


King Saud University  
College of Medicine  
2nd Year, 2nd Block

# GIT BLOCK

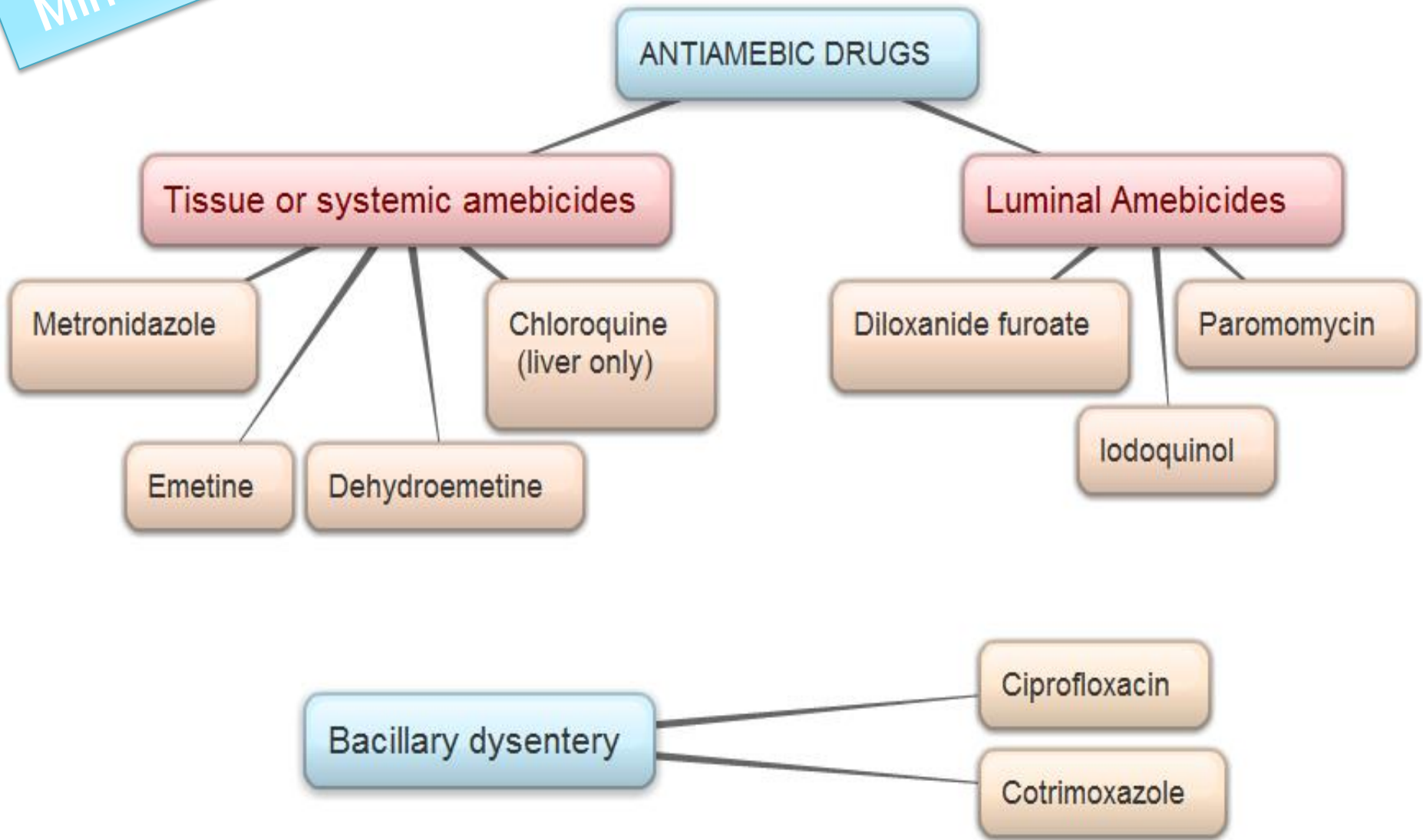


## L3: Treatment of dysentery and amebiasis

# Learning objectives

- To understand different causes of dysentery.
- To describe different classes of drugs used in treatment of both bacillary dysentery and amebic dysentery.
- To be able to describe actions, side effects of drugs for treating bacillary dysentery.
- To understand the pharmacokinetics, actions, clinical applications and side effects of antiamebic drugs.
- To be able to differentiate between types of antiamebic drugs; luminal amebicides, and tissue amebicide.

