List of drugs

- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

Table of content

L1: H2 Blockers and Proton Pump Inhibitors

Drug	MOA	Uses	ADRs	Precaution
Proton pump inhibitors				
Omeprazole **Lansoprazole** **Pantoprazole** **Rabeprazole**	◦ **Irreversible** inhibition of proton pump (H+/K+ ATPase). ◦ they are the most potent inhibitors of acid secretion ◦ PPIs heal ulcers faster than H2 blockers and have H.pylori inhibitory properties.	◦ Eradication of H. pylori w/antibiotics. ◦ Hypersecretory conditions as Zollinger Ellison syndrome and gastrinoma (first choice). ◦ Resistant **severe** peptic ulcer. ◦ GERD.	◦ CNS: headache ◦ GIT: diarrhea, abdominal pain ◦ Achlorhydria & Hypergastrinemia. ◦ Gastric mucosal hyperplasia. ◦ Infection ◦ Long term use: ◦ Vitamin B12 deficiency ◦ Hypomagnesemia ◦ Osteoporosis.	◦ Omeprazole (CYT2c19 inhibitor) should not be combined with clopidogrel. ◦ Dose reduction is required in severe liver failure. ◦ PPIs should **not** be combined with H2 blockers or antacids.
H2 receptor blockers				
Cimetidine most ADRs **Ranitidine** **Famotidine** most potent **Nizatidine** greatest bioavailability	◦ They **reversibly** and competitively block H2 receptors on the parietal cells. ◦ Block 90% of nocturnal acid secretion, given before night sleep.	◦ GERD (heartburn/dyspepsia). ◦ Acute ulcer healing. in moderate cases. ◦ **Pre**anesthetic medication (to prevent aspiration pneumonitis). ◦ Post–ulcer healing maintenance therapy. ◦ Prevention of bleeding from **stress-related gastritis.**	◦ Nausea & vomiting. ◦ Headache, confusion (in elderly, hepatic/renal dysfunction) ◦ Bradycardia & hypotension in rapid I.V injections. **- Only cimetidine:** ◦ **CYT-P450 inhibition** (↓metabolism of Warfarin, phenytoin, Benzodiazepine) ◦ **Galactorrhea** (hyperprolactinemia) ◦ **Antiandrogenic actions** (gynecomastia, impotence)	Dose reduction in severe renal or hepatic failure and elderly.
Prostaglandin analogues (PGE1)				
Misoprostol	◦ ↓ **HCL** secretion. ◦ Prostaglandin analogues (PGE1) ◦ ↑ protective measures (↑ mucus /bicarbonate & gastric mucosal blood flow).	◦ Drug of choice for NSAIDs induced peptic ulcer. ◦ Labour Induction.	◦ Abdominal cramps, diarrhea. ◦ **Uterine contraction** (dysmenorrhea or abortion). #in pregnancy. ◦ **Vaginal bleeding.**	-
Antacids (Inorganic salt)				
NaHCO3	◦ Direct chemical neutralization of HCL. ◦ ↓ pepsin activity.	◦ **Relieve pain** of peptic ulcer & dyspepsia. ◦ All antacids ↓absorption of some drugs as tetracycline, fluoroquinolones, iron.	◦ Systemic alkalosis. # CVS patients.	
CaCO3			◦ Hypercalcemia. ◦ Milk-alkali syndrome. ◦↓absorption of tetracycline. ◦ Renal failure.	
Al(OH)3			◦ Constipation. ◦Hypophosphatemia. ◦Seizures.	
Mg(OH)2			◦Diarrhea. ◦Cardiac arrest, hypotension.	

L2: Antiemetic Drugs

Serotonin (5-HT3) antagonists

Drug	MOA	P.K	Uses	ADRs
Ondansetron **Granisetron**	• Act by **blocking 5-HT3** receptor **centrally** (CTZ) & **peripherally** (GI). • the most potent antiemetic drug.	• Orally or parenterally. • Have a long duration of action,first pass effect.	• 1st choice of Prevention of **moderate to severe** emesis • **Chemotherapy** induced nausea & vomiting **(CINV)** especially **cisplatin.** • Their effects are augmented by combination with corticosteroids & NK1 antagonists. • Post-radiation NV & Post-operative NV	• Well tolerated in general. • Headache,dizziness &constipation. • Minor ECG abnormalities **(QT prolongation).**

D2 receptor antagonists

Drug	MOA	P.K	Uses	ADRs
Domperidone (Prokinetic)	• **Block D2** dopamine receptors in the **CTZ**. • **Prokinetic** agents (**5-HT4** agonist activity) increase upper GI motility and gastric emptying.	• Given orally or IV • Does not cross BBB	• **D2 blocker**: vomiting, gastroenteritis, surgery, toxins, uremia, radiation • **5-HT4 agonist:** gastroesophageal reflux disease (GERD), Gastroparesis.	Safer as it doesn't cross the BBB
Metoclopramide (Prokinetic)		• Given orally or IV • Cross BBB		- Dyskinesia (extrapyramidal side effects) -Postural hypotension,Sedation, drowsiness. - Galactorrhea, menstrual disorders, impotence
Chlorpromazine (Neuroleptic) **Droperidol (Neuroleptic)**	Block D2 dopamine receptors in the CTZ.	-	Postoperative vomiting & Chemotherapy-induced emesis.	• Extrapyramidal symptoms. • Sedation. • Postural hypotension.

