

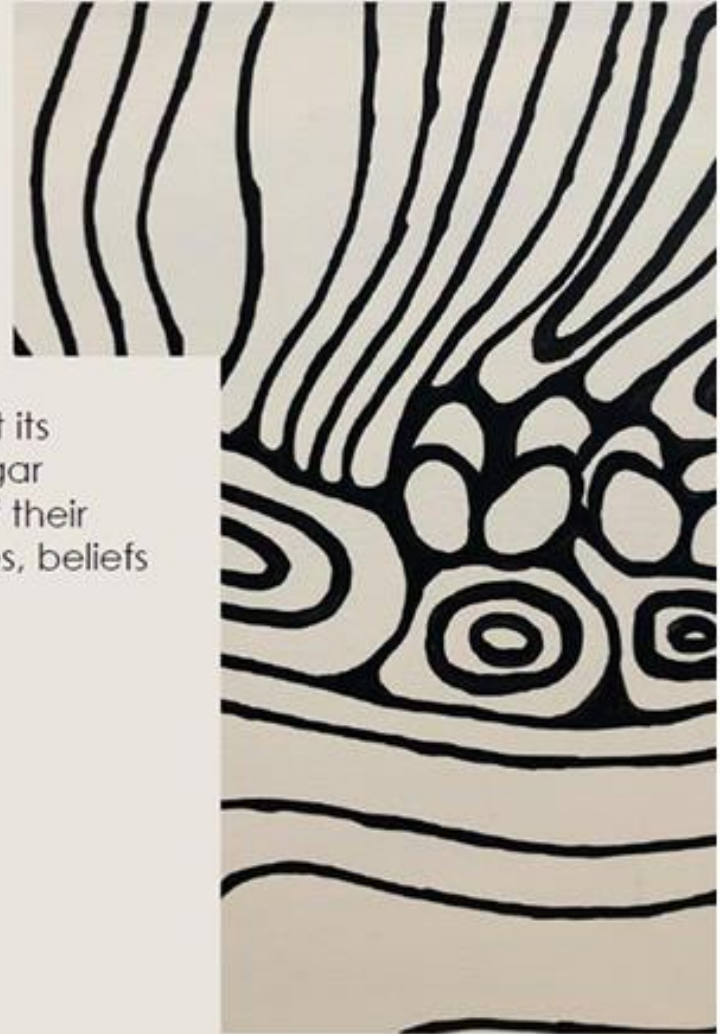
# DENT 3005: Introduction to Pharmacology

## **Gastrointestinal drugs**

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# Acknowledgement of country