Mind map



# DYSENTERY

introduction

## Definition :

is an inflammatory disorder of the intestine (colon), that results in severe diarrhea containing mucus and/or blood in the feces with fever and abdominal pain.

## Causes:

- 1- viral infection
- 2- bacterial infection
- 3- parasitic infestations

The two most common causes are:

### -**Amebic dysentery**

(protozoal infection mainly by *Entamoeba Histolytica*).

### -**Bacillary dysentery**

(or shigellosis) (bacterial infection mainly by shigella).

## Treatment :

-Maintain fluid intake using oral rehydration (due to severe diarrhea) therapy or I.V fluid therapy.

Antimicrobial agents should not be given until stool analysis is done (**empiric therapy should be started after sample of stool taken for analysis**). After stool results & detecting the pathogen we give more specific drugs.

# AMOEBIASIS

introduction

## Definition

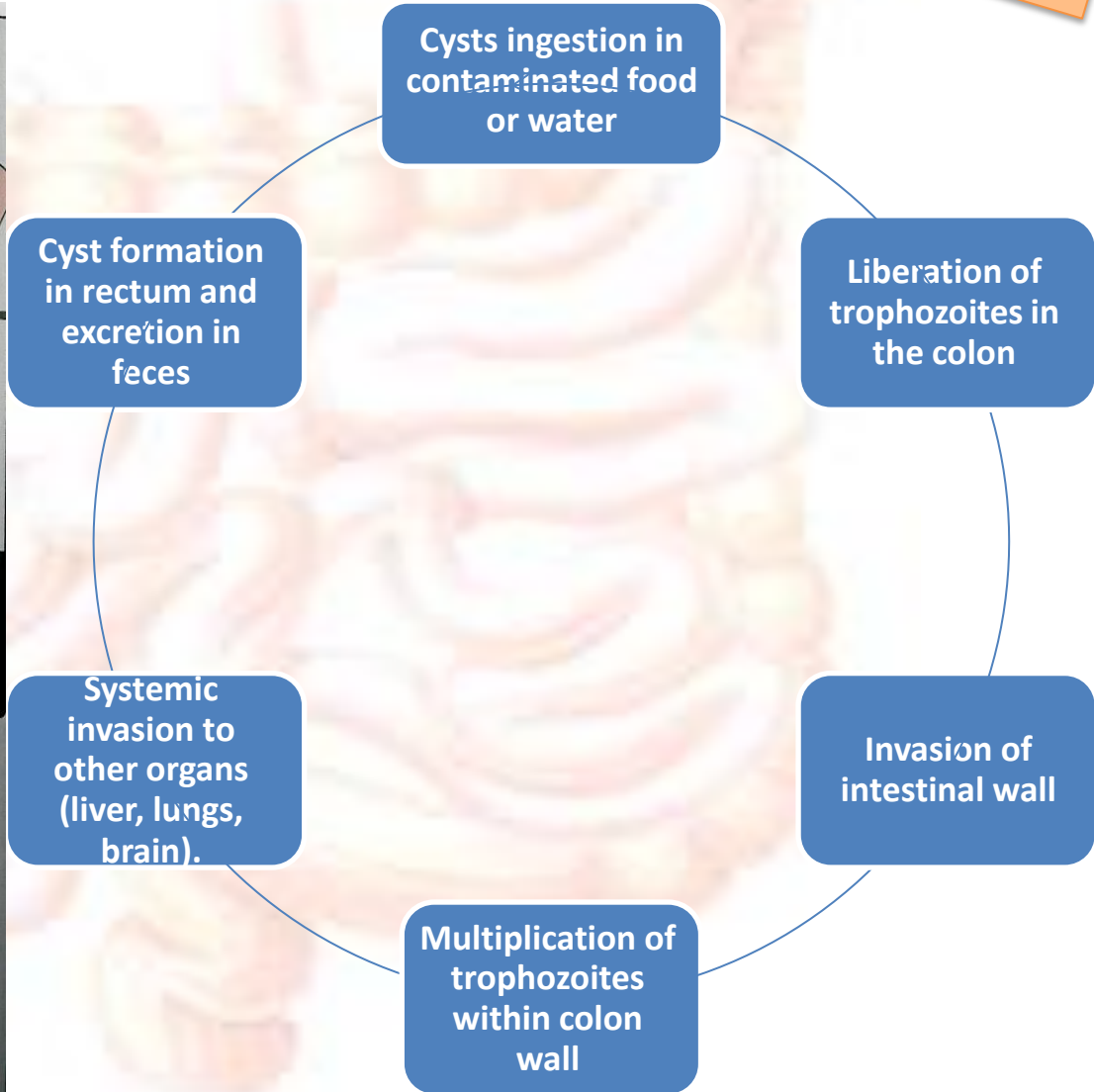
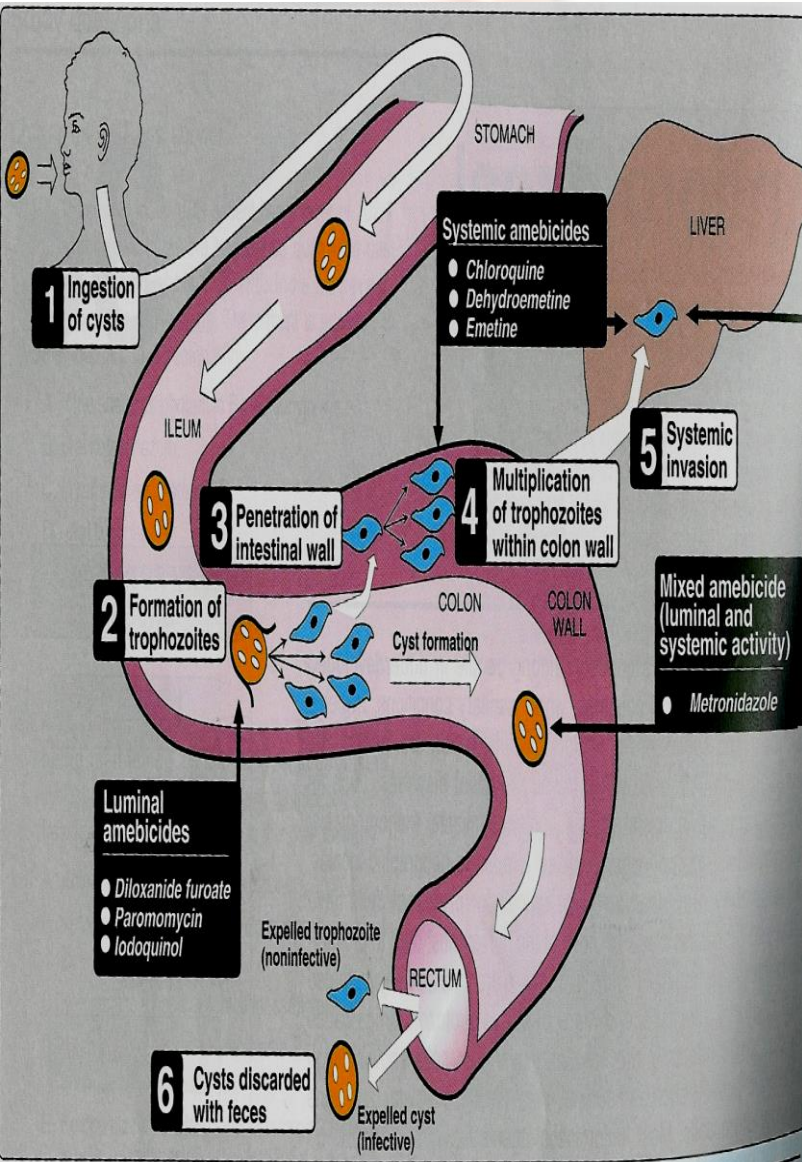
- Amebiasis is a **protozoal infection** of the intestinal tract that occurs due to ingestion of foods or water contaminated with **cysts of Entameba Histolytica**.
- The patients show varying degree of illness from no symptoms to mild diarrhea to severe dysentery.

## Clinical presentation

- Asymptomatic intestinal infection (Carriers, passing cysts in stool)
- Mild to moderate intestinal disease (colitis)
- Severe intestinal infection (amoebic dysentery) present sometimes with blood and mucus.
- Ameboma (localized granulomatous lesion of colon).
- Hepatic abscess, and other extra-intestinal diseases.

