

Treatment of Dysentery

1-Maintain fluid intake using:

oral rehydration therapy or
intravenous fluid therapy

2-Antimicrobial agents:
used against the two most
common causes which are

A-Amebic dysentery (*protozoal*
infection mainly by Entameba
Histolytica).

ANTIAMEBIC DRUGS

A- Luminal Amebicides

1-Diloxanide furoate
2-Iodoquinol
3-Antibiotics
Paromomycin+Tetracyclin

B-Tissue or systemic amebicides

1-Metronidazole
2-Tinidazole
3-Emetine +Dehydroemetine
5-Chloroquine (liver only)

B-Bacillary dysentery
(*bacterial infection mainly by*
shigella).

1-Fluoroquinolones e.g: Ciprofloxacin
2-Cotrimoxazole (trimethoprim and
sulfamethoxazole)
3-Ceftriaxone and cefixime



ANTIAMEBIC DRUGS : A- Luminal Amebicides

Drugs	Diloxanide furoate	Iodoquino	Paromomycin
MOA	unknown	unknown	*Has direct amebicidal action (causes leakage b action on cell membrane of parasite) * Indirect killing of bacterial flora essential for proliferation of pathogenic amoebae.
P.K + other features	<ul style="list-style-type: none"> ▪ Ester of diloxanide + furoic acid ▪ Given orally. ▪ It splits in the intestine, most of diloxanide is absorbed, conjugated to form a glucuronide which is excreted in urine (90%). ▪ The unabsorbed diloxanide is the amebicidal agent (10%). ▪ Direct amebicidal action against luminal forms. ▪ NOT active against trophozoites in (intestinal wall or extra-intestinal tissues) 	<ul style="list-style-type: none"> ▪ Is given orally ▪ Not absorbed (90%), excreted in feces. ▪ 10% enter circulation, excreted as glucuronide in urine. ▪ effective against the luminal trophozoites. 	<ul style="list-style-type: none"> ▪ Aminoglycoside antibiotic. ▪ It is given orally and Not absorbed from GIT ▪ Effective against luminal forms of ameba ▪ Small amount absorbed is excreted unchanged in urine (<i>may accumulate with renal insufficiency</i>)
USES	1- Drug of choice for asymptomatic intestinal infection (drug of choice in cysts passers). 2-For complete eradication of amebic infections given along with tissue amebicides eg metronidazole .	1-luminal amebicide for asymptomatic amebiasis	1-in chronic amebiasis to eliminate cysts, in cyst passers (Diloxanide and iodoquinol are best for purpose)
A.E	<ul style="list-style-type: none"> ▪ Flatulence ▪ Nausea, vomiting, abdominal cramps. ▪ No serious adverse effects 	<ul style="list-style-type: none"> ▪ GIT: Nausea, vomiting, diarrhea. ▪ Peripheral neuropathy including optic neuritis ▪ Enlargement of the thyroid gland. ▪ Iodine sensitivity interference with thyroid function tests (increase protein-bound serum iodine, decrease in measured (¹³¹I uptake)) 	▪ Gastrointestinal distress and diarrhea.
Contraindications #	<ul style="list-style-type: none"> ▪ Pregnancy (Because it crosses the placenta) ▪ Children (less than 2 years). 		
Pre-caution		-Iodoquinol should be used with caution in patients with optic neuropathy, renal or thyroid disease	<ul style="list-style-type: none"> ▪ Severe renal disease ▪ patients with GIT ulceration

❖ **discontinued** if it produces persistent diarrhea or signs of iodine toxicity (dermatitis, urticaria, pruritus, fever).

+ ANTIAMEBIC DRUGS : B- Tissue or systemic

	1-Metronidazole	3-Emetine and dehydroemetine	4-Chloroquine
MOA	Inhibits DNA replication		
P.K. + Other features	<ul style="list-style-type: none"> ▪ Tissue amoebicide. ▪ Acts on trophozoites. ▪ Does not eradicate cysts from intestines ▪ Given orally or IV. ▪ Absorption is rapid and complete. ▪ Wide distribution to all tissues and body fluids (CSF, saliva, milk) ▪ Plasma half life is (8 h) ▪ Metabolized in liver by mixed function oxidase followed by glucuronidation (consider drug interactions). ▪ Excreted in urine. ▪ Clearance is decreased in liver impairment 	<ul style="list-style-type: none"> ▪ Emetine is an alkaloid derived from ipecac while dehydroemetine is a synthetic analog. ▪ Both are effective against (tissue trophozoites of E. histolytica) causing irreversible block of protein synthesis. ▪ Because of major toxicity concerns they have been almost completely replaced by metronidazole. ▪ Have erratic oral absorption. ▪ Given preferably subcutaneously but could be given by IM, NEVER I.V. ▪ Has long plasma half life about 5 days. ▪ Metabolized & excreted slowly via kidney so they have a cumulative effect. ▪ Should not be used for more than 10 days (usually 3-5 days) why? b/c of the cumulative effect. 	<ul style="list-style-type: none"> ▪ Anti-malarial drug ▪ Used in combination with metronidazole or dehydroemetine and luminal amebicide for amebic liver diseases. ▪ Now NOT commonly used in amebiasis.
Uses	<p>Drug of choice for treating invasive amebic infections (intestinal wall & extra-intestinal).</p> <ul style="list-style-type: none"> ▪ Extra-luminal amebiasis: is the drug of choice in all tissue amebiasis (<i>should be combined with luminal amebicide</i>) ▪ Giardiasis (cause by G. lamblia & common in children) ▪ Trichomoniasis ▪ Broad spectrum of anaerobic bacteria e.g., <ul style="list-style-type: none"> ○ Helicobacter pylori infection ○ Pseudo-membranous colitis (<i>Clostridium difficile</i>) 	<ul style="list-style-type: none"> ▪ Amoebic liver abscess. ▪ Intestinal wall infections. ▪ Severe forms of amebiasis acute amoebic dysentery 	

