ANTACIDS

used for dyspepsia (indigestion, feeling of fullness & burning) and acid peptic disorder, Now replaced by H2RA & PPI, however still use by pts for treatment of intermittent heartburn & dyspepsia and for pain relief.

ACTION

Antacids + Gastric HCl → Salt + water.
(weak bases)

After a meal → 45meq/h of HCl secreted

(1) single dose of 156meq of antacid given after 1hr of meal. Neutralize acid upto 2hrs.

Acid-Neutra. capacity (ANC) depends:
- rate of disso (tab v/s liq)
- water solubility
- rate of rex ē acid
- rate of gastric emptying

(2) 40-80meq ANC when needed or (after meal & at bed time)

*-SODIUM BICARBONATE:- (Baking soda, Alka seltzer)

$NaHCO_3 + HCl \rightarrow CO_2 + NaCl + H_2O$.

- unreacted alkali readily abs. → cause metab. alkalosis when give high doses or to given pt. of renal insuff.
- CO_2 → gastric distention, Belching (release of gas)
- absorp. → use fluid retention in pt ē HT, HF or R.insuff

Prescriptioncracker.com

*-Ca-carbonate:- (Tums, Os-cal)

react slowly ē HCl than $NaHCO_3$ to form CO_2 and $CaCl_2$, also can cause meta. alkalosis

belching

* Excessive dose of these antacids ē Ca-containing daily products → Hypercalcemia, renal insuff., milk-alkali syn

- Most potent - may cause constip.

*-Mg-Hydroxide OR Al-hydroxide:- Reacts slowly ē HCl

produce $MgCl_2$ or $AlCl_3$ and water

* - NO gas generated
- alkalosis is uncommon becoz of efficiency of neutraliz. re

⇒ unabsor. mg salt → osmotic diarrhea
⇒ Al-salt → constipation

← Alone they're not really effective, esp. Al-containing antacids are weakest ANC.

Both (Mg & Al-) antacid are adm. together in formulation (Gelusil, Maalox, Mylanta) to avoid bowel movemen.

- Both excr. by Kidney.

Ren Insu (long term) ← Avoid all Anacids.

→ As all antacids affect abs. and gastric pH, of other drugs. Therefore Antacids shouldn't be given within 2hr of doses of Tetracyclines, FQ, Itraconazole & iron., Digoxin.

...upon in concomitant disease

H_2-Receptor Antagonist

Ach, Histamin, Gastrin → activate protein Kinase → (Ach → Ca^{2+} ion → PK activ; Hist → ATP → cAMP → PK activ; Gastrin → Ca^{2+} release → PK activ) → Activate/stimulate H^+/K^+ ATPase proton pump to secrete H^+ in exchange for K^+

Cimetidine → First agent H_2RA
↳ ↑ ADR profile

ACTION/MOA

- Selective on H_2 (No effect on H_1 & H_3)
- Competitive antag. and are fully reversible (dose-dependent)

REDUCE secretion from Ach & gast

- Histamin release from ECL cells by gastrin or vagal stimul. is blocked from binding to parietal cell H_2 recep.
- Direct stimul. of P.C by gastrin or Ach. has ↓se effect in presence of H_2-recep. Antag.

H_2 mast cells
ECL = enterochromaffin-like cells
most prevent in acid-secreting region
- release Histamin

THERAPEUTIC USES

Peptic ulcer

All 4 agents are equally effective

For NSAIDs induce ulcer
1 ↳ Stop NSAIDs + Start H_2RA
2 ↳ If need to continue NSAIDs, start co-adm of PPIs to promote ulcer healing.

For H. Pylori
- H_2RA → No signif. role → Recurrence occur.
- Start 10–14 day therapy ≈ PPI + 2 antibiotics

Cime (less potent)	Rani/Nazi	Famo
800mg Hs OR 400mg Bd	300mg HS or 150mg Bd	40mg Hs or 20mg BD

Hs = Bed time.

Acute stress ulcer

- To prevent and manage ASU esp in ICU pts
  ↳ GIVEN IV
  ↳ Replaced Now by PPI
- Sometimes bleeding also occur

H_2RA/PPI → ↑pH → ↓se bleeding incidence.

Cime: 50mg/h IV infus. continu.
Rani: 6.25mg/h C. inf. or 50mg IV q 6-8hr
Niza → Not avail
Famo 20mg IV q 12hr.