Neurokinin-1 (NK1) receptor antagonists

Drug	MOA	P.K	Uses	ADRs
Aprepitant	Acts centrally as **substance P antagonist** by blocking **neurokinin 1 receptors** in vagal afferent fibers.	Given orally	**Combined** with 5-HT3 antagonists and corticosteroids in prevention of chemotherapy-induced nausea and vomiting and post-operative NV. "Not effective alone, must be combined"	-

L2: Antiemetic Drugs

H1- receptor antagonists

Drug	MOA	Uses	ADRs
Diphenhydramine	H1- receptor antagonists.	**Morning sickness in pregnancy if only essential** Promethazine: severe morning sickness of pregnancy Motion Sickness	• Prominent sedation. • Hypotension. • Anticholinergic effects (atropine like actions).

Muscarinic receptor antagonists

Drug	MOA	P.K	Uses	ADRs
Hyoscine (Scopolamine)	Reduces impulses from vestibular apparatus by blocking muscarinic receptors.	Orally, injection, patches	• Motion sickness. • Not in chemotherapy-induced vomiting	• Sedation. • Atropine-like actions

Glucocorticoids

Drug	MOA	Uses	ADRs
Dexamethasone	Potentiate the effect of antiemetic drugs	• **Chemotherapy induced vomiting.** • combined with 5-HT3 antagonists or NK1 receptor antagonist	• **Hyper**tension • **Hyper**glycemia. • **High** intraocular pressure. • **Increased** appetite & obesity. • Cataract. • Osteoporosis. • Superinfections
Methylprednisolone			

L3: Drugs used in IBD

1st : 5-Aminosalicylic acid AKA(Aminosalicylates 5-ASA)

M.O.A	Have TOPICAL anti-inflammatory action due to: 1- inhibition of PGs and leukotrienes 2-Decrease neutrophil chemotaxis 3- Antioxidant activity (scavenging free radical production)
Uses	1. Induction and maintenance of remission in mild to moderate IBD (First line of treatment) 2. Rheumatoid arthritis (Sulfasalazine only) 3. Rectal formulations are used in distal ulcerative colitis, ulcerative proctitis and proctosigmoiditis
P.K	• 5-ASA itself is absorbed from the proximal small intestine • **All aminosalicylates are used for induction and maintenance of remission**

A) Azo compound

Drug	Overview	P.K	ADRs
Sulfasalazine	- **Azo** structure reduces absorption of 5-ASA in small intestine. - In the terminal ileum and colon, azo bond is cleaved by **azoreductase enzyme** produced by bacterial flora releasing **5-ASA** in the **terminal ileum and colon .**	In the terminal ileum and colon, sulfasalazine is broken by azoreductase Into: 1. 5-ASA (not absorbed, active moiety, acting locally) 2. Sulphapyridine (absorbed, causes most of side effects)	Only Sulfasalazine (Azulfidine): 1. Crystalluria 2. Folic acid deficiency 3. Megaloblastic anemia 4. Bone marrow depression 5. Impairment of male fertility (oligospermia). 6. Interstitial Nephritis due to 5-ASA
Olsalazine		-	
Balsalazide		-	

B) Mesalamines

Drug	Overview	Oral formulations	Rectal formulations
Asacol **Pentasa** **Canasa** **Rowasa**	- Well tolerated - Sulfa free - Less ADRs than sulfasalazine - Useful in patient sensitive to sulfa drugs	Releases 5-ASA in the distal small bowel secondary to pH changes. **1. Asacol:** 5-ASA coated in pH-sensitive resin that dissolve at pH 7. (delayed release tablet) **2. Pentasa**: micro granules that release 5-ASA throughout the stomach, colon. (sustain released)	-Release 5-ASA in the distal colon. **1.Canasa**: (suppositories),. **2. Rowasa**: (enema)

2nd: Glucocorticoids

M.O.A	• Inhibits phospholipase A2 • Inhibits gene transcription of NO synthase, cyclooxygenase-2 (COX-2) • Inhibit production of inflammatory cytokine
Uses	• Indicated for acute flares of disease **(active moderate to severe IBD).** • Not useful in maintaining remission (not effective as prophylactic therapy). • Asthma • Rheumatoid arthritis • Immunosuppressive drug for organ transplants • Antiemetic during cancer chemotherapy

Drug	Route	P.k	Uses
Prednisone Prednisolone	Oral preparation		Oral glucocorticoids is commonly used in active condition
Budesonide	Oral perpetration	-Low oral bioavailability (10%) -Extensive first pass metabolism -Low bioavailability	Used in treatment of **active mild to moderate** Crohn's disease involving ileum and proximal colon.

L3: Drugs used in IBD

2nd: Glucocorticoids cont.