# LIFE CYCLE

introducin



slide

doctor's note

important

explanation

# Antiamoebic Drugs

\*after we finish from systemic amoebicides treatment we have to follow the Luminal Amoebicides treatment to clear the Lumen

## A-Tissue or systemic amoebicides\*

## B-Luminal Amoebicides

Action

Act on **ameba in tissues** e.g. the intestinal wall and/or other extra-intestinal tissues as liver, brain and lung.

Acts on the parasites in the **lumen of the bowel**. (non-systemic)

uses

Used for treatment of **systemic form of the disease (invasive amoebiasis)** e.g. intestinal wall infection or liver abscesses.

used for treatment of **asymptomatic amoebiasis (carriers)**.

include

- 1.Metronidazole
- 2.Emetine
- 3.Dehydroemetine
- 4.Chloroquine (liver only)

Diloxanide furoate  
Iodoquinol  
Paromomycin

# 1. METRONIDAZOLE

Metronidazole	Pharmacokinetics	Clinical Uses
<p>-Tissue ameobicide.</p> <p><b>-Acts on trophozoites.</b></p> <p>-inhibits DNA replication.</p> <p>-Does not eradicate cysts from intestine.</p> <p><b>-Drug of choice for treating invasive amebic infections</b> (intestinal &amp; extra-intestinal amebiasis)</p>	<p>Given orally or IV.</p> <p>Absorption is rapid and complete.</p> <p><b>Wide distribution</b> to all tissues and body fluids (CSF, saliva, milk).</p> <p>Plasma half life is (8 h)</p> <p><b>Metabolized in liver by mixed function oxidase*</b> followed by glucuronidation (consider drug interactions).</p> <p>Excreted in urine.</p> <p>Clearance is decreased in liver impairment</p> <p><b>*Cytochrome p450</b></p>	<p><b>1-Extra-luminal amoebiasis: is the drug of choice in all tissue amebiasis</b></p> <p>(should be followed by luminal amebicides) to get rid off pathogens from tissue + lumen (not becoming a carrier)</p> <p>2-Giardiasis</p> <p>3-Trichomoniasis</p> <p><b>4-Broad spectrum</b> of anaerobic bacterial infections</p> <p>e.g.</p> <p>Peptic ulcer (Helicobacter pylori)</p> <p>Pseudo-membranous colitis (Clostridium difficile). <b>Dental infection</b></p>

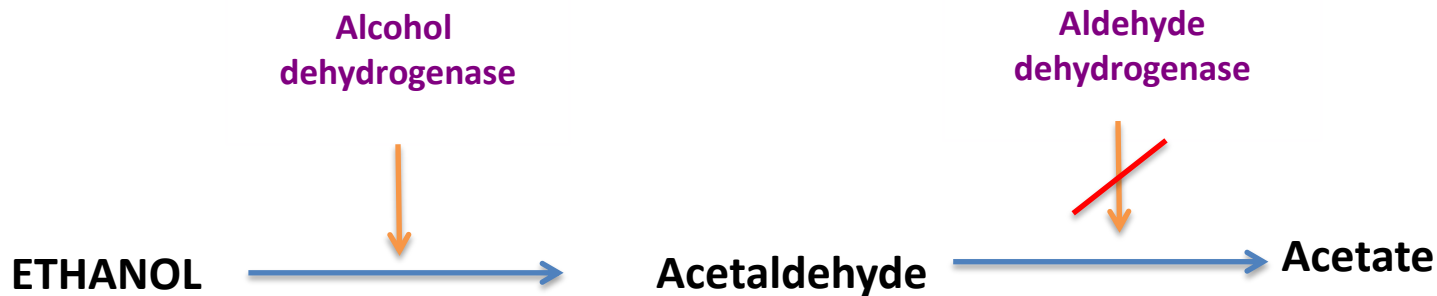


# 1. METRONIDAZOLE

Adverse affects	Drug interactions	CONTRAINDICATIONS
<p><b>*GIT:</b> Dry mouth, metallic taste, Nausea, vomiting, diarrhea (NVD), Oral Thrush (Moniliasis, yeast infection).</p> <p><b>*CNS:</b> <b>Neurotoxicological effect,</b> Insomnia, dizziness, <b>Peripheral neuropathy</b>, paresthesia Encephalopathy, convulsion (IV infusion, rare).</p> <p><b>*Dysuria</b>, dark urine.</p> <p><b>*Neutropenia.</b></p> <p><b>*Disulfiram-like effect</b> if taken with alcohol.(next slide)</p>	<p>▪Enzyme inhibitors <b>(cimetidine, ketoconazole)</b> ↑ duration of action of metronidazole</p> <p>▪Enzyme Inducers <b>(phenytoin and phenobarbitone).</b> ↓ duration of action of metronidazole</p> <p>Metronidazole inhibits CYP-450 ( 2C9 &amp; 3A4) so:</p> <p>-Increases anticoagulant effect of warfarin.</p>	<p><b>*Pregnancy and breast feeding women.</b></p> <p><b>* Alcohol intake.</b></p> <p><b>*CNS diseases.</b></p> <p><b>*Severe renal disease.</b></p> <p><b>*Severe hepatic disease.</b></p>