GERD

- low doses of H_2RA → effective in 50% pts (OTC)
- provide relief by ↓sing Acid secretion ≈ in 45min
- Antacids → Rapid-but short Term relief. upto 2hr
- PPIs → preffered esp in severe Heartburn

- Cime = 800mg BD
- Rani and Niza = 150mg BID
- Famo = 20mg BID

KINETICS

- Oral adminisn.
- Widely distn (Across placenta and in B. milk)
- excreted via urine
- Cime, Rani & famid → Avail as IV
- $t_{1/2}$ ↑se in pt ≈ renal dysfunction.

Efficacy ↓se of
- Drug that req. acidic medium eg ketoconazole

ADRs

mostly by cimetidine
↳ have endocrine effect bcoz it act as non-steroidal anti-androgen
↓
cause gynecomastia & impotence, galactorrhea (↑prolactin)
→ CNS :- confusion etc
→ Inhibit CYP450 → effect metab. of
- Warfarin
- Diazepam
- phenytoin, Carbamazep.
- Quinidine
- Theophylline
- Imipramine. (↑se serum conc.).
- atorvastatin

* Rapid IV infusion causes bradycardia & HYPOtension through blockade of cardiac H_2-recept.
* NOT to be given < 12 year of age.

Avoidin PG + B. Feed

Pharmaco-Study YouTube channel

PPIs

These agents are pro-drugs
ē acid-resis-enteric coating
↓
(oating removed in alkaline duodenum → produg, weak base abs & transported to parietal cell

Form stable covalent bond ē H⁺/K⁺ ATPase enzyme
↑
There it converted to active dug
↑ cations
1) sulphenic acid
2) sulphenamide &
sulfenamide

- It takes 18 hrs for enzy to be resynthesi and acid secretion is inhibited during this time. - Inhibit both basal & stimulated secre at standard dose by MT 90%

Oral product (Omepraz + NaHCO3) — better absorp and avail as OTC + presrip.

THERAPEUTIC USES

GERD and other

↓
*PPIs are preffered drugs for
- Stress ulcer treatment
- Prophylaxis & treatment of
  - ✓ GERD ✓ active duoden. ulcer
  - ✓ Erosive esophagitis
- ✓ Pathologic Hypersecretory condition (Zollinger:- Hypersec. of HCl by a Gastrin secreting tumor cells) -Ellison syndrom

- OD PPI → partially effective for GERD
BID PPI or PPI in morning & H_2A bedtime improve symp.

→ H_2RA should be taken well after PPI bcoz H_2A ↓ activity of proton pump and PPI require proton pump to be in active state to be effective.

PPI → ↓se risk of bleeding from aspirin ulcer and other NSAIDs.
→ use to prevent / treat NSAID induc ulcers.

H. Pylori ulcers

(gra - ve) bacillus.

Mechanism
antimicrobial proper. (minor) ↑se pH intragastric

Treatment Regimen

Triple therapy (14 days).
- PPI BD
- clarithro 500mg BD
- amoxic 1g BD (OR)
- metronida. 500mg BD

In penicillin allergy

After completion of therapy PPI continued for 4-6 weeks to ensure comp. healing

Sequential Treatment (10 days)
Day 1-5: PPI BD + Amoxi 1g BD
Day 6-10: 5 addi. days of PPI BD + clarithro 500mg BD and Tinidazole 500mg BD.

∴ Amoxi is preffered over augmentin to use S.E profile of clavunic acid

PHARMACOKINECTICS:-

All effective orally
PPI adm. 30-60min before breakfast or largest meal
$t_{1/2}$ = few hrs (1.5 hrs), however (24 hrs) duration due to cova bond. ē H^+/K^+ ATPase enzyme. (48 hrs)
metab. excret. in urine.
-Dexlansoprazole has dual delayed release formulation → can be taken without reg aud to food.
Esmo, lanso and panto → avail as IV.
PEL → IV

ADVERSE REC.

(1) ome & esom ↓se effectiveness of clopidogrel, as they inhib. CYP2C19, so prevent conversion → active metab. However ↑se risk of CV events
(2) Fracture = ē ↑↑ duration of use MT 1 year
(3) ↓ Vit B_{12} level = as acid req. for its absorp
(4) Impair Ca-carbon abs = due to ↑ pH (Ca-citrate - alternative for supple
(5) Diarrhea & clostridium difficile colitis may occur. (Pt. should dis. PPI at that time of diarrhea)
(6) Hypomagnesemia & ↑se risk of pneumonia.