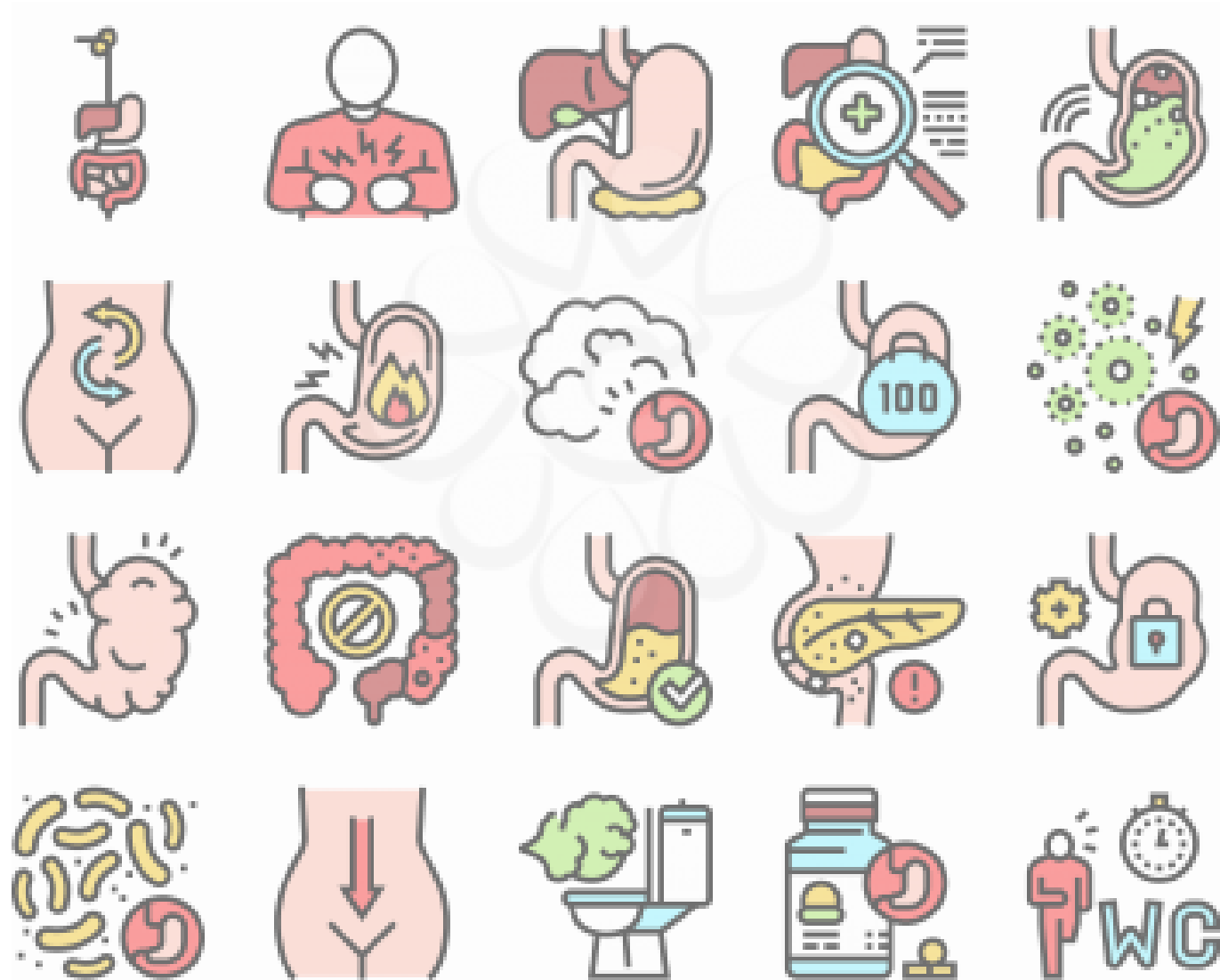
The University of Western Australia acknowledges that its campus is situated on Noongar land, and that Noongar people remain the spiritual and cultural custodians of their land, and continue to practise their values, languages, beliefs and knowledge.



# Learning Outcomes

## Learning objectives

- 1) Understand the classes and mechanisms of major classes of GI drugs
- 2) Recognise common GI conditions managed with these drugs
- 3) Recognise oral and dental side effects of GI drugs
- 4) Understand the oral impact of GI conditions
- 5) Understand drugs interactions with dental medications
- 6) Applied knowledge to clinical scenarios



# Gastrointestinal drugs

- Ulcers
  - Dyspepsia: chronic/recurrent pain, burning or discomfort centered in upper abdomen
  - GORD: chronic & relapsing condition
  - PUD: H-pylori most common cause, others medication induced
  - Drug therapy: Antacids, H2 antagonists, PPIs, other drugs for ulcer
- Laxatives
- Anti-emetics
- Anti-diarrheal
- Inflammatory bowel disease
- Obesity
- Perianal disorder

## Antacids

- **MOA:** neutralize hydrochloric acid secreted by gastric parietal cells
- **Dental implications:** nil
- **Drug interaction:** reduce absorption of many drugs

## H<sub>2</sub> antagonists

- **MOA:** competitively block H<sub>2</sub> receptors on parietal cells, Reduce gastric acid secretion
- **Dental implication:** dry mouth, taste disorder
- **Drug interaction:** reduce absorption of azoles

Generic name	Brand Name
Aluminum hydroxide	Alu-tab
Combo antacids	Mylanta, Rennie