# Disulfiram like-effect

Combining metronidazole and alcohol causes nausea, vomiting, abdominal distress, flushing, headache, tachycardia, hyperventilation

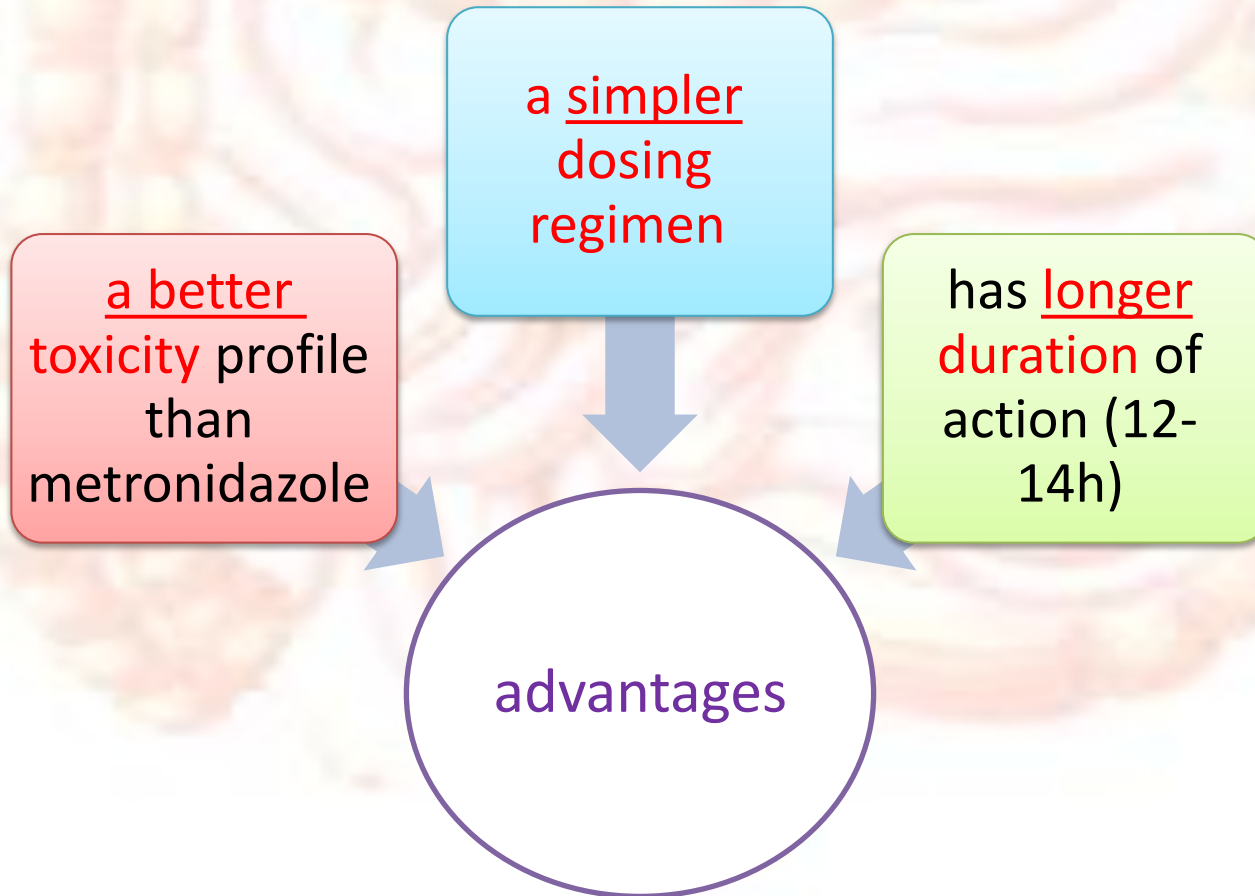


Metronidazole inhibits this enzyme and this will lead to accumulation of acetaldehyde

# TINIDAZOLE

has similar activity to metronidazole but better potency\*

\*the dose is less than metronidazole but it has the same action



## 2. EMETINE 3. DEHYDROEMETINE

( Emetine is an alkaloid derived from ipeca while dehydroemetine is a synthetic analog ).