*- Mucosal PROTECTIVE AGENTS

AKA: Cytoprotective compounds.

prevent mucosal injury, reducing inflam, heal existing ulcers

Sucralfate

Complex of $Al(OH)_3$ and sulfated sucrose

- Binds to positively charged grps of protein of both normal & necrotic mucosa at pH<4
- By forming complex gel ē epithelial cells it creates a physical barrier,

⇩

Thus protect ulcer from pepsin & acid and allow it to heal

- Limited use → DIs → As it binds ē groups
- ⇩ require acidic pH for activation, so sucralfate shouldn't co-adm ē H_2RA or PPI or antacids
- ADR = constipation
- ✓ Doesn't prevent NSAID induced ulcers, neither heal gastric ulcers → But need to take big tablet 4 time a day (Drawback)
- ✓ Effective for duodenal ulcers.

⇒ DOC = ulcer + CRF

Bismuth sub-salicyl. [CBS]

colloidal

- use as component of quadruple therapy to heal peptic ulcer
- Action → anti-microbial [H. pylori] → inhibit pepsin activity → ⇩se mucus secretion.

interact ē glycoprotein in necrotic mucosal tissues to coat & protect ulcer.

(Quadruple therapy :- Bis. sub + metronida + Tetracy + PPI
(use in this therapy is use increase of Clarithromycin resistance)

ANTI-MICROBIALS

ulcer due to H-pylori require anti-microbial

Diagnosis

- endoscopic biopsy of gastric mucosa
- Non-invasive methods
  - Serology
  - urea breath Test

Subj are given urea labelled ē ^{13}C orally → ⇩

H-pylori produce urease which hydrolyze labelled urea → $^{13}CO_2$ and ammonia

⇩

$^{13}CO_2$ dissolved in blood & Traveled to lungs

⇩

exhaled $^{13}CO_2$ is analyze. The presence of H. pylori → ⇩se ratio of $^{13}CO_2$ to $^{12}CO_2$ in expired breath

*- PROSTAGLANDINS

Prostacyclin

- Prostaglandin E, [E_1, E_2, I_2] → I_2 a.k.a Prostacyclin produce by gastric mucosa
  - → inhibit acid secretion
  - → stimulate bicarbo. & mucus secre = healing ulcer effect
- prog. ē deficiency is thought to be involved in pathogen of peptic ulcer.
- Misoprostol, analog of pro. E_1 → approved for NSAID> indu. ulcer
- prophylactic use is also conside in high risk pts e.g elder or pt ē previous ulcer.
- PG — as it ⇩se uterine contrac. → miscarriage.
- DOSE-related diarrhea & Nausea — most common adr.

Thus PPIs are preffered for prevention. NSAID indu ulcer. due to chronic use

MANAGEMENT of GERD
(American college of Gastroenterology)

→ They work best when stomach is empty. ↑

Uncomplicated GERD, NERD and EE
↓
non-erosive

⇒ ① Lifestyle modific
② Empiric PPI OD 30-60 min before 2 or 2 hr after food breakfast for 8 weeks

⇓

RESPONSE

← Complete
↓
GERD Maintainace
⇓
- Reassess sympt. atleast annually
- Titrate to lowest dose based on symp.

→ NO/partial
⇓
- optimize/tailor the therapy
- ↑se PPI BID
- Adjust timing

⇓

Symp. relief ← Yes
↓
No
↓
- Review Diagnosis
- consider need for investigational procedure such as pH. metry, impedance etc

- Omeprazole
- pantoprozole

⇒ Dex-lansoprozole
⇓
can be taken irrespective of food.

Avail as:- "Dexilant" — recommended in ramzan.

- PPI — for long-term recomm. only when ulcer, lymphoma etc
- Some pt even take it on alternate days.

5, 3)

depen on concomitant disea

LAXATIVES

Bulk forming (1st line) | Hyperosmotic (2nd line) | Stimulant lax (3rd line)

Bulk-forming Laxatives

Natural or synthetic polysacc. or cellulose derivatives
↓
absorb H_2O to soften stool
↑se bulk of stool
↓
Stimulate peristalsis

- given ē 8oz of water (approx 240ml) to prevent choking
- ONSET: 12–24 → 72 hrs
- ADR: Bloating, cramping and flatulence
- CI: -Obstructing bowel lesion
  - Crohn's disease (type of IBD) → due to risk of perforation.
  - In pt ē fluid restriction → HF/renal impair

- Sugar-free formula.
  - Diabetics
  - Avoid in phenylketonuria
- ★ For treatment
  - use must be limited to 1 week.
  - For prevention can be use for long-term.

HYPEROSMOTIC LAX.