Drug	Route	P.k	Uses
Hydrocortisone	Rectal	-As enema or suppository, give topical effect. -Less absorption rate than oral. -Minimal side effects & maximum tissue effects	Rectal glucocorticoids are preferred in IBD involving rectum or sigmoid colon
Hydrocortisone Methylprednisolone	Parenteral	-Higher rate of absorption -More adverse effects compared to rectal administration	

3rd : Immunomodulators

Drug	M.O.A	ADRs	Uses
Methotrexate Orally,S.C,I.M	- Folic acid antagonist -Inhibits **dihydrofolate reductase** required for folic acid activation (tetrahydrofolate) -Impairs DNA synthesis	-Bone marrow depression -Megaloblastic anemia -Teratogenic	- Induce and maintain remission in **IBD** in active **moderate to severe** conditions or steroid dependent or steroid resistant patients (refractory) -IBD , Rheumatoid arthritis & Cancer
Purine analogs: Azathioprine, 6-mercaptopurine	- Azathioprine is **pro-drug** of 6-mercaptopurine. - Inhibit **purine** synthesis and inhibits synthesis of DNA, RNA, and proteins. - It may decrease proliferation of immune cells, which lowers autoimmune activity.	-Bone marrow depression: leucopenia, thrombocytopenia -Hepatic dysfunction -Gastrointestinal toxicity -CBC & LFTs are required in all patients	Induce and maintain remission in **IBD in active moderate to severe** conditions or steroid dependent or steroid resistant patients(refractory)

4th : Monoclonal antibodies used in IBD (TNF-α inhibitors)

Drug	M.O.A	Overview	ADRs	Uses
Adalimumab (Humira)	- Act by binding to TNF- α thus preventing its binding to cell surface receptors. - Increase apoptosis of T-lymphocytes and monocytes.	-**Fully humanized** IgG antibody to TNF-α (TNF-α inhibitor) -It binds to TNF-α, preventing it from activating TNF receptors -Has an advantage in that it is given by **subcutaneous injection**.	-	- Moderate to severe - Crohn's disease - Rheumatoid arthritis - Psoriasis
Certolizumab pegol (Cimzia)		-**Fab fragment** of a **humanized** antibody directed against TNF-α -Attached to polyethylene glycol to increase its half-life in circulation	-	- Crohn's disease - Rheumatoid arthritis
Infliximab		- A chimeric mouse-human monoclonal antibody, (25% murine -75% human - Inhibits soluble or membrane –bound TNF-α located on activated T lymphocytes - Given intravenously as **infusion**	1. Allergies : - Acute or early infusion reactions(Allergic reactions or anaphylaxis in 10% of patients) - Delayed type hypersensitivity reaction (serum sickness- like reaction, in 5% of patients). - Pre-treatment with diphenhydramine, acetaminophen, corticosteroids is recommended 2. Loss of response to infliximab over time due to the development of antibodies to infliximab. 3. Infection complication (Latent TB, sepsis, hepatitis B) 4. Severe hepatic failure. 5. Rare risk of lymphoma	-In **moderate to severe active** Crohn's disease and ulcerative colitis -Patients not responding to immunomodulators or glucocorticoids - Rheumatoid arthritis -Psoriasis

L4: Antiplatelets

Drug	MOA	Uses	ADRs
Arachidonic acid pathway			
Aspirin (Acetylsalicylic Acid)	• **Irreversible inhibition of cyclooxygenase enzyme (COX-1) via acetylation** • **A small dose** inhibits the synthesis of thromboxane **(TXA2)** in platelets **but not prostacyclin (PGI2)** synthesis in the endothelium **(larger dose)**.	• **Prophylaxis** of thromboembolism e.g. **prevention of transient ischemic attack, ischemic stroke, and myocardial infarction** • **Prevention of ischemic events in patients with unstable angina pectoris.** • **Combined** with other antiplatelet drugs: **(clopidogrel)** or anticoagulants **(heparin)**.	★★ Risk of peptic ulcer (#) • **Epigastric pain & hyperacidity** • ↑ incidence of GIT bleeding (aspirin prolongs bleeding time).
Glycoprotein IIb/IIIa receptor inhibitors			
Abciximab	Inhibits platelet aggregation by **preventing the binding of fibrinogen, von Willebrand factor, and other adhesive molecules to GP IIb/IIIa receptor sites** on activated platelets.	With **heparin and aspirin** as adjunct to PCI for the prevention of cardiac ischemic complications.	
Tirofiban	• Act by **occupying the site on GP IIb/ IIIa receptor that is required to bind the platelet to fibrinogen (act as fibrinogen-mimetic agents).**	Given I.V. for the reduction of the incidence of thrombotic complications during coronary angioplasty (PCI)	
Eptifibatide			
Adenosine Diphosphate Pathway (ADP) Inhibitors			
Clopidogrel *less side effects (neutropenia) than ticlopidine	• They specifically and **irreversibly inhibit adenosine diphosphate (ADP) receptors of subtype P2Y12**, which is required for platelet activation and thus prevents platelet aggregation • **P2Y12** is purinergic receptor and is a chemoreceptor for adenosine diphosphate **(ADP).**	○ **a history of recent (MI), stroke, or established peripheral arterial disease.** ○ **acute coronary syndrome** ○ **2ry prevention of ischemic complications after myocardial infarction, ischemic stroke, and unstable angina.** ○ **replaced ticlopidine**	○ **GIT:** nausea, dyspepsia, diarrhea. ○ Bleeding (prolongs bleeding time) ★★**Severe neutropenia,** CBC should be done monthly during treatment. ○ Allergic reactions ○ **Inhibit** CYT P450 causing ↑ plasma levels of drugs such as **phenytoin** and **carbamazepine**.
Ticlopidine		○ **2ry prevention of ischemic complications after myocardial infarction, ischemic stroke, and unstable angina.**	
Prasugrel more rapid than clopidogrel	**Irreversible** inhibitor of the **P2Y12** receptor	↓ the rate of thrombotic cardiovascular events (including stent thrombosis) in patients with acute coronary syndrome who are to be managed by PCI.	○ Both increase bleeding risk ○ **Ticagrelor**: dyspnea
Ticagrelor more rapid than clopidogrel	**Reversible** inhibitor of the **P2Y12** receptor		
Phosphodiesterase PDE inhibitors			
Dipyridamole	• **Vasodilator** • Inhibits phosphodiesterase thus increasing cAMP and causing decreased synthesis of TXA2 and other platelet aggregating factors.	○ Secondary prevention of **stroke** and transient ischemic attack **with aspirin**. ○ Adjunctive therapy: prophylaxis of thromboembolism in cardiac valve replacement **with warfarin**.	• Headache • Postural hypotension

