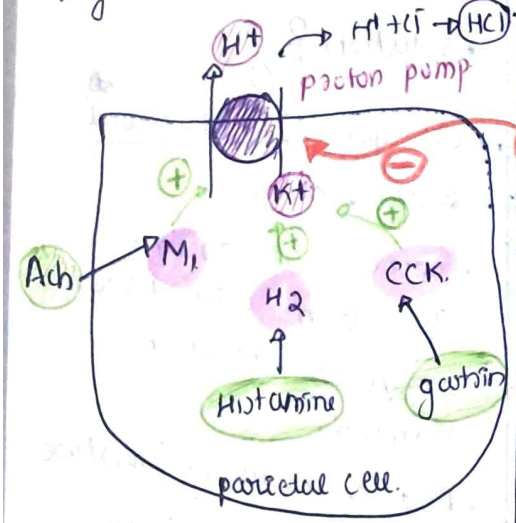
Peptic Ulcer Disease

- we all know, ulcer occurs due to ↑ acid effect, so first Rx → to decrease acid production

① ↓ acid production

how is acid formed?

→ from parietal cell.



- On parietal cell, there is proton pump - H+ - K+ pump.
- Ach, Histamine, Gastrin activate that pump through various receptors and ↑ acid production
- PGE_2 blocks / inhibits the pump.

So, treatment can be done by:

M1
H2
CCK
} receptor blockers.

OR

PGE_2 → Level ↑

OR

(-) proton pump itself.

- we don't have CCK blocker.

So, Rx is by (4) ways.

- M_1 receptor blocker
- H_2 receptor blocker
- PGE_2
- proton pump inhibitors

I. M1 Blocker.

- pirenzepine
- Telenzepine.

II. H2 blocker.

Cimetidine. XX not used now.
Ranitidine. → (-) me
Famotidine. → Disco.
Loxatidine.
Nizatidine.

Cimetidine - not used now.

① Strong microsomal enzyme (-), so many drug interaction.

② Disco drug.

Digoxin
↑ "
Spironolactone.
Cimetidine.
Oestrogen.
↓
Gynaecomastia.

III. PGE_2

- protect stomach by:

① ↓ HCl → PPT.

② mucous, HCO_3^- secretion ↑

③ vasodilation
↓
↑ blood flow to stomach.

" Gastro protective action".

- so, NSAIDs.
↓
peptic ulcer.
↓
NSAID induced peptic ulcer.
↓
Specific drug for NSAID induced PUD
↓
misoprostol (PGE_1) XX not used.

- S/E ↑↑
- less effective.

so what will we see:

Proton Pump Inhibitors

↓

They are the

DOC for

NSAID induced PUD

↓

not just that, But

↓

PPI are the

DOC of PUD

due to any reasons.

4) PPI

- They are the strongest as they directly act on proton pump. (pyzoles)
  - omeprazole.
  - Esomeprazole.
  - Pantoprazole.
  - Lansoprazole.
  - Dexlansoprazole.
  - Rabeprazole.

They are the strongest and ~~has~~ is very Safe

So, DOC in PUD due to any cause.

NOTE:

PPI are the drug of choice for PUD due to any cause, be it stress, vagal, NSAID induced.... anything.

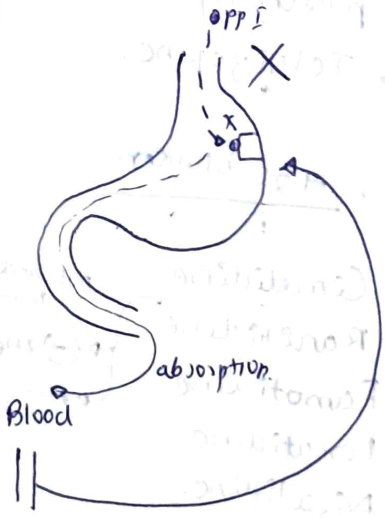
- apart from that, they are also drug of choice in other conditions:

PPI

DOC

↓

- PUD ✓
- GERD ✓
- Zollinger Ellison ✓ syndrome



- PPI's action is not (local) X

ie, they don't reach stomach and directly act on PPI in stomach X

- they go to intestine, get absorbed, and then act on parietal cell.

1) systemic action ✓

- But they are acid labile.

- solution ?

2) we give Enteric coated drugs - always

- Enteric coat doesn't degrade in acid medium so remains intact in stomach
- But on reaching Intestine in alkaline medium. the Enteric coat will dissolve to release the PPI.

3) they are pro drugs

- they need slightly acidic medium for activation.

↓

In blood pH = 7.4

So, they won't get activated.

But on reaching inside parietal cell.

↓

Intracellular medium is slightly acidic.
{not too much that it degrades}

↓

PPI only gets activated on reaching inside parietal cell.

④ They are Irreversible Inhibitors.

↓

once bound they won't let that particular parietal cell to function.

↓

acid secretion resumes only after new parietal cells are formed.