Create osmotic gradient → that pulls water in intestine → peristalasis & motility

Glycerin

(Fleet Gly Supp. , Fleet pedia-Lax)
- effective when used rectally.

DOSING

6yr → adult: 2g regular suppos. | 5.4g liquid supp
2–5yrs: 1g neg. suppo. | 2.8g liq. suppo.

- ONSET: 15min → 1hr
- ADR: rectal burning

PEG 3350

(Miralax, Balance)
- approv. for self-care use in age 17≤age
- Dose: 17g stirred into 4–8 oz of fluid, OD
- ONSET: 1–3 days
- ADR: N/D, bloating etc

⚠ Kidney DS | IBS | PG | BF → for short-term it can allow

SALINE LAXATIVES

Non-absorbable salts & sugars.
Works by drawing water into colon

- ONSET: 30min–3hr (orally)
  2–5 min (rectally).
- ADRs: N/V/Dehydration
  - excessive diuresis
  - abdom. cramping
  - ⇒ 20% magnes. absorbed from these products → HYPERmagnesemia in pt. ē pre-existing renal impair.
  - ⇒ Excessive dose = Diarrhea of mg.

WARNING/counselling
- Mg-citrate = adult dose = one full bottle
  ↳ refrigration ↑se palatibi & prevent crystall
- Na-salt — HF, edema, RF, kidney DS
- mg-salt (6hr onset)
- OSP — oral sod. phosph. → Non-prescrip med. for constip.
  ↓
  Some pt. report AKI
  ↓
  Thus FDA removed it from market due to non-efficacy
  For constipt as well as potential for AKI

Bulk-forming lax → prevention
depen on concomitant disease

Bulk former for = IBS + spastic constipation

This is pro-drug. Sulfasalazine = IBD

Sulfasalazine → Sulfapyridine → ↓ R.A.

Sulfasalazine → 5-Aminosalicylic acid (5ASA) → ↓ treat IBD

Mesalazine (coated 5ASA).
- treat IBD
- Take as enema
- Less ADR.

★ STIMULANT LAXATIVES

Works by altering water & electrolyte transport by intestines → stimulate motility
Also work by stimulation of enteric nervous syst. [propulsive peristaltic activity]
– Third line – for general constip. → 1st line for opiate induced constip.

SENNA

(1) Single-entity
- Senokot
- Ex-Lax
- Pevdiem
- Fletcher's Laxa.
- for kids.

(2) Comb ē stool-softner
- Senokot-S
- Peri-colace

avail as standardize conc. or as sennosides.
↓
from senna leaf

Dose: solid oral formul. 187–374mg stand. conc.
8.6 – 17.2mg sennosides
Avail as Tab, syrup or chocolate chew.

Bisacodyl

- (Dulcolax, correctol)
- avail as oral & rectal

Adult		Pediatric (age 6 & more)
oral	rectal	5mg OD (oral/rectal)
5–15mg	10mg OD	

Oral ONSET: 6–12hrs
Rectal: 15–60 min (like giving supp)

★ – ADRs:- All stimulant Lax:- Abd. cramp., Electro. fluid depletion, enteric loss of protein, malabs., hypokalemia, Suppository → rectal burning

WARNING & counselling

- Undiagnosed rectal bleeding
- Intestinal obs.
- Spastic constipation
- Avoid chronic use of cathartic (stimulant) Lax.

Laxative = elimin. of soft, formed stool
Purgative/cathartic = produce more fluid evacuation

Sennosides
- Wine discolor (pink, yellow, red, brown)
- This is harmless.
- Bluish pigment of mucus (melanin)

Bisacodyl
- Tablets shouldn't be crushed or chewed due to enteric coating.
- Milk, H_2RA & antacids also erode this coating, so should be separated in dosing by atleast 1 hr.

★ – EMOLLIENT LAXAT./SURFACTANTS

– Works by allowing water to move more easily into stool. → soft st
– useful for those who should avoid straining to pass hard stool
e.g (recent myocardial surgery, rectal surg). less effective than

- They're salts of surfactant docusate
- contain insigni amount of Ca^{2+}, Na or K+
- products includes:
  - ✓ docusate Na^+ (colace)
  - ✓ Docusate Ca^{2+} (kaopectate stool softner) or surfak (OD)
    - same manufacturer
- each dose should be taken ē 8oz of H_2O
- Avoid in N/V (appendi)

Adult	paed/child <24yr
50–300mg/day	50–150mg/D

- ONSET: slow: 24–72hr (1–3day)
- ADR: Diarrhea, cramps.