Generic name	Brand Name
Famotidine	Ausfam, Pepzan
Nizatidine	Nizac, Tazac
Ranitidine	Ausran, Rani

# Proton Pump Inhibitors

- **MOA:** irreversibly inactivate proton pump
  - Suppress stimulated & basal acid secretion
- **Dental implications:** dry mouth, taste disturbance
  - Implant failure???
- **Drug interaction:** reduce absorption of azoles

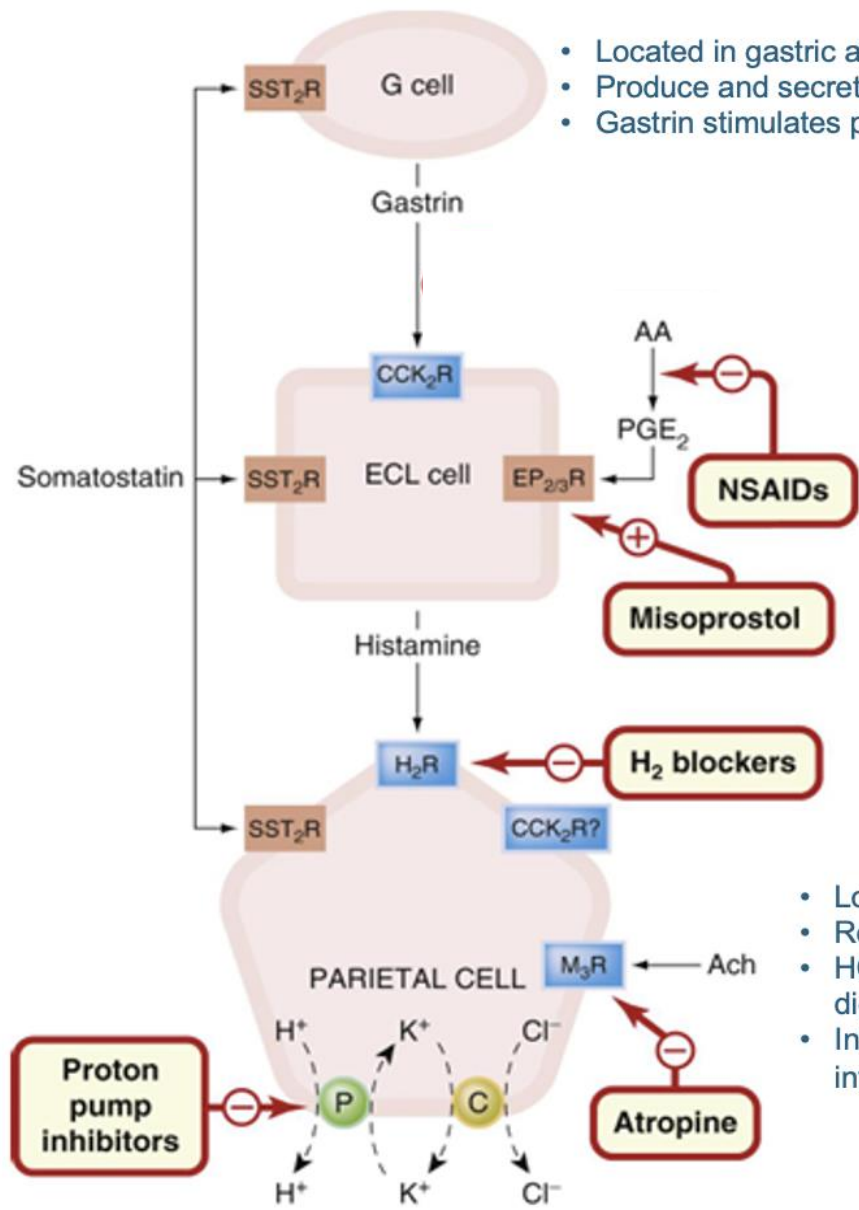
## Other drugs for ulcers

- **Bismuth subcitrate & sucralfate**
  - **MOA:** forms acid & pepsin resistant coating at ulcer site
  - [Bismuth Sub] ADR: darkening of teeth & tongue
  - [Sucralfate]: Dry mouth
- **Misoprostol**
  - Prostaglandin E analogue: increase mucus secretion in stomach