L5: Cytochrome System and Drug Metabolism

(responsible for oxidation reactions)

Class	Substrates	Inhibitors	Inducers
1A2	• Imipramine • Clozapine • Propranolol • Theophylline • Caffeine	• Fluoroquinolone • Fluvoxamine • Cimetidine	• Smoking tobacco
2C9	• Most NSAIDs (including COX-2) • S-warfarin • Phenytoin • Tolbutamide	• Fluconazole •Sulphaphenazole	•Rifampicin •Barbiturates
Genetic Variations 2C9	• Warfarin, phenytoin, & tolbutamide are examples of drugs with narrow therapeutic index. • Clearance of these drugs is impaired in genetic variation.		
2D6	• Codeine • Many B-blockers • Many TCAs •Debrisoquine • Sparteine	• Fluoxetine, Paroxetine • Haloperidol • Quinidine	• Rifampicin
Genetic Variations	Most frequent polymorphisms in all CYT P450, those who exhibit the polymorphism become poor metabolizers: 1. Metabolism of some drugs neuroleptics, tricyclic antidepressants, antianginals agent (perhexiline), antiarrhythmics (propafenone & metoprolol) are suppressed, so side effects & toxicity develop. i.e.: a. Neuropathy after therapeutic doses of perhexiline. b. Bradycardias & arrhythmias on therapeutic dose of propafenone or metoprolol. 2 . The pro-drugs cannot be converted to their therapeutically active metabolite e.g. poor analgesia with codeine & tramadol because they are not transformed into active forms.		
3A4 **Responsible for metabolizing a large number of drugs**	• Immunosuppressants (Cyclosporine) • Macrolides (Erythromycin , Clarithromycin) • Anti Fungal (★Fluconazole, Ketoconazole, Itraconazole)		• Rifampicin/Rifampin • Rifabutin • Barbiturates • Carbamazepine • Dexamethasone • Phenytoin • Progestins
	• CCB (Amlodipine, Verapamil,Nifedipine) • Benzodiazepines (Midazolam, Clonazepam) • Statins (★ Atorvastatin) • non-sedating H1-blockers (Astemizole) • Chemotherapy (Cyclophosphamide, Tamoxifen) • HIV protease inhibitors • Cisapride	• Antibiotics (Troleandomycin, Chloramphenicol) • H2 Blocker (Cimetidine) • Protease Inhibitors (Ritonavir) • Nefazodone • Grapefruits Gestodene	
1A2	• Imipramine • Clozapine • Propranolol • Theophylline • Caffeine Tacrine	• Fluoroquinolone antibiotics • Fluvoxamine Furafylline • Cimetidine	• Smoking tobacco
2C19	• Omeprazol • Diazepam • Phenytoin Mephenytoin	• Omeprazole • Isoniazid • Ketoconazole Fluconazole	• Rifampicin • Barbiturates
Genetic Variations	• Polymorphism shows increased & prolonged action of its substrates as omeprazole. • This has been an advantage as in those variants there is ↑ cure rates in peptic ulcer patient with Helicobacter pylori (beneficial effect).		

L6: Hepatotoxic Drugs

Type A (Intrinsic)		Type B (Idiosyncratic)	
Increased Dose	**Cumulative Dose**	**Immunoallergic**	**Metabolic**
• Acetaminophen • Salicylates • Statins	• Amiodarone • Oral contraceptive	**Inflammatory cholestasis**	**Interfere with bilirubin**
Both		• Chlorpromazine • Chlorpropamide • Erythromycin	• Erythromycin • Rifampicin
• Methotrexate • Alcohol		**Viral hepatitis-like pattern**	**Interfere with protein synthesis**
		• Isoniazid • Phenytoin • Methyldopa	• Corticosteroid • Tetracycline

Clinical Presentation of Drug-Induced Hepatotoxicity

1- Latency period

Latency period	Type of Hepatotoxicity	Example
Short (hrs to days)	Direct Dose-Dependent	Acetaminophen (toxic does)
Intermediate (1-8 w) may continue to evoke even after drug withdrawal	Direct Type A (cumulative)	Amiodarone
	Indirect (Immunoallergic)Idiosyncratic	Phenytoin, Isoniazid
Long (1-12 m)	indirect (metabolic) Idiosyncratic	Tetracycline, Oral contraceptive

2- Clinical Patterns

- **Asymptomatic: Phenytoin, Statins, Sulfonamides, Sulfonylureas.**
- **Symptomatic:**

Injury	Hepatocellular	Cholestatic	Mixed
Symptoms	Flu-like, malaise, weakness, muscle aches, loss of appetite, diarrhea,jaundice, urine discoloration, GI symptoms	Yellowish discoloration of skin, dark urine, rash, pruritus, stool may be light.	Symptoms of both
↑ Enzymes	**ALT only**	**ALP** only	**Both ALT & ALP**
Examples	•NSAIDs • Isoniazid • Amiodarone • Acetaminophen	CORE •Chlorpropamide • Erythromycin • Rifamycin • Oral contraceptives	CAPS • Carbamazepine • Phenytoin • ACE inhibitor • Sulfonamides

Lines of treatment

- No specific treatment
- Immediate withdrawal of any suspected drug.
- Emergency liver transplant: for fulminant hepatic failure.