(They have also marketed kaopectate – bismuth subsalicylate = Treat diarrhea)

★ Bulk-forming lax → prever

depen on concomitant disea

LUBRICANT LAX.

(Mineral oil) — paraffin oil and petrolatum

OPOID Receptor Antagonist

- Acute or chronic therapy ē opoids → constipation.
(mu,(μ) opoid recep).

μ-opoid recep. antagonists

methylnaltrexone

- Use for opoid-induce treat. in pt. who don't respond to other treatme.
- ADMINISTR.
  S/c injec (0.15mg/kg) q 2 days

Alvimopan

These agents don't cross BBB → so inhibit peripheal μ-recep ēout effecting analgesic effect.

For short term treatm to shorten the period of post-opera. ileus in hosp. patients

Dose:- 12mg capsule adm orally ein 5hrs before surgery & BD after surg until bowel function recovered —
Don't use MT 7 days.

Due to risk of CV-toxic, It is currently restricted in short-term use.

Pospoperitileu = intolerance of good/oral intake due to disruption of (Propulsive motor activity (power to propel)

Specific population

Paediatrics

First use non-pharmaco. therapy
↳ ↑se fluid intake or sugar
↳ ↑se bulk content of diet (fruit, fiber, cereals, vege)

Age <2yrs — 90 medical provider

Age >2yr — Glycerin supp.

Laxative Abuse: leads to cathartic colon (loss of tone of intestinal muscle)
Most often ē taken ē lifestyle modifi ↑ water & exercise (↑ bowel tone)

PGs

- may be by enlarged uterus, ingestion of Pre-natal vitamins iron & calcium. & influence of progesterone (↓motility)

* Bulk formers and stool softeners are recommend.

Geriatrics

may be due to
↓ fluid intake,
concurrent disease (Hypothyroidism)
or medication (opiates, anticholi.)

Major concern:-
Fluid loss induce by aggressive laxa. treatment (enemas, high-dose saline laxat.)

* - Hyperosmotic or Stimulant laxatives for treatm
* Bulk-former lax → prevention

depen on concomitant disease

LUBRICANT LAX.

(Mineral oil) — paraffin oil and petrolatum

Work at colon to ↑se water retention in stool

Availability
- Oral / rectal

Dose
- Adult
  - Oral: 15-45ml orally
  - rectal: 118 ml r
- Child (≤12yr)
  - 6-11yrs
    - Oral: 10-15ml
    - rectal: 59ml.

Kinetics
- ONSET: 6-8hr (oral)
  5-15min (rectal)
- ADR: anal seepage
  ↓
  Itching & perianal discomfort

Warnings
- can ↓se absorp. of fat-soluble vitamin so DON'T use on chronic basis
- can be Taken on EMPTY stomach
- NOT TO BE Taken → AT BED-TIME
  ⇓
  Due to risk of lipid pneumonitis
- Elders, debilitated pt or pt ē dysphagia → at ↑ risk ↙
- NOT TO Be co-Adm ē Emolients (Docusate) → as absor. of mixed oil ↑ses

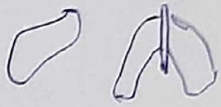
Swallowing difficulties

Rectal bleeding

Appendicitis

Hepatotoxicity ←

age < 6yr



CHLORIDE-CHANNEL ACTIVATOR

Lubiprostone
(Prostanoid acid derivative)
- Chronic constip
- IBS

MOA: Stimulate Type-2 Cl-channel (ClC-2) → ↑se Cl⁻ rich fluid in intestine
↓
Stimulate intestinal motility

DOSE: 24mcg PO BD — chronic constip.

ONSET: within 24hrs

Recurrence of constip. — after discontinu.

- minimal sys. absorption.

Pg — category-C

- Nausea in 30% pt due to delayed gastric empty.

Linaclotide
(minimaly absorb. 14 A.A peptide).
- Chronic constip
- IBS.

Lina. binds to and activate Guanylyl cyclase-C on luminal epith. surface of intestine
⇓
↑se Intra & extra cell cGMP
↓
Activate CFTR → ↑se Cl⁻ rich secretion & ↑se intest. transit
(Cystic fibrosis transmembrane 145)

DOSE: 145mcg OD → 1-2 bowel mov. per week.

upon discontinu. → bowel movem. ↓ became normal ē in 1 week

ADR: severe diarrhea in 20% pts

Category C → Pg

Paediar

- Breast MRI
- pathology review [ER, PR & Her-2/neu]