## 4. CHLOROQUINE

M.O.A	<ul style="list-style-type: none"><li>-Both are effective against tissue trophozoites of E.histolytica causing irreversible block of protein synthesis.</li><li>-Because of major toxicity concerns they have been almost completely replaced by metronidazole.</li></ul>	-Anti-malarial drug
Pharmacokinetics	<ul style="list-style-type: none"><li>-Have erratic oral absorption.</li><li>-Given preferably <u>subcutaneously</u> but could be given by IM, NEVER I.V.</li><li>-Has long plasma half life about 5 days.</li><li>-Metabolized &amp; excreted slowly via kidney so they have a cumulative effect.</li><li>-Should not be used for more than 10 days (usually 3-5 days).</li></ul>	-----
Clinical Uses	<ul style="list-style-type: none"><li>-Amoebic liver abscess.</li><li>-Intestinal wall infections.</li><li>-Severe forms of amebiasis <u>acute amoebic dysentery</u> dehydroemetine is preferable due to less toxicity (3-5 days).</li></ul>	Used in combination with metronidazole or dehydroemetine for <b>amebic liver diseases</b> .
Adverse Effects	<ul style="list-style-type: none"><li>-<b>Dehydroemetine is less toxic than emetine.</b></li><li>-GIT: nausea, vomiting, diarrhea.</li><li>-<b>Serious toxicities:</b> cardiotoxicity, Hypotension, cardiac arrhythmias, heart failure.</li></ul> <p><u>Caution:</u> the drug should not be used in patients with cardiac or renal disease, in young children, or in pregnancy.</p>	<ul style="list-style-type: none"><li>-<b>pruritus is</b> common</li><li>-Nausea, vomiting, abdominal pain, anorexia.</li><li>-Blurring of vision.</li><li>-<b>Hemolysis in G6PD deficient patients.</b></li></ul>

# B.LUMINAL AMOEBICIDES

used to eradicate cysts of *E histolytica* after treatment of invasive disease.

-Include: Diloxanide furoate , Iodoquinol, Paromomycin

## Paromomycin Sulphate

### M.O.A

- Effective only against **luminal forms of ameba**
- Has **direct amebicidal action** (causes leakage by its action on cell membrane of parasite).
- Indirect killing of bacterial flora** essential for proliferation of pathogenic amoebae.

### Pharmacokinetics

- Aminoglycoside antibiotic.      -Given orally      -**Not significantly absorbed from GIT**
- Small amount absorbed is excreted unchanged in urine (may accumulate with renal Insufficiency\*).

### Clinical Uses

- Use in **chronic amebiasis to eliminate cysts** (in cysts passers).

### Adverse Effects

- Gastrointestinal distress** and diarrhea.