ANTIAMEBIC DRUGS : B- Tissue or systemic

A.E	<p>1-GIT: Dry mouth, metallic taste, Nausea, vomiting and Oral Thrush (Moniliasis, yeast infection).</p> <p>2-CNS: Neurotoxicological effect: Insomnia, dizziness + peripheral neuropathy, paresthesia + encephalopathy, convulsion (IV infusion, rare).</p> <p>3-Dysuria : dark urine.</p> <p>4-Neutropenia (decrease the numbers of neutrophils in the serum)</p> <p>5-Disulfiram-like effect (if taken with alcohol): Combining metronidazole and alcohol causes nausea, vomiting, abdominal distress, flushing, headache, tachycardia, hyperventilation</p>	<p>Dehydroemetine is less toxic than emetine</p> <ul style="list-style-type: none"> GIT: nausea, vomiting, diarrhea. Serious toxicities: cardiotoxicity <ul style="list-style-type: none"> Hypotension cardiac arrhythmias heart failure 	<ul style="list-style-type: none"> pruritus is common Nausea, vomiting, abdominal pain, anorexia Blurring of vision. Hemolysis in G6PD deficient patients
Drug interactions	<p>Metronidazole inhibits Cytochrome p450, so it will increase the effect of other drugs:</p> <ul style="list-style-type: none"> increases anticoagulant effect of warfarin. Increases lithium toxicity. <p>Also it is affected by :</p> <ul style="list-style-type: none"> Enzyme inhibitors (cimetidine, ketoconazole) increase duration of action of metronidazole Inducers (phenytoin and phenobarbitone) decrease duration of action of metronidazole 		
Contraindications	<p>1-Pregnancy and breast feeding women</p> <p>2-CNS diseases) 3-Severe hepatic disease</p> <p>4-Alcohol intake 5-Severe renal disease</p>		
Precaution		<ul style="list-style-type: none"> The drug should not be used in patients with cardiac or renal disease, in young children, or in pregnancy 	

2. Tinidazole

Tinidazole has similar activity to metronidazole but **better potency**

Advantages of tinidazole:

- 1- has **longer** duration of action (12-14h), so the frequency of administration will be less
- 2- a **simpler** dosing regimen
- 3- a **better** toxicity profile than metronidazole



Bacillary dysentery : Treated by

1-Fluoroquinolones e.g: *Ciprofloxacin*

Active against a variety of BOTH gram-positive and gram-negative bacteria (**board spectrum**)

- Mechanism of action :
 - Block bacterial DNA synthesis.**
- Used in treatment of :
 - Bacterial diarrhea (caused by shigella, salmonella and E coli).
 - Urinary tract infections
 - Respiratory tract infections
 - Soft tissues, bones, and joint infections
- Side effects:
 - Arthropathy (damage of growing cartilage).
 - GIT disorders (nausea, vomiting, diarrhea).
 - CNS disorders (headache, dizziness).
 - CVS disorder (prolonged QT interval)
 - Phototoxicity.
 - Liver toxicity.
- Contraindication :
 - **Children, pregnancy**, nursing mother
 - Epilepsy
 - Arrhythmias.
 - Should not be combined with antacids, divalent cations

2-Cotrimoxazole (trimethoprim and sulfamethoxazole) :

- Uses:

Commonly used in **travelers diarrhea**.
- Contraindication:

Children or patient allergic to sulpha drugs

3-Ceftriaxone (penatrally) and cefixime (oral): (3dr gen cephalosporin)

- **Ceftriaxone** Third-generation cephalosporin with broad-spectrum, gram-negative activity. It acts by inhibiting cell wall synthesis
- **Cefixime** Third-generation oral cephalosporin with broad activity against gram-negative bacteria.

BOTH are safe and effective