↓

and the time taken for that is

↓

24 hours

- ie, Irrespective of each PPI half life. Or duration of action, we always give any PPI for 24 hours duration.

- i.e, till new p.cells are formed.

- we need not focus about duration of A or half life.

eg: Omeprazol - 30 min $T_{1/2}$

↓

still we only give once per day.

↓

So, they are hit & Run drugs

↓

ie, Even after drug has been excreted from body, their effect still remains for 24 hours.

- Irreversible drugs are mostly Hit & run drugs.

eg: Aspirin
MAO - inhibitors.

- Normally, PPIs are very safe

- But if we are giving PPIs for prolonged duration {years} then those substances that needs acidic medium to get absorbed, will be deficient.

(years)

In long term PPI users

↓

↓ Ca → osteoporosis.

↓ Vit B_{12} → megaloblastic anemia

ie, If we are planning to give long term PPIs

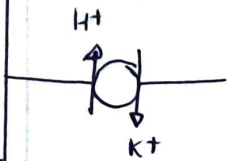
↓

ensure Ca & Vit B_{12} supplementation.

* also Long-term uses has also been associated with ↑ infections overall {not just GIT, pneumonia like too}

K-CAB

K - Competitive Acid blocker



- KCAB - competes with potassium for binding and block proton pump.
- They are faster acting than PPIs
- They are reversible.

• K CAB are reversible PPIs ends in (Prazan).

eg: Vonoprazan.

Antacids. (2)

• See, those blockers, PPI, PGE_2 etc... further acid production.

But, what about pain on ulcers caused by already present acid.

↓

So we need to neutralize already present acid, right?

↓

So that we can relieve pain.

↓ for that we use.

ANTACIDS

↓

fastest pain relief method in epigastric pain due to ulcers.

• $Mg(OH)_2$ - diarrhea

• $Al(OH)_3$ - constipation

~~were~~ our IQ is 1000+.. so we give them both together.

→ Antacids have both Mg & Al hydroxides

:)

(3) Ulcer protective Drugs.

• they protect ulcers from HCl action, so that they can heal. & don't worsen further.

• they form layer on ulcer.

• Drugs →

• Sucralfate.

• Colloidal Bismuth Subcitrate (CBS)

• problems... Hein...

• Sucralfate is small molecule right?

• So for it to form a layer... it should polymerise.

• only then, it can polymerize.

→ for it's polymerization (PH < 4).

• So NEVER GIVE antacids with Sucralfate.

- If both needs to be given...

we leave a time gap of

120 min

- we give Sucralfate 1st
  ↓
  give time for it to polymerize
  ↓
  then give PPI after 120min

another problem...

- Since it forms a layer in stomach, it will inhibit absorption of drugs in stomach.
  ↓
  So we that drugs that needs acidic environment in stomach for absorption
  ↓
  doesn't get absorbed.

- So, for that too, we require min 120 min. gap if we are planning to give any drug that is absorbed from stomach
- eg: Phenytoin.

CBS

- If CBS is overdosed.
- there will be Bismuth poisoning.

Bismuth poisoning.

- Bone → Osteodystrophy
- Brain → Encephalopathy

antidote: BAL.

- Bi
- Arsenic
- lead.

BAL is the antidote for. Bismuth, Arsenic, lead poisoning.

4) Antibiotics.

OK?

Lemme ask u a question....

what is DOC in PUD?

– PPI.

- what is DOC in PUD caused by H. pylori?

Still PPI

- we said earlier right?

PPI are the DOC in PUD due to any cause.

- A person has PU due to H. pylori...
- Can PPI cure that ulcer?

- of course it can!
- ulcer will be cured...

The problem is if we don't kill H. pylori... it'll cause ulcer again after sometime.

ie, The problem with H. pylori is

Relapse.

- If we are treating a patient for PU and if he gets it again & again, that's when we suspect H. pylori.

So for H. pylori caused ulcer

↓

Treatment:

- PPI
- Antibiotic for preventing recurrence.

3 Ab are approved.

- Amoxycillin
- Clarithromycin.
- Metronidazole.

Treatment

TRIPLE DRUG THERAPY.

PPI + 2 AMA

↳ any 2 of above.

- Triple drug therapy – 2 weeks.

India

TDT → C.A.P.

PPI

Clarithro

Amoxi

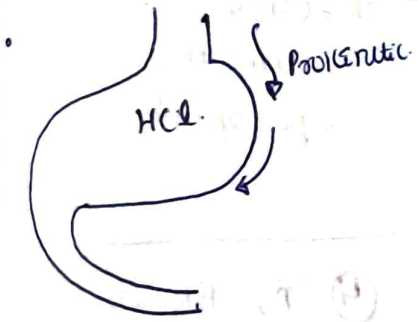
Anti-Emetics & Prokinetics

UQ antiemetic
1. metoclopramide
2. Ondansetron
3. Aprepitant

(M+O) in chemo vomiting
- Ond - MOA, ADR.
- meto - MOA

prokinetics
- Super ORS

GERD



- In GERD - acid is refluxing into esophagus
- stomach has protection so acid won't cause problems
- But Oesophagus has no protection like stomach
- burns

GERD
DOC = PPI
but clinically, Combinations are given

How to treat it?