Generic name	Brand Name
Esomeprazole	Nexium
Lansoprazole	Zopral, Zoton
Omeprazole	Acimax, Losec
Pantoprazole	Somac
Rabeprazole	Pariet

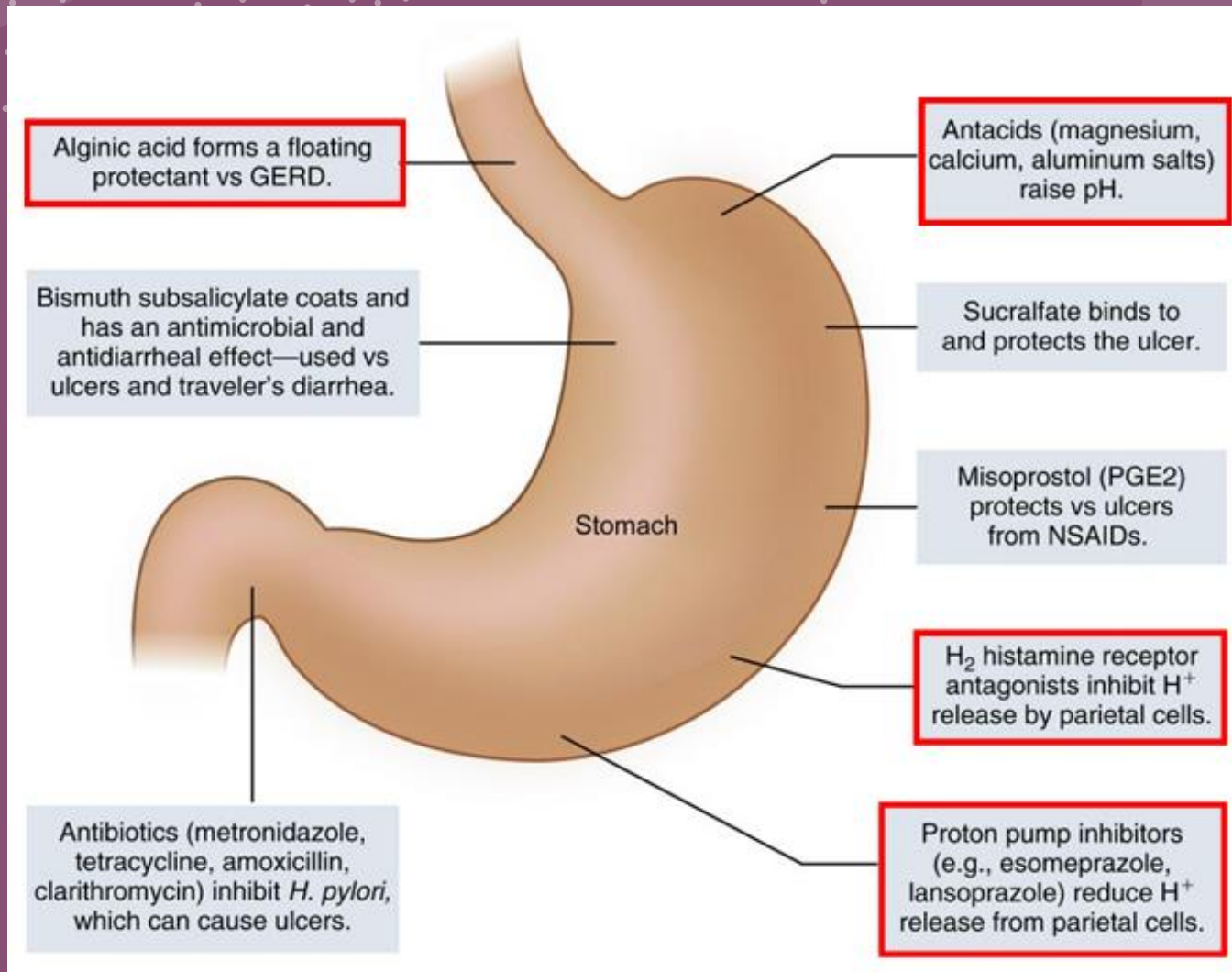
