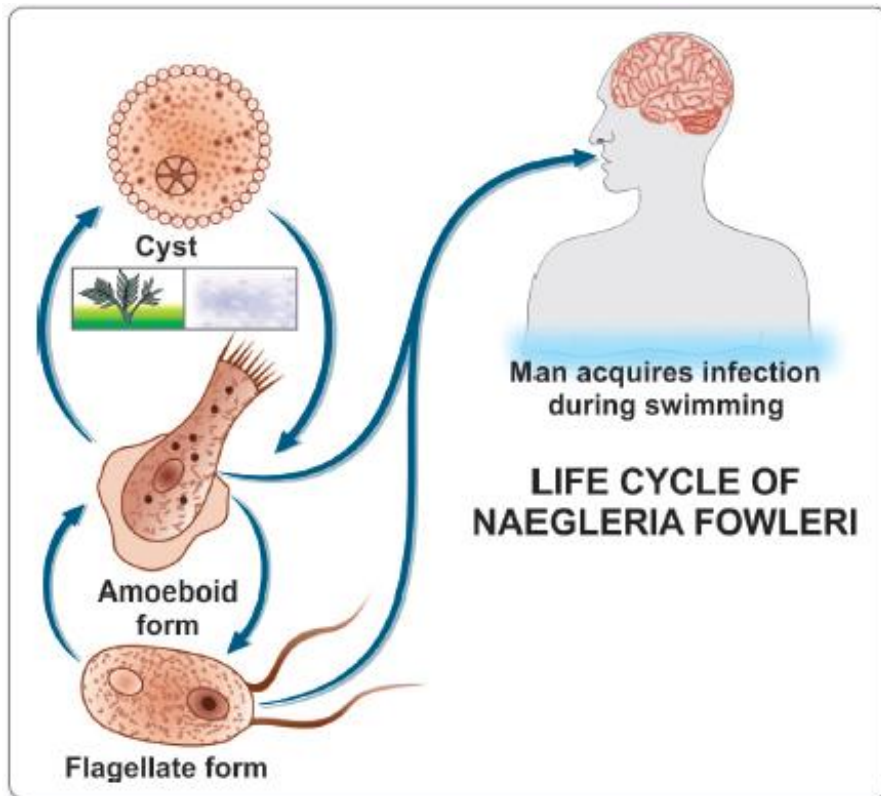




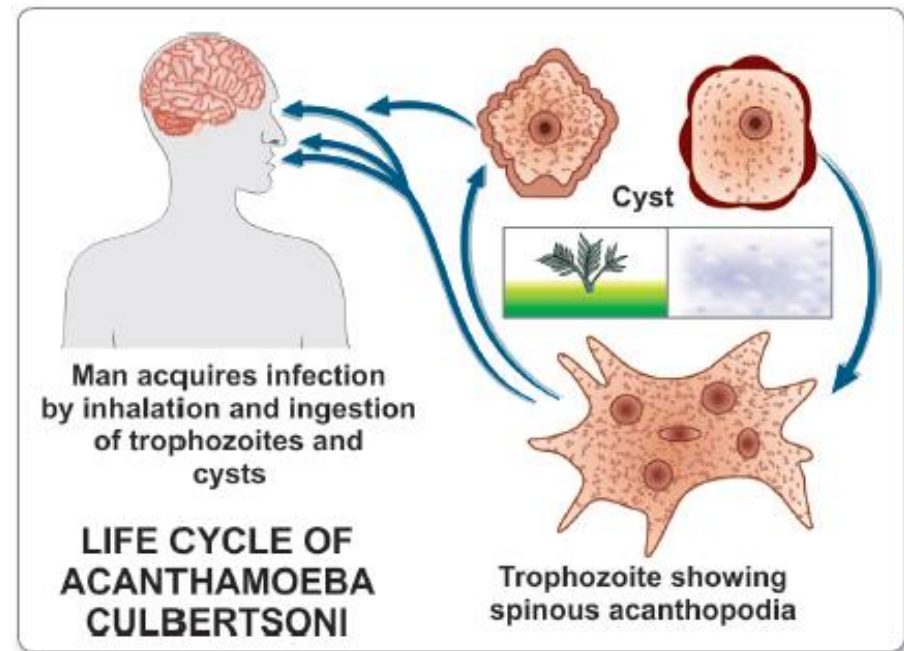
## Table 3.5: Differential features of *Naegleria* and *Acanthamoeba*