#### Precautions

- \*Severe renal disease**
- patients with GIT ulceration**

# B.LUMINAL AMOEBICIDES

	Diloxanide furoate	Iodoquinol
M.O.A	<ul style="list-style-type: none"> <li>-Mechanism of action is unknown</li> <li>-<b>Direct amoebicidal action against luminal forms.</b></li> <li>-<b>Not active against trophozoites</b> in intestinal wall or extra-intestinal tissues.</li> </ul>	<ul style="list-style-type: none"> <li>-Mechanism of action is unknown.</li> <li>-effective against the <b>luminal forms of amebiasis= asymptomatic</b></li> </ul>
Pharmacokinetics	<ul style="list-style-type: none"> <li>-Ester of diloxanide + furoic acid .</li> <li>-Given orally.</li> <li>-It splits in the intestine liberating diloxanide</li> <li>-<b>The unabsorbed diloxanide is the amoebicidal agent.</b></li> <li>-The absorbed portion is <u>excreted in urine.</u></li> </ul>	<ul style="list-style-type: none"> <li>-Is given orally</li> <li>-Poorly absorbed, <u>excreted in feces.</u></li> </ul>
Clinical Uses	<ul style="list-style-type: none"> <li>-Drug of choice <b>for asymptomatic intestinal infection</b> (cysts passers) .</li> <li>-<u>to eradicate cysts of E histolytica after treatment of invasive disease with systemic amebicides.</u></li> </ul>	<p>luminal amoebicide for <b>asymptomatic amebiasis.</b></p>
Adverse Effects	<ul style="list-style-type: none"> <li>-Flatulence</li> <li>-Nausea, vomiting, abdominal cramps.</li> </ul>	<ul style="list-style-type: none"> <li>-<b>GIT:</b> Nausea, vomiting, diarrhea.</li> <li>-<b>Peripheral neuropathy</b> including <b>optic neuritis.</b></li> <li>-<b>Enlargement of the thyroid gland.</b></li> <li>-<b>Iodine sensitivity.</b></li> <li>-<b>interference with thyroid function tests</b> (increase protein-bound serum iodine, decrease in measured <sup>131</sup>I uptake).</li> </ul>
Contra indications	<ul style="list-style-type: none"> <li>- <b>Pregnancy</b></li> <li>- <b>Children</b>(less than 2years)</li> </ul>	<ul style="list-style-type: none"> <li>-<b>Iodoquinol</b> should be <b>used with caution in patients with optic neuropathy, renal or thyroid disease.</b></li> <li>-<b>discontinued if it produces persistent diarrhea or Signs of iodine toxicity</b>)dermatitis, urticaria, pruritus,</li> </ul>

# C.BACILLARY DYSENTERY

- Fluoroquinolones such as ciprofloxacin.
- Cotrimoxazole (trimethoprim- sulfamethoxazole).
- Cotrimoxazole is commonly used in traveler's diarrhea.
- Children or patient allergic to sulpha drugs parenteral ceftriaxone or oral cefixime are safe and effective.

## Ciprofloxacin

M.O.A	-active against a variety of gram-positive and gram-negative bacteria. -block bacterial DNA synthesis.
Clinical Uses	- <u>Bacterial diarrhea (caused by shigella, salmonella and E coli)</u> . -Urinary tract infections. -Respiratory tract infections. -Soft tissues, bones, and joint infections.
Adverse Effects	- <b>Arthropathy</b> (damage of growing cartilage). -GIT disorders (nausea, vomiting, diarrhea). -CNS disorders (headache, dizziness). -CVS disorder (prolonged QT interval ) - <b>Phototoxicity</b> . - <b>Liver toxicity</b> .
Contraindications	-Children, pregnancy, nursing mother. -Epilepsy. -Arrhythmias. -Should not be combined with antacids, divalent cations.

# SUMMARY

-Maintain fluid intake (oral rehydration therapy or Intravenous fluid therapy).

-asymptomatic luminal amebiasis is treated by luminal amebicides (diloxanide, or iodoquinol or paromomycin ).

-Metronidazole is the mainstay of therapy for invasive amebiasis (followed by luminal amebicides to prevent relapse).

-Chloroquine has also been used for patients with hepatic amebiasis.

-Dehydroemetine is useful but not preferable due to CVS toxicity

-Ciprofloxacin is the drug of choice in bacillary dysentery. **In children and pregnancy, ceftriaxone or cefixime is the choice.**



# SUMMARY

	Drugs	Therapeutic Uses	Adverse effects
Luminal Amebicides	Diloxanide furoate	<ul style="list-style-type: none"> <li>• Drug of choice for <b>asymptomatic intestinal infection</b></li> <li>• eradicate cysts of E histolytica after treatment of invasive disease</li> </ul>	<ul style="list-style-type: none"> <li>• Flatulence</li> <li>• Nausea, vomiting, abdominal cramps</li> </ul>
	Iodoquinol	<ul style="list-style-type: none"> <li>• luminal amoebicide for <b>asymptomatic amebiasis.</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Peripheral neuropathy</b> including optic neuritis</li> <li>• <b>Enlargement of the thyroid gland.</b></li> <li>• Iodine sensitivity</li> </ul>
	Paromomycin	<b>chronic amebiasis to eliminate cysts</b>	<ul style="list-style-type: none"> <li>• Gastrointestinal distress and diarrhea.</li> </ul>
Tissue or systemic amebicides :	Metronidazole	<ul style="list-style-type: none"> <li>• Extra-luminal amoebiasis</li> <li>• Giardiasis</li> <li>• Trichomoniasis</li> <li>• Broad spectrum of anaerobic</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth,</li> <li>• metallic taste</li> <li>• Insomnia, dizziness</li> <li>• <b>Peripheral neuropathy</b></li> </ul>
	Emetine dehydroemetine	<ul style="list-style-type: none"> <li>• Amoebic liver abscess.</li> <li>• Intestinal wall infections.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>GIT:</b> nausea, vomiting, diarrhea.</li> <li>• <b>Serious toxicities</b></li> </ul>
	Chloroquine	<ul style="list-style-type: none"> <li>• Anti-malarial drug</li> <li>• Used in combination with metronidazole or dehydroemetine</li> </ul>	<ul style="list-style-type: none"> <li>• pruritus is common</li> <li>• <b>Blurring of vision.</b></li> <li>• Hemolysis in G6PD deficient patients</li> </ul>