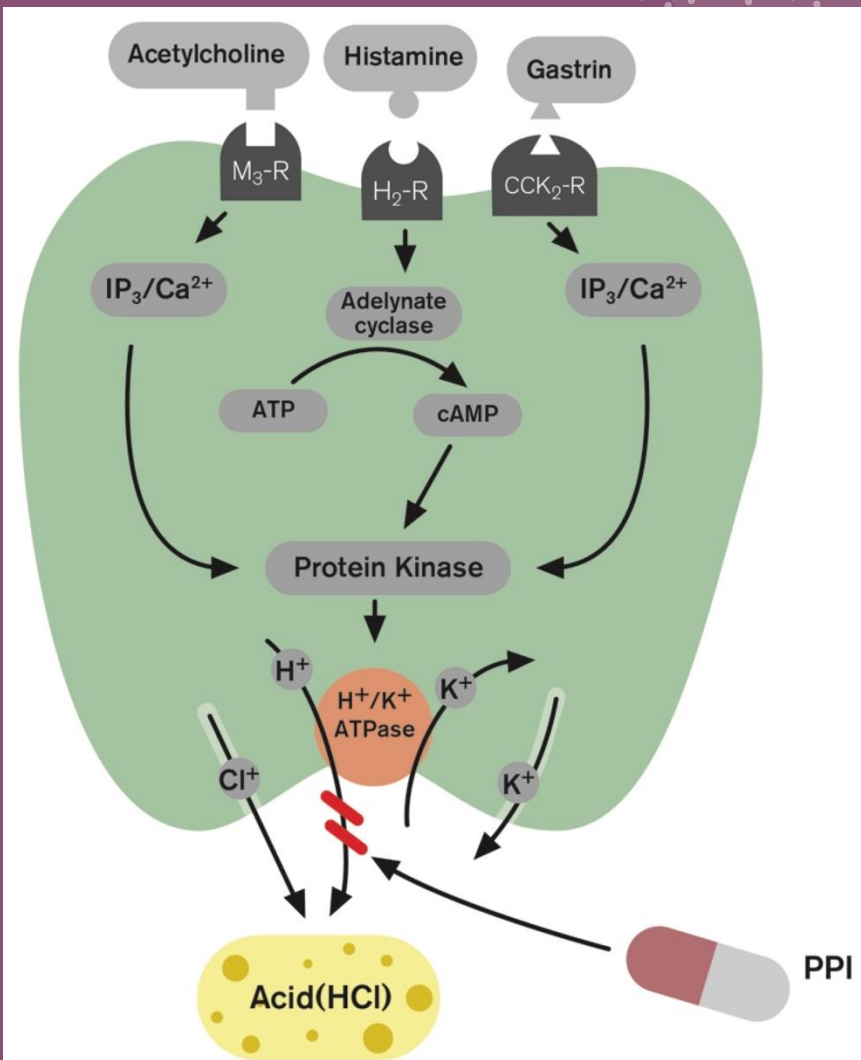
Generic name	Brand Name
Bismuth subcitrate	Bismuth subcitrate
Sucralfate	Ulcyte
Misoprostol	Cytotec