	<i>Naegleria</i>	<i>Acanthamoeba</i>
<b>Disease</b>	Primary amoebic meningoencephalitis (PAM)	Granulomatous amoebic encephalitis (GAE) and keratitis
<b>Portal of entry</b>	Nose	Upper Respiratory tract (?), cornea
<b>Clinical course</b>	Acute	Subacute or chronic
<b>Pathogenicity</b>	Acute suppurative inflammation	Granulomatous inflammation
<b>Morphological forms</b>	3 stages: trophozoite, cyst and flagellate form	2 stages: trophozoite and cyst.  Flagellate form absent

## Naegleria



## Acanthamoeba



## Table 3.5: Differential features of *Naegleria* and *Acanthamoeba* (continued)

	<i>Naegleria</i>	<i>Acanthamoeba</i>
<b>Trophozoite</b>	10–20 $\mu\text{m}$ , with a single pseudopodia	20–50 $\mu\text{m}$ , with spine-like pseudopodia
<b>Cyst</b>	7–10 $\mu\text{m}$ , round with smooth wall	15–25 $\mu\text{m}$ , polygonal double-walled with wrinkled surface
<b>Nuclear division</b>	By promitosis, nucleolus divides, nuclear membrane persists	Nuclear membrane dissolves
<b>WBC in CSF</b>	Predominantly neutrophils	Predominantly lymphocytes

**Table 3.5: Differential features of Naegleria and Acanthamoeba (continued)**

	<i>Naegleria</i>	<i>Acanthamoeba</i>
<b>Treatment</b>	<ul style="list-style-type: none"> <li>•The drug of choice is amphotericin-B intravenously.</li> <li>•It can also be instilled directly into the brain.</li> <li>• Treatment combining miconazole and sulfadiazine has shown limited success, only when administered early.</li> <li>• More than 95% cases of PAM are fatal despite of treatment.</li> </ul>	<ul style="list-style-type: none"> <li>•In <b>acanthamoeba keratitis</b>, current therapy involves topical administration of biguanide or chlorhexadine with or without diamidine agent.</li> <li>•In severe cases, where vision is threatened, penetrating keratoplasty can be done.</li> <li>•No effective treatment is available for GAE.</li> <li>•Multidrug combinations including pentamidine, sulfadiazine, rifampicin, and fluconazole are being used with limited success.</li> </ul>

# References

- [https://www.google.com/search?q=amoebic+ulcer&rlz=1C1GCEA\\_enJO788JO788&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiOxp-c977eAhWBy6QKHV3tDYsQ\\_AUIDigB&biw=1366&bih=657](https://www.google.com/search?q=amoebic+ulcer&rlz=1C1GCEA_enJO788JO788&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiOxp-c977eAhWBy6QKHV3tDYsQ_AUIDigB&biw=1366&bih=657)
- <https://www.bigstockphoto.com/image-182596567/stock-photo-entamoeba-histolytica-protozoan-isolated-on-white-background-parasite-which-causes-amoebic-dysentery-and-ulcers%2C-3d-illustration>
- [https://www.google.com/search?q=charcot-leyden+crystals&rlz=1C1GCEA\\_enJO788JO788&source=lnms&tbm=isch&sa=X&ved=0ahUKEwii--KvnL\\_eAhWGNOWkHT95A4AQ\\_AUIDigB&biw=1366&bih=608#imgcr=kpLxQFqJWyhjcM](https://www.google.com/search?q=charcot-leyden+crystals&rlz=1C1GCEA_enJO788JO788&source=lnms&tbm=isch&sa=X&ved=0ahUKEwii--KvnL_eAhWGNOWkHT95A4AQ_AUIDigB&biw=1366&bih=608#imgcr=kpLxQFqJWyhjcM)
- **Paniker's Textbook of Medical Parasitology.** Paniker CKJ. and Ghosh S. 7<sup>th</sup> ed. Jaypee Brothers Medical Publishers (P) Ltd, 2013. ISBN: 978-93-5090-534-0. **ONLINE REFERENCE:** [https://www.academia.edu/30595207/Panikers\\_Textbook\\_of\\_Medical\\_Parasitology\\_7th\\_Edition\\_2013\\_PDF](https://www.academia.edu/30595207/Panikers_Textbook_of_Medical_Parasitology_7th_Edition_2013_PDF) . Retrieved on October 15, 2018.