Pronunciation:- M. Gulzaib's presentation 3/6 - sugar + 4 tsp - salt

ANTI-EMETICS

Four important sources of afferent input to vomiting centre

- Chemoreceptor Trigger Zone (CTZ)
  - Or area postrema
  - located at caudal end of 4th ventricle, outside BBB
  - Rich in D_2 recep. & opioid (cannabinoid) recep. and possibly 5-HT_3 and NK_1 receptors.
  - CINV = Chemotherapy - induced Nausea and vomiting
- vestibular system
  - important in motion sickness via Cranial nerve VIII
  - Rich in M_1 and H_1 recept.
- vagal & spinal afferent nerves (periph → CNS)
  - These afferent nerves are rich in 5-HT_3 recep.
  - (GI irritation via chemotherapy, radiation therapy, distention or acute infectious gastroenteritis leads to release of mucosal serotonin and activ. of these recep.
- CNS (Central nervous system)
  - Role in vomiting due to psychiatric disorders, stress and anticipatory vomiting prior to chemo.

★-PHENOTHIAZINES (anti-psy)

- Act by blocking dopamine receptors
- Prochlorperazine → Fluorouracil & doxorubicin INV
  - low/moderate effective

★-5-HT_3-Receptor Blocker

- Block 5-HT_3 recep in periphery (visceral vagal afferent fibers) and in Brain CTZ.
- Prefer in chemo → long duration → superior efficacy
- can be adm prior to chemo (IV/orally)
- Ondan. & gani (GO) → Prevent cisplatin induced N/V in 50-60% pts
- Also use in post-operative N/V
- Metab. by liver
- Excreted in urine
- Prolong QTc interval — esp. dolasetron and high doses of ondansetron
  - ↓ Due to this Dolasetron is not used in Proph of CINV.
  - ↑QTc
- ADR = Headache.

Substituted Benzamide:-

- metoclopramide → cisplatin INV in (High doses) 30-40% pts
- Inhibit dopamine in CTZ (dop. anti. effect → extrapyramidal symp & high/long term use.)
- Metclo. — previously used as Pro-kinetic drugs (which ↑se GI motility by ↑sing freq. & strength of contrac) for the cure of GERD
  - ↓ Replac By PPI due to ADR
- Also use in pts ē documented gastric paresis (partial paralysis of stomach)
  - metclop : similar to anti-dopaminergic. (anti-psy)

★-BUTYROPHENONE:

- Act by blocking dopamin recep.
- moderately effective.
- Dorperidol (in comb ē → opioid/BZ) → For sedation in endoscopy and surgery.
- Prolong QTc interval — reserve for pt. who don't respond to other
- Haloperidol (High dose) = Metclopr (High dose) → cisplatin induce N/V.

Dor Dola QTc↑

Vestibular sys:- Sensory apparatus of inner ear that keep body maintain its postural balance
The info. furnished by V.S is also essential for coordinating position of head & movement of eyes

CN-VIII :- brings sound & info about one's position & movement in space into brain
↓
vestibulocochlear nerve.

Metclop ← Anti-dopamin
Anti-seroli 5HT3

↑ACh = so can be blocked by atropine

Prokinectic
↓ (gastric but NOT large intestine)

↑se LES tone.

Domperidon = D2 act
Blocks action of levodopa.

+ Dehydration :- M. Gulrajani's Presentation

*-Benzodiazepines :-

- antiemetic potency = low
- Beneficial due to = sedative, anxiolytic & amnesic properties.
  ⇩
  useful for treating anticipatory vomiting
- Concomitant use of alco = avoided due to ↑se CNS effects

*-Substance P, NK1-recep block

Aprepitant → Target NK-recep in brain
Thus ⊖ binding of sub-P to NK-recep

- Used for highly or moderately emetogenic chemo. regimen
- Usually adm ē Dexa & a 5HT3 antag
- metab by CYP3A4 — affect metab of other drugs metab by CYP3A4
- ↑g-Warfarin (↓se INR) (apprep)
- cross BBB.

Several chemo drugs 're mētab. by this path
Docetaxel, paclitaxel, etopo; irinotecan, imatinib
vinblas and vincristine.

⇒ Fosaprepitant (IV formul) → converted to aprepitant after 30 min of infusion

- Taxanes
- MT- Inhibitor
- EI²

∴ Also has Anxiolytic/Antidep effect

*-CORTICOSTEROIDS

used for mild to moderately emetogenic chemotherapy

- mostly use in combin.
- MOA = may be due to blockade of prostaglandin

*-COMBINAT. Regimen

- Anti-emetic 're often combined to ↑se activity & ↓se toxicity

- Dexameth + odansetron ⟶ 91% response
- Dexametha Diphenhydram Metclopram Domperidol ⟶ 76% response
- Lorazepam = Dexametha → 63% response.
  Metclopra
- Diphenhydram Dexam Metclop ⟶ 58% resp

DO > MD3 > MLD > MD²

∴ Diphenhydram = anti-histamine (Benadryl brand).
- Also as sedative
- Tremors in parkinson
- INVERSE AGONIST AT H1-receptor (vestibular sys).