- Located in gastric mucosa
- Secrete histamine – stimulates parietal cells to produce HCl
- Histamine released by ECL binds to the H<sub>2</sub> receptor on parietal cells enhancing acid secretion



- Located in gastric antrum of stomach and duodenum
- Produce and secrete gastrin- secretes gastric acid secretion
- Gastrin stimulates parietal cells to secrete HCl

- Located in gastric mucosa
- Responsible for secreting HCl and intrinsic factor
- HCl – creates an acidic environment – for protein digestion/ activation of digestive enzymes.
- Intrinsic factor- for vitamin B12 absorption in small intestine



# Laxatives

- **Stool softener:** docusate, liq paraffin, poloxamer
- **Stimulant laxative:** bisacodyl, senna, sodium picosulfate
  - Act on nerve endings in colonic mucosa → increase intestinal motility
- **Osmotic laxative:** glycerol, lactulose, macrogol, saline laxatives, sorbitol
  - Non-absorbable sugar → draw water into feces
- **Other**
  - Bulk forming: absorb water in colon → increase fecal bulk
  - Methylnaltrexone: Mu opioid receptor antagonist
  - Prucalopride: 5HT4 receptor agonist → increase GI motility

## Laxatives

### Stool softeners

Docusate

Liquid paraffin

Poloxamer

### Stimulant laxatives

Bisacodyl

Senna

Sodium picosulfate

### Osmotic laxatives

Glycerol

Lactulose

Macrogol laxatives

Saline laxatives

Sorbitol

### Other laxatives

Bulk-forming laxatives

Methylnaltrexone

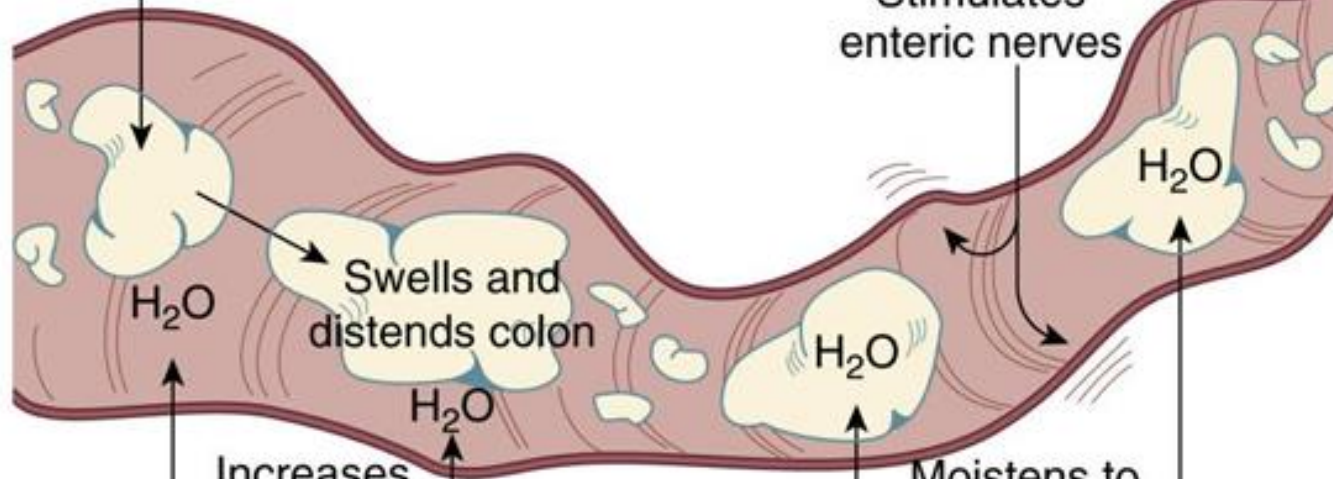
Prucalopride

### Bulk-forming

Examples:

- psyllium
- methylcellulose
- polycarbophil

Increases stool mass



Swells and distends colon

Increases fluid volume

### Osmotic

Examples:

- magnesium hydroxide
- lactulose
- polyethylene glycol (PEG)

### Stimulant (irritant)

Examples:

- bisacodyl
- senna
- castor oil

Stimulates enteric nerves

Moistens to ease passage

### Wetting agents

Examples:

- docusate
- mineral oil

# Anti-emetics

- **Nausea & vomiting**
  - Rationale: prevent/ relieve sx
  - Prevent complications (dehydration, electrolyte disturbance)
- **Dopamine antagonists**
- **Sedating antihistamines**
  - Pheniramine & promethazine: px motion sickness
- **Anticholinergics**
  - Hyoscine hydrobromide: px motion sickness
- **5HT3 antagonists, substance P antagonists, corticosteroids**
  - Px nausea & vomiting assoc w/ chemotherapy