Symptomatic	- Severe allergy → Corticosteroids, -Pruritus → Cholestyramine, -Cholestatic liver injury → Ursodiol
Supportive	High-carb, moderate protein diet adequate in calories
Specific Antidotes	• N-acetylcysteine for Acetaminophen toxicity • L-Carnitine for Valproate toxicity

L7: Anticoagulants

Direct thrombin inhibitors: hirudin/ Lepirudin

MOA	exert their anticoagulant effect by **direct binding to thrombin**.
Effect	◦ The first DTI to be developed was hirudin, which was isolated from the saliva of the leech ◦ Lepirudin is a polypeptide that binds directly to the active site of thrombin ◦ Recombinant hirudin "Lepirudin" IV anticoagulant in patients with HIT
Advantage	◦ rapid and potent. ◦ not associated with thrombocytopenia development.

Indirect thrombin inhibitors

drug	Heparin (UFH)	Heparin fragments (Enoxaparin - Dalteparin)	Synthetic pentasaccharide (Fondaparinux)
MOA	★ Heparin binds to antithrombin III and thrombin → conformational changes (ternary complex) → ↑ rate of action **1000x**. (no heparin → slow inactivation). ★ ↑ **Activity of** endogenous anticoagulant [**Antithrombin III**] → inhibits activated clotting factors mainly thrombin and **Xa**. ★ **Drug of choice** anticoagulant during **pregnancy**	◦ chemical or enzymatic degradation of UFH → fragments. ◦ Equal efficacy without frequent laboratory monitoring ◦ Have a more predictable anticoagulant response ◦ Binding to platelets/osteoblasts is low with LMWH ◦ ↑ Action of antithrombin III on factor Xa but not its action on thrombin	
ADRs	◦ Bleeding (major ADR). ◦ ★ **HIT (serious ADR)** ◦ Allergic reactions (chills - fever - urticaria) → of animal origin, caution in allergic patients. ◦ Long-term therapy associated with osteoporosis ◦ IM → Hematomas (IV / SC is the choice of administration)	Less (bleeding, HIT, osteoporosis)	
Therapy setting	Hospital	Hospital & OPC	
Monitoring	Needed aPPT	Not needed	
Reversal of Action	● Discontinuation of drug. ★ strongly acidic → neutralized by i.v. **protamine sulfate**	-	
#	○ Bleeding disorders: hemophilia. ◦ Recent surgery ○ Hypersensitivity to drug. ◦ Threatened abortion.	-	

Warfarin

MOA	★ Inhibits biologically active forms of vitamin K-dependent clotting factors **[II - VII - IX - X]** , and anticoagulant proteins C and S synthesis. ★ No effect on already-synthesized coagulation factors → effects are not seen until these factors are depleted.
Monitoring	○ Monitoring anticoagulant effect by measuring **PT** [*International Normalized Ratio* (***INR***)].
ADRs	○ The most common adverse effect of oral anticoagulants is **bleeding** ○ Treatment of bleeding may include a decrease in dosage and the administration of phytonadione (vitamin K1) ○ Oral anticoagulant: teratogenicity
Reversal of Action	○ Stop the drug, Fresh frozen blood. ★ IV **Vitamin K** , administration of phytonadione (vitamin K1)
#	★ **Pregnancy [Cross placental barrier → abortion - hemorrhagic disorder in fetus - birth defects] , (category D)**

L7: Anticoagulants

Heparin Vs. Warfarin

Drug	Heparins	Coumarin (Warfarin)
Chemical Nature	• Large polysaccharide • Water soluble	• Small molecule • Lipid soluble derivative of Vit. K
★ M.O.A.	• ↑ activity of Antithrombin III → inactivation of coagulation factors IIa - IXa - Xa - XIa - XIIa. • Action in **vivo and vitro** • Rapid / variable	• ↓hepatic synthesis of Vitamin K- dependent factors II, VII, IX, X - cournarins prevent their γ-carboxylation. • Has no effect on factors already present. • Action in **vivo only.** • Slow / latency / variable.
P.K.	• **Administration:** parenterally (IV/SC). • **Half-life:** 2 h • **Elimination:** hepatic & reticuloendothelial. • No placental access.	• **Administration:** orally. • 98% protein bound. • PO • **Metabolism:** liver. • **Half-life:** 30+ h • Placental access.
Monitoring	• Partial thromboplastin time (PTT) 1.5-2.5 times normal (30 sec) • Clotting time 2-3 times normal (5-7 min)	• Prothrombin time (PT) • Expressed as International Normalized Ratio (INR)
Antagonist (Anti-dote)	★ Protamine sulfate I.V (1mg/100 units UFH) (chemical antagonism, fast onset) • + Fresh blood	★ ↑ Vit K cofactor synthesis (slow onset) ★ Fresh frozen plasma (fast onset) • Fresh blood + needs de novo synthesis - Has clotting factors → manage bleeding fast.
Uses	• **Rapid anticoagulation (intensive,** emergency**) for:** - Thromboses - Emboli - Unstable angina - Disseminated intravascular coagulation (DIC) - Open heart surgery	• **Long term anticoagulation (controlled,** prophylaxis**) for:** - Thromboses - Emboli - Post MI - Heart valve damage - Atrial arrhythmias
★ Toxicity	• Bleeding • Osteoporosis ★ Thrombocytopenia (HIT) • Hypersensitivity	★ Bleeding • Skin necrosis (if low protein C) • Drug interactions ★ Teratogenic (Bone dysmorphogenesis)