H1 recep = similar to muscarinic recept

Hyoscin (or) Scopolamine (DOC), MD3/MD2/ diphenhydramine

[usually taken 1 hr before journey] ← Motion sickness } Acetazola, dicyclic Promethazine, Cyclizine

Anti-histamines for vomiting

* - anti-vertigo = cinnarizine (DOC) - ↓ Ca^{2+} influx from endolymph into vestibular sensory cells which mediate Labyrinthine reflexes

* Morning sickness = Doxylamine.

* - Motion sickness: Diphenhydramine, Cyclizine
Diyclic promethazine

*. Introduction:- M. Guzaab's presentation

SEROTONIN: Types of recep 5HT 1, 2, 3, 4.

5-HT3 = present in GIT - peristalsis ← 5HT4 | 90% of all present in ECL.

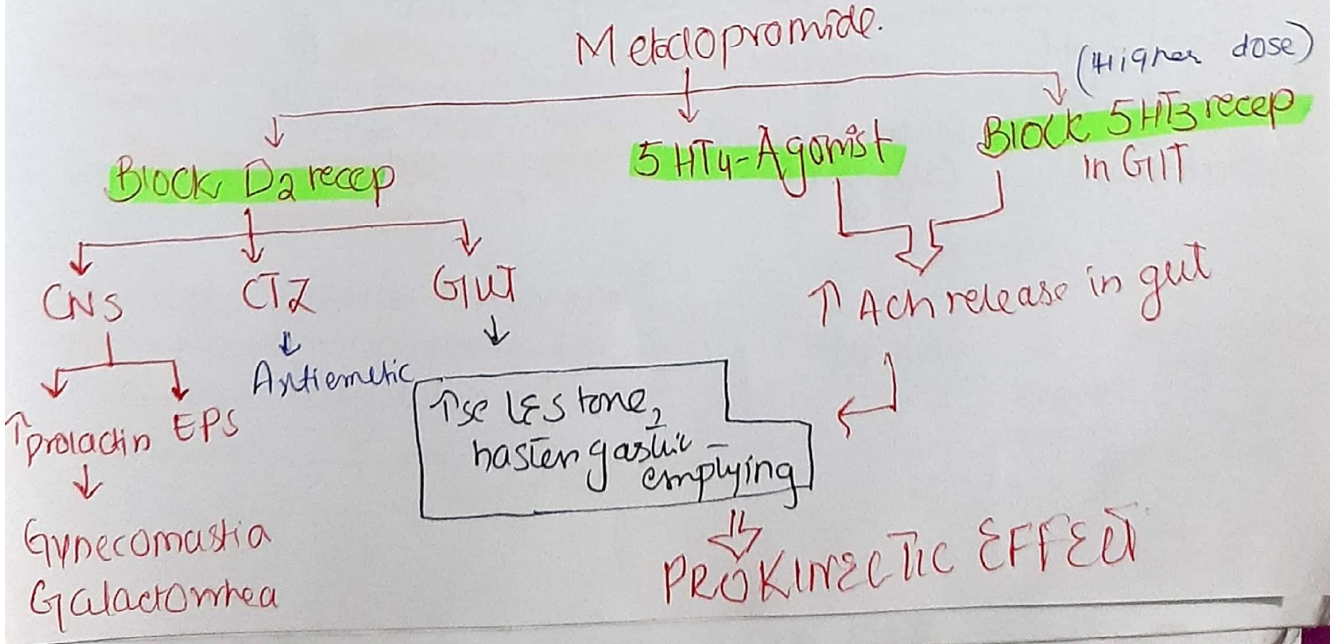
5HT = Brain (1, 2, 5, 6, 7).

5HT (location)	Role	Antagonist
• 5HT3 = CTZ, NTS, Parasym (GIT)	vomiting, Peristals	Ondansetron, Gran (AGONISTS) • Metclopr • proclaupride • cisapride (↑QTC). Mosaprid • Tegaserod
• 5-HT4 = GIT, CNS	peristalsis (Forward move)	

5HT2 CNS

Influence
- Anxiety
- Aggression
- Appetite
- mood • sleep
- Thermo regul.