## Dopamine antagonists

- **MOA:** block dopamine receptor in CTZ
- **Dental implications:** dry mouth
- **Drug interaction:** prolongation of QT interval
  - +Clarithromycin, erythromycin, fluconazole, moxifloxacin

## 5HT3 antagonists

- **MOA:** block serotonin (5-HT3) receptors in the brain and gut
- [Granisetron] ADR: dry mouth, taste disturbance
- **Dental implications**
  - Not directly but normally use adjunct in chemotherapy

Generic name	Brand Name
Domperidone	Motilium
Droperidol	Droperidol inj
Haloperidol	Serenace
Metoclopramide	Maxolon
Prochlorperazine	Stemetil

Generic name	Brand Name
Granisetron	Kytril
Ondansetron	Ondaz
Palonosetron	Aloxi inj
Tropisetron	Tropisetron inj

## Sedating antihistamines

- **MOA:** H<sub>1</sub> receptor and stabilising it in an inactive form
- **Dental implications:** sedation, dry mouth
- **Drug interaction:** nil in dental setting

## Anticholinergics

- **MOA:** Block muscarinic actions of acetylcholine
- **Dental implications:** sedation, dry mouth
- **Drug interaction:** nil in dental setting

Generic name	Brand Name
Cyclizine	Nausicalm
Promethazine	Allersoothe, Phenergan

Generic name	Brand Name
Hyoscine hydrobromide	Kwells, Travacalm

# Substance P antagonists

- **AKA:** Also known as neurokinin-1 (NK1) receptor antagonists
- **MOA:** antagonize substance P/neurokinin-1 receptors.
- **ADR:** hiccups
- **Drug interaction**
  - [CYP3A4 inH] azoles, clarithromycin, erythromycin: increase conc of substance P antagonist

Generic name	Brand Name
Aprepitant	Aprepitant
Fosaprepitant	Emend inj
Fosnetupitant (+palonosetron)	Akynzeo inj

# Anti-diarrheal

- **Rationale for drug therapy**
  - Px dehydration & electrolyte disturbance
  - Sx relief
  - Tx of infection
- **Acute diarrhea:** self limiting
- **Chronic diarrhea:** underlying disease req investigations
- **Drug therapy choice**
  - ORS: 1<sup>st</sup> line in children
  - Opioid antidiarrheals: short term tx

Generic name	Brand Name
Codeine	Codeine phosphate Actacode linctus
Diphenoxylate + Atropine	Lofenoxal Lomotil
Loperamide	Imodium

# Inflammatory bowel disease

- **Crohn's disease & ulcerative colitis**
  - Tx rationale: relieve sx & improve QOL, induce & maintain remission, px complications
- **Corticosteroids**
  - Budesonide (oral), prednisolone (rectal)
  - Adrenal suppression possible w/ budesonide
  - Steroids ADRs
- **5-aminosalicylates**
  - Mesalazine, Olsalazine, Sulfasalazine

Crohn's	Ulcerative colitis
5-aminosalicylates	5-aminosalicylates
Azathioprine & mercaptopurine	Azathioprine & mercaptopurine
Corticosteroids	Corticosteroids
TNFa antagonists	TNFa antagonists
	Cyclosporin
MTX	
Antibacterials for perianal fissures - Metronidazole - Ciprofloxacin	



# Corticosteroids ADRs

- Infection
- Delayed wound healing
- Steroid rosacea
- Perioral dermatitis
- Skin atrophy
- Bruising
- Acne
- Facial flushing
- Pupura
- Depigmentation
- Telangiectasia
- Steroid induced crushing's

## 5-Aminosalicylates

- **MOA**
  - Anti-inflammatory, immunosuppressant.  
Exact mechanism unknown
  - Sulfasalazine: also indicated for RA (see RA lecture)
- **Indication:** UC, Crohn's
- **ADR & drug interaction:** no dental implication

Generic Name	Brand Name
Mesalazine	Mesasal Salofalk
Olsalazine	Dipentum
Sulfasalazine	Pyralin Salazopyrin