1. problem is due to acid so ↓ acid production
   - use: PPI — DOC
2. Increase motility - ↑ forward motility so that stomach contents are going down and not back up!
   - use prokinetic drugs
   - drugs that increases ↑ upper GI motility ✓ (not lower OK?)

Prokinetics

1. 5HT4 agonists
   - Cisapride (XX not used) — QT prolongation (CAT drugs)
   - Mosapride
   - Prucalopride.
2. D_2 blocker.
   - dopamine acts on dopamine receptors in stomach and brain (CTZ) and induce vomiting.

Pan D
Pantoprazole + Domperidone

1. dopamine induces vomiting. (by increasing gastric emptying time → so food in stomach can't go to intestine... so it induces vomiting
2. dopamine ↓ Ach release

- when dopamine receptors are blocked

dopamine induced
1. Vomiting ✗
2. Ach ↑ contractions & motility ↑

eg: METOCLOPRAMIDE
DOMPERIDONE
Itopride
↳ this pride isn't 5HT4 agonist
don't be confused

3. Macrolides.
   - stimulate motilin receptors in stomach.
   - ↓
   - not that used.

Anti-emetic

① DOC for prophylaxis of motion sickness.

↓

Hyoscine {Scopolamine}

Oral — 30 min before travel.

Transdermal — 12-24 before ↓ slowly absorbed.

⇒

② First generation anti-histaminic.

↓

Promethezine

② Morning sickness

DOC: Doxylamine

1st gen antihistaminics

③ Chemotherapy Induced Vomiting. (CINV)

- many cell destruction
↓
loss of serotonin release
↓
⊕ CT_2 receptor of brain
↓
Vomiting

Drugs used.

① $5HT_3$ receptor blocker

Ondansetron
Granisetron
Tropisetron
Palanosetron — most potent setron.

DOC

② Substance P antagonist — PITANTS

- APREPITANT
- FOSAPREPITANT
- ROLAPITANT
- NETUPITANT

③ steroid.

DEXAMETHASONE.

④ D_2 blockers

- doc in CINV
→ setrons
- in delayed vomiting
→ substance P analogues

Chemotherapy

early (<24 hrs) → setrons.

delayed (>24 hrs) → Substance P antagonists (DOC)

Substance P → NK_1 receptor (Neurokinin)

antagonist acts on

DOC in

- CINV
- radio-INV
- post op INV

④ D_2 Blockers

Metoclopramide	Domperidone
BBB ✓	✗
$5HT_4$ ⊕	✗
$5HT_3$ ⊕	✗

more effective: metoclop as ⊕ acts on other receptors.

metoclopramide crosses BBB

↓

Excess block of D_2 receptors in brain

↓

cause Extrapyramidal symptom

↓

Dystonia : earliest s/e

↓

Caused by metoclopramide

- treatment : dystonia.

- to relive that →

D_2 receptor blocker.

- what to use ?

metoclopramide / domperidon ?

- metoclopramide crosses BBB and will block D_2 inside brain too...

ie, cancel parkinsonism treatment also.

- that's not good :'

- So, use domperidone that only blocks peripheral D_2 receptors.

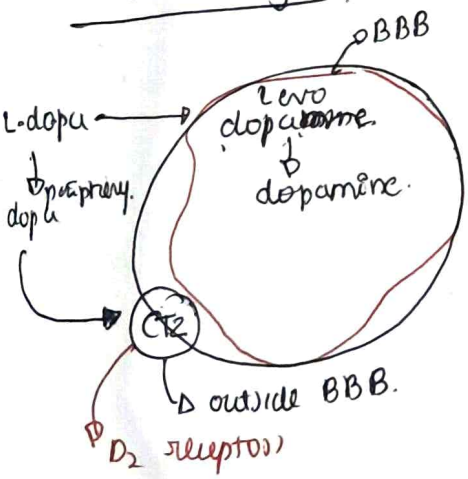
Infectious diarrhea

- Bacterial → DOC → FQ
- amoebic → DOC → nidazole / nitranidazole.

Bact - fever + vomit

Amoeba - diarrhea only

Levodopa Induced vomiting



- L-dopa → dopamine inside & outside too.

↓

- act on CT2 receptors outside BBB
- dopamine can't cross BBB. (formed out)
- but will act on D_2 receptors on CT2.

LINV → DOC

↓

Domperidone.

Diarrhea.

1. ORS

- Sodium chloride
- potassium chloride
- Trisodium citrate
- Glucose.

Electrolyte replacement

⊖ acidosis

help in sodium absorption.

(2) If any cause, treat cause.