L8: Antimalarial drugs

Drug	M.O.A	Uses	ADRs
Artemisinin	• Blood schizonticides against all malaria parasites. • No effect on hepatic stages. • they have endoperoxide bridges cleaved by heme to carbon-centered free radicals that will: - Alkylate membranes of food vacuole & mitochondria → no energy. - Irreversibly bind to SER Ca2+-ATPase → no growth - Inhibit formation of transport vesicles → no food vacuoles	**Due to its short DOA:** • Monotherapy should be extended beyond disappearance of parasite • or Combining the drug with long- acting antimalarial drugs (e.g. mefloquine). **For severe complicated cases as cerebral malaria:** - IV or IM Artesunate (24h) + complete course of ACT	Transient heart block • ↓ neutrophil count (rare) • Brief episodes of fever • Resistance •High rate of Recrudescence
Chloroquine	•Chloroquine & Quinine inhibit heme polymerase enzyme → inhibiting detoxification of heme (toxic to the parasite) • Eradicate blood schizonts of Plasmodium Not active against tissue schizonts	•Hepatic amebiasis. • Rheumatoid arthritis. • Safe in pregnancy.	• Mild headache and visual disturbances • GIT upsets; Nausea and vomiting • Pruritus and urticaria **Prolonged therapy and high doses:** • Ocular toxicity • Ototoxicity • Weight loss • Bolus injection → hypotension and dysrhythmias
Quinine		•Parenteral treatment of severe falciparum malaria. • Oral treatment of falciparum malaria. • Nocturnal leg cramps. • Safe in pregnancy.	• **With Higher doses**: •Cinchonism → (tinnitus,deafness,headaches,nausea & visual disturbances) • Blood dyscrasias; anaemia, thrombocytopenic purpura • **Blackwater fever** • (IV □) neurotoxicity: tremor of the lips and limbs, delirium,depression of respiration and coma **C.I:** Prolonged QT Interval • G6PD deficiency. • Myasthenia Gravis. • Hypersensitivity. • Optic Neuritis and auditory problems. • Dose reduction in renal insufficiency. **DDI:** • Antacids: containing aluminum/magnesium → delay absorption • Mefloquine • Quinine can raise plasma levels of warfarin & digoxin
Primaquine	• Hypnozoitocides, against liver hypnozoites. • Gametocytocidal, against the 4 human malaria species • Radical cure of P.ovale and P. vivax • MOA: Generating ROS	• Radical cure of relapsing malaria,15 mg/day for 14d **Doses** 1.Normal → 15 mg\day * 14 days. 2.Mild G6PD deficiency → 45mg\week*8 weeks 3. Severe G6PD deficiency → 30 mg\week*30 weeks.	• **At regular doses:** - Patients with G6PD deficiency → hemolytic anemia - ROS: Oxidative damage of RBCs → Hemolysis • **At larger doses:** - Epigastric distress,abdominal cramps,anemia, cyanosis & methemoglobinemia **Contraindicated in :** • Pregnancy • G6PD deficiency

L8: Antimalarial drugs

Therapeutic classification

Class	Drug	M.O.A / Uses
1-Causal prophylaxis	• Primaquine	Destroys parasite in liver cells and prevent invasion of erythrocytes
2- Suppressive prophylaxis	• Chloroquine • Mefloquine • Doxycycline	Suppresses the erythrocytic phase and thus attack of malaria fever
3- Clinical cure (Erythrocytic schizonticide)	**Fast acting high efficacy:** - Chloroquine - Mefloquine - Artemisinin - Quinine **Slow acting low efficacy:** - Pyrimethamine - Proguanil - Sulfonamides	Used to terminate an episode of malarial fever
4- Radical cure	• Suppressive drug • Hypnozoitocidal	Eradicate all forms of vivax from the body
5- Gametocidal	**Against vivax:** • Chloroquine • Quinine **Against all species:** • Primaquine	Destroys gametocytes and prevent transmission
6- Sporozoitocides	• Proguanil • Pyrimethamine	Destroys sporozoites

WHO treatment guidelines

In Plasmodium. falciparum	**Uncomplicated:** • ACT	**Complicated:** • IV Artesunate for 24 hrs followed by ACT • Artemether+ Clindamycin /doxycycline • Quinine + Clindamycin /doxycycline
In Plasmodium. viva	**If sensitive** • Chloroquine for 3 days followed by • Primaquine For 14 days	If Resistant: • ACT / 3 days followed by • Primaquine for 14 days.
Special Risk group in falciparum	• Pregnancy (2nd and 3rd trimester) • Lactating women Infants and • young children : ACT	**Pregnancy (1st trimester):** • Quinine +Clindamycin (7 days)

Prophylaxis in travelers

Chloroquine	**Mefloquine**	**Doxycycline**
Areas without resistant P.falciparum	Areas with chloroquine- resistant P.falciparum	Areas with multidrug-resistant P.falciparum

Begin 1◦2 weeks before departure (except for doxycycline 2 days) and continue for 4 weeks after leaving the endemic area.