Antagonist
Mirtazapine (Atypical anti-dep)



*- Defination:- M. Gulzaeb's

⇨ ANTI-DIARRHEAL ⇦

Major causes → Increased motility; ↓se absorption of fluid

*- Anti-motility agents

(Diphenoxylate and loperamide → widely used)

Both are analogs of meperidine

- Have opoid-like action on Gut → activate pre-synap opoid recep in enteric nervous system → inhibit Ach release → ↓se peristalsis ⇩ ↓se clonic transit time and fecal water absorption

Dipheny. At high doses – affect CNS

Loperamide: - non-presc. opoid • NOT cross BBB ↓ NO potential for abuse
- No analgesic properties.

Use:- 2mg QD → QID

Diphenoxylate: prescription opoid. • prolong use → dependence.
↓
commercial prep:- contain Atropine (2.5mg Dip + 0.025mg atropine) to avoid overdose. — synergistic effect

✓ Atropine → anti-chol → anti cholinergic

*- AGENTS MODIFYING FLUID & Electo. Transp.

Bismuth subsalicy. → For Traveler's Diarrhoa
↓se fluid secretion in bowel

Action may be due to its salicylate compound/component as well as its coating Action.

ADRs:- Black tongue & Black stool.

*- ADSORBENTS: presumbaly act by ADSORBING intestinal toxins or micro-org and/or by coating or protecting intes. mucosa.

⇨ less effective than other • interfere ē absor. of other drugs
- Safe because NOT abs. system.

BILE-SALT BINDING RESIN

Conjugated B.S normally abs. in Terminal Ileum.

Disease in Ileum ile. (Crohn's disease) ↓ malabs. of bile salt → Secretory Diarrhea due to excess bile acid.

ADRs. ↓ Bloating, Flatulence, Constip., fecal impacti ↓ Unable to push out large, hard mass of stool that get stuck badly in colon

Cautions ↓
- In pts ē diminish bile salts/acid further removal of bile acid ↓ Use fats malabsorption.
- cholestyram & colistipol bind a no. of drug, so they should n't be given ēn 2hr of other drugs

avail in powder & pills
- once → thrice before meal.

OCTREOTIDE:

Analog of natural hormone somatostatin

↓

release in GIT from and pancreas

(Paracrine signaling = cell produce a signal/hormone to induce changes in nearby cells)

Autocrine: Act on same cell which produce that hormone.

paracrine cell (Delta) → D-cells (somatostatin producing cells present in stomach, intestine, pancreatic islets) → enteric nerve → Hypothalamus

Roles of somatostatin

- Inhibit secretion of numerous hormones & transmitters
  - ✓ Gastrin (Stimulate gastric acid prodn)
  - ✓ cholecystokinin (Fat & protein absorption in GIT)
  - ✓ Glucagon - α-cells = ↑ Glucose
  - ✓ Growth hormone - (use in acromegaly)
  - ✓ Insulin
  - ✓ secretin - release by duodenum → ① gastric acid regulation ② Pancreatic bicarbonate regul. ③ Osmoregulation (salt & H_2O balance) ← secretin release in response to acidity
  - ✓ pancreatic polypeptide → regulate pancreatic & gastric secretion - mainly inhibition → ↓ motility
  - ✓ 5-HT (Stabilize mood & happiness)
- ↓se intestinal fluid and pancreatic secret.
- slow GIT motility and inhibt Gallbladder contraction
- ↓se portal & splanchnic Blood flow → Thus use in internal bleeding
- ↓se secretion of anterior pituitary hormone

KINETICS:-

Somatostatin $t_{1/2}$ = 3 min when adm IV

Octreotide $t_{1/2}$ = 1.5 hrs IV, can also be given s/c — 6-12 hr duration.

↓

I/M → once monthly

USES

Inhibition of Endocrine Tumor effects

- Carcinoid & VIPoma
  - (Neuroendocrine tumor)
  - (endocrine tumor = ↑ VIP → vasodilator → ↑ BF, regulate S/m activity; ↑ secretion → vasoactive peptide)
  - → Secretory diarrhea, flushing, wheezing.
- So in pts in which tumor can't be removed - Octreotide ↓se diarrhea & by inhib. of other hormones → ↓se tumor progression.

Dose-related effect

- low dose → ↓ Stimulate motility (50 mcg s/c)
- High doses (100-250 mcg s/c) → ↓ inhibit motility

ADRs

- N/V/ Abdom. pain
- Hormone related effects
- Gallstone formation
- long-term use.