# Quiz yourself

1- which one of the following used in amoebic liver abscess?

- A- Emetine
- B- Tinidazole
- C- Iodoquinol

2- a 83 years old man developed severe renal disease which of the following drugs is precautions in this case?

- A- Iodoquinol
- B- Diloxanide furoate
- C- Paromomycin
- D- Chloroquine

3- the 1<sup>st</sup> drug of choice in the treatment of extra-luminal amoebiasis is ?

- A- Iodoquinol
- B- Paromomycin
- C- dehydroemetine
- D- Metronidazole

4- patient comes with peripheral neuropathy which drug should we avoid?

- A- Metronidazole
- B- Iodoquinol
- C- Paromomycin

5- which one of the following is not use for pregnancy?

- A- Paromomycin
- B- dehydroemetine
- C- Metronidazole
- D- Diloxanide furoate

6- patient comes with enlargement of the thyroid gland which drug should we avoid?

- A- Iodoquinol
- B- Paromomycin
- C- dehydroemetine

7- which one of the following block bacterial DNA synthesis?

- A- Metronidazole
- B- Diloxanide furoate
- C- Paromomycin
- D- ciprofloxacin

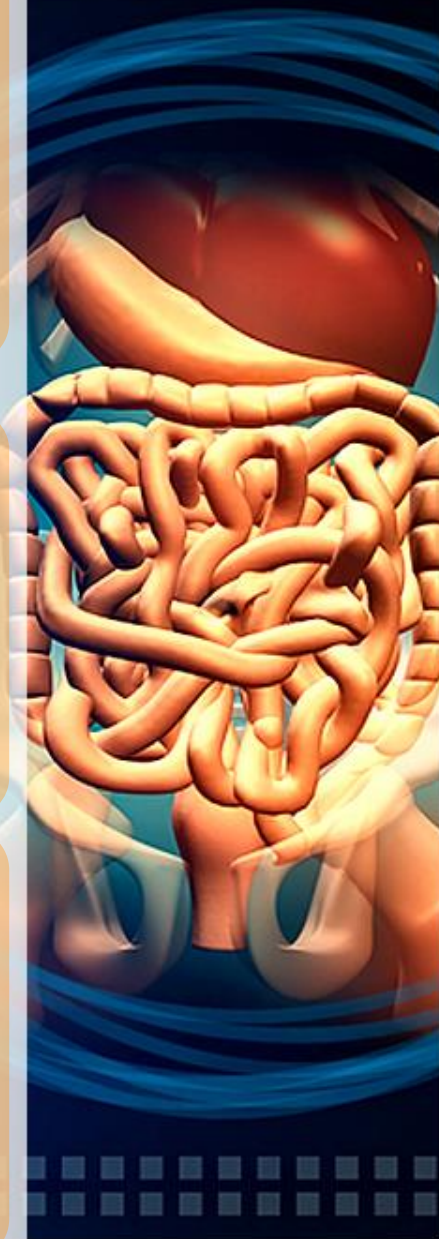
8- which one of the following should not be used in patient with cardiac or renal disease?

- A- Metronidazole
- B- Diloxanide furoate
- C- Emetine

9- which one of the following is inhibits DNA replication?

- A- Metronidazole
- B- Iodoquinol
- C- Paromomycin

Answers 1-A, 2- C, 3-D, 4-B, 5-D 6-A, 7-D, 8-C, 9-A



*Done by*

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*It always seems  
impossible until it is done*

**BEST OF LUCK**



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