L9: Drugs Used in Treatment of Constipation & IBS

Drug	M.O.A	Uses	ADRs
1. Bulk Forming Laxatives			
Dietary fibers -Indigestible parts of vegetables & fruits -Bran powder **Hydrophilic colloids** -**Psyllium seed** (soluble fiber) -Methyl cellulose -Carboxymethyl cellulose (CMC)	Dietary fibers and hydrophilic colloids are **non absorbable substances**→ increase the bulk of intestinal contents by water retention→ Distend the colon→↑ Mechanical pressure on the walls of intestine→ Stimulation of stretch receptors→ ↑**Peristalsis** → Evacuation of soft stool.	**Delayed onset of action (therefore avoided in acute constipation) (1-3 days)** "Not in acute constipation, only chronic"	●Intestinal obstruction (should be taken with enough water). ●Bloating, flatulence, distention. ●Interfere with other drug absorption e.g. iron, cardiac glycosides.
2-Osmotic Laxatives			
Salts(saline laxatives) — **Lactose**	They remain in the bowel, **attract & retain water** by" osmosis thereby increasing the volume of feces → ↑ Peristalsis → Evacuation of stool.	Prevention of **chronic constipation (ex: liver cirrhosis)**	● Delayed onset action (2-3 Days) ● Abdominal cramps & flatulence. ● Electrolyte disturbance.
Salts(saline laxatives) — **Magnesium sulphate** (Epson's salt) **Magnesium hydroxide** (milk of magnesia) **Sodium & Potassium phosphate**		Treatment of **acute constipation**	● **Disturbance of fluid and electrolyte balance.** ● May have systemic effects. #: **Magnesium salts:** 1- Renal failure 2- Heart block 3- CNS depression 4- Neuromuscular block #:**Sodium salts**: CHF
Balanced Polyethylene Glycol		◦ whole bowel irrigation **before colonoscopy or surgery** (4L over 2-4h) ◦colonic lavage solution	**Advantages**: ●Safe for all patients & Limited fluid or electrolyte imbalance ● Less flatulence and cramps
3-Stimulant Laxatives			
Anthraquinone derivatives — **-Senna** **-Cascara** **-Aloe Vera** (Active by-product: Emodin)	● Act via **direct stimulation of enteric nervous system**→ increased peristalsis & purgation and increased fluid and electrolyte secretion. ● The **most powerful group among laxatives** and should be used with care.	-	● Abdominal cramps may occur. ● Prolonged use → dependence & destruction of the myenteric plexus leading to atonic colon. ● **Dark pigmentation of colon** #: **Senna: breastfeeding** **Castor Oil**: pregnancy→ reflex contraction of the uterus → abortion.
Bisacodyl			
Castor Oil (Active by-product: **Ricinoleic acid)**		after oral ingestion of a toxin	

L9: Drugs Used in Treatment of Constipation & IBS

Drug	MOA	Uses	ADRs
4. Stool Softeners (Lubricants)/Surfactants			
Docusate	Act by either **decreasing surface tension** (allowing water to interact with stool) or by **softening feces** thus promoting defecation.	Treat constipation in patients with hard stool or specific conditions and for people who should avoid straining. "patients that can't push hard after surgeries" **Paraffin Oil** is good for radiology preparation	-
Glycerin			-
Paraffin oil			Impairs absorption of fat soluble feces thus promoting vitamins
5. Other Anti-Constipation Drugs			
Prucalopride	A selective, high affinity **serotonin (5-HT4)** receptor agonist with enterokinetic activities	-	-
Lubiprostone	Stimulates type 2 chloride in the small intestine	chronic constipation & IBS-C	
Linaclotide	Stimulates chloride secretion		
Methylnaltrexone	**μ- receptor antagonist**	opioid induced constipation in advanced illness	
Symptomatic Treatment of IBS			
Alosetron	• Selective **5-HT3 antagonist** • 5-HT3 receptors antagonism of the enteric nervous system of the GIT results into: **inhibition of colon motility, inhibition of** unpleasant visceral **afferent pain sensation** (nausea, pain, bloating).	**Used in IBS with severe diarrhea** in women who not had success with any other treatment. (IBS-D)	Constipation and ischemic colitis may occur.
Tegaserod	• **5-HT4 agonist** • Stimulation of 5-HT4 of enteric nervous system of GIT → **increases peristalsis**	• Short term treatment of **IBS-associated constipation in women older than 55** with no history of heart problems, • may still be used in limited emergency situations. **(IBS-C)**	CVS side effects

L10: Treatment of dysentery and amoebiasis

amoebiasis

Amoebiasis	treatment
Asymptomatic dysentery "cyst carriers"	1. **Luminal amebicides:** Diloxanide or iodoquinol or Paromomycin
Amebic colitis Dysentery ameboma Extra-intestinal disease	1. Metronidazole or tinidazole Extra-intestinal disease 2. Luminal amebicides
Hepatic abscess	1. Metronidazole or tinidazole or chloroquine or dehydroemetine