## TNF $\alpha$ antagonists

- **MOA:** binds & antagonize TNF $\alpha$  (cytokine involved in inflammatory & immune responses)
- **Common adverse effect include infections**
  - Persistent fever, other signs of infection, bruising, bleeding → Pt need to contact medical GP urgently
- **Also indicated for RA (see RA lecture)**

Generic name	Brand Name
Adalimumab	Humira inj
Golimumab	Simponi inj
Infliximab	Remicade inj

# Drugs for obesity

- **Orlistat**
  - **MOA:** inH GI lipases
  - Fecal urgency/incontinence
- **Phentermine**
  - **MOA:** sympathomimetic w/ CNS stimulatory effect
  - CNS overstimulation
    - Restlessness, nervousness, tachycardia, agitation, HTN, dry mouth!
- **Dietary and lifestyle factors**

Generic name	Brand Name
Orlistat	Xenical
Phentermine	Duromine

# Total parenteral nutrition

- **Total parenteral nutrition**
  - Method of feeding - Bypasses the gastrointestinal tract
  - Nutrition is given into a vein
  - Used when a person cannot or should not receive feedings or fluids by mouth
- **Pancreatic enzymes**
  - Pancreatic enzyme insufficiency: cystic fibrosis
  - Amylase, Lipase, Protease
  - Irritation of skin around mouth & anus

Generic name	Brand Name
Pancreatic enzymes	Creon
Ursodeoxycholic acid	Ursofalk



# Gastrointestinal drugs Dental implications

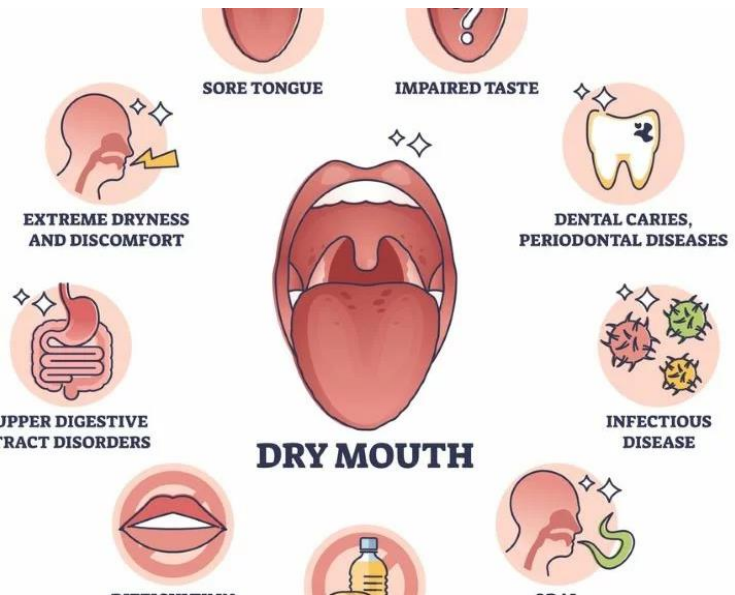
- **Drugs for gastric ulcer**
  - No real dental implications
  - However, uncontrolled acid secretions → dental erosions
  - Use of NSAIDs: close monitoring, risk Vs benefit
- **Drug interactions**
  - Antacids: most interaction avoided by dosing interval of at least 2hrs
  - Esomeprazole/omeprazole & diazepam
  - H2 antagonists & PPIs: decrease absorption of itra- & ketoconazole → reduce antifungal effect
  - Phentermine & tramadol: risks of seroT toxicity



# IBD

## Dental implications

- **Oral manifestations of Crohn's disease & UC**
  - Pyostomatitis vegetans: rare, abscess & pustular lesions
  - Recurrent aphthous ulcers: 1 or more
  - Atrophic glossitis: red glossy tongue appearance
  - Burning mouth syndrome
  - Angular cheilitis: scaling & crusting corner of mouth
  - Taste disturbance
  - Dry mouth
  - Halitosis
  - Periodontitis



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