Drug	MOA	Uses	ADRs	#
Tissue/systemic amoebiasis				
Metronidazole	◦ Inhibit **trophozoites** DNA replication. ◦ Doesn't eradicate cysts from intestine.	◦ **Drug of choice in all invasive amebic infections (ex: liver abscess)(followed by luminal amebicides).** ◦ Giardiasis ◦ Trichomoniasis ◦ Anaerobic bacterial infections: - Pseudomembranous colitis (C. difficile). - Peptic ulcer (H. pylori)	◦ **GIT**: dry mouth - metallic taste - NVD - oral thrush (Moniliasis: yeast infection) ◦ **CNS**: paresthesia - insomnia -dizziness - neurotoxicological effect - convulsion - encephalopathy - peripheral neuropathy ◦ Dysuria / dark urine ◦ Neutropenia	**A. DDI:** -Enzyme **Inhibitors (cimetidine | ketoconazole):** ↑DoA. -Enzyme **Inducers (phenytoin | phenobarbital):** ↓DoA. - **Alcohol: blocks aldehyde dehydrogenase →disulfiram like effect: flushing, tachycardia** ,NV - **Inhibits** CYP-450 (2C9 & 3A4) →↑ **warfarin** & **lithium** toxicity **B. #:** ◦ Pregnancy / breastfeeding ◦ Alcohol intake ◦CNS diseases ◦ Renal/hepatic diseases
Tinidazole	Similar to metronidazole. **Simpler** dosing regimen.	-	Better **potency & toxicity** profile than metronidazole	-
Emetine **dehydroemetine**	◦ **Irreversible** block of **protein** synthesis ◦ Toxicity concern → replaced by metronidazole.	○ Tissue trophozoites of E. histolytica ○ Intestinal wall infections ○ **Amoebic liver abscess** ○ Severe amebiasis (acute amoebic dysentery).	◦ GIT: NVD ◦ CVS: hypotension - cardiac arrhythmias - heart failure. ○ **Toxicity**: dehydroemetine (preferred) < emetine ○ Cardiotoxicity	**A. Precaution**: Not used for more than 10 days (3-5 days). **B. #:** ○ Pregnancy ○ Young children ○ Renal/cardiac diseases
Chloroquine	◦Anti-malarial drug	◦ Amebic liver diseases with metronidazole / dehydroemetine	○ Pruritus ○ **GIT**: NV - pain -anorexia ○ Blurring of vision ○ Hemolysis (in **G6PD** deficiency)	-

L10: Treatment of dysentery and amoebiasis

amoebiasis

Drug	MOA	Uses	ADRs	#
Luminal Amebicides				
Diloxanide Furoate	◦ Direct: amoebicidal action against luminal forms ◦ Not active against trophozoites in intestinal / extra-intestinal tissues	◦ **Drug of choice** in all **asymptomatic** intestinal infections (cysts carriers/ luminal amoebiasis). ◦ **Eradicate** E. histolytica **cysts** (after treatment of invasive disease invasive)	◦ GIT: - NV - Flatulence - abdominal cramps	**#:** ◦ Pregnancy ◦ Children (<2 yo)
Paromomycin Sulphate	◦ **Direct ambecidal action**: leakage by acting on parasite's cell membrane. ◦ **Indirect**: killing bacterial flora essential for proliferation.	◦ Chronic amebiasis to eliminate cysts (in cysts passers). ◦ Eradicate E.histolytica cysts (after treatment of invasive disease). ◦ Effective only against luminal forms of amoeba	◦ **GIT**: - distress - diarrhea	- **Precautions**: ◦ Severe renal disease: toxicity ◦ GIT ulcer pts.
Iodoquinol	Effective against luminal forms of amoeba	**Asymptomatic** amebiasis.	◦ **GIT**: NVD (persistent diarrhea → discontinue). - ◦ **Peripheral neuropathy including** optic neuritis (**caution** in optic neuropathy pts). ◦ Enlargement of **thyroid gland** (**caution** in thyroid disease pts). ◦ Iodine sensitivity (signs of iodine toxicity → discontinue): dermatitis - urticaria - pruritus - fever ◦ Interfere with **Thyroid FTs**:↑ protein-bound serum iodine →↓measured 131I uptake.	
Bacillary dysentery				
Fluoroquinolones (Ciprofloxacin)	Block bacterial **DNA synthesis** (DNA gyrase & topoisomerases) in Gram + & - bacteria	◦ [First-Line Treatment] of shigellosis. ◦ Bacterial diarrhea: [shigella - salmonella - E. coli] ◦ Infections: UTI - RTI - Soft tissues, bones, & joint infections.	◦ Arthropathy ◦ GIT: NVD ◦ CVS: Prolonged QT interval ◦ CNS: headache - dizziness ◦ Phototoxicity ◦ Liver toxicity	◦ **Pregnancy** / nursing ◦ **Children** ◦ Epilepsy ◦ Arrhythmias ◦ Shouldn't be combined with antacids, divalent cations.
3rd Generation Cephalosporins (Cefixime - Ceftriaxone)	Interfere with synthesis of peptidoglycan (major structural component of bacterial cell wall).	◦ [Second-Line Treatment] of shigellosis. ◦ Children and pregnant (then azithromycin). ◦ Patient allergic to sulfonamides (then azithromycin).	-	

1. Maintain fluid intake (oral rehydration therapy/Intravenous fluid therapy).
2. **Asymptomatic** luminal amebiasis → luminal amebicides (diloxanide/iodoquinol/paromomycin).
3. **Invasive**/intestinal amebiasis → **metronidazole** (mainstay of therapy) followed by luminal
4. **Hepatic** amebiasis → chloroquine - dehydroemetine (CVS toxicity → not preferable).
5. **Bacillary dysentery → ciprofloxacin (drug of choice), in Children & pregnancy → ceftriaxone/cefixime.**

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