Farmakoterapi

OBAT-OBAT YANG BEKERJA PADA SISTEM PENCERNAAN

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2024

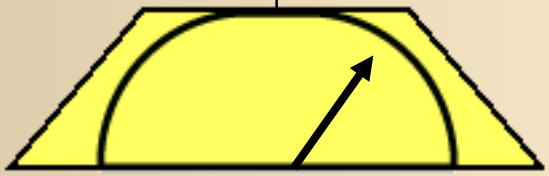
Topik

- Obat yang Mempengaruhi Sekresi HCl di lambung
- Obat yang Melindungi Mukosa Lambung (Mukoprotektan)
- Obat yang Mempengaruhi Peristaltik GIT

Lambung

Faktor yang meningkatkan keasaman (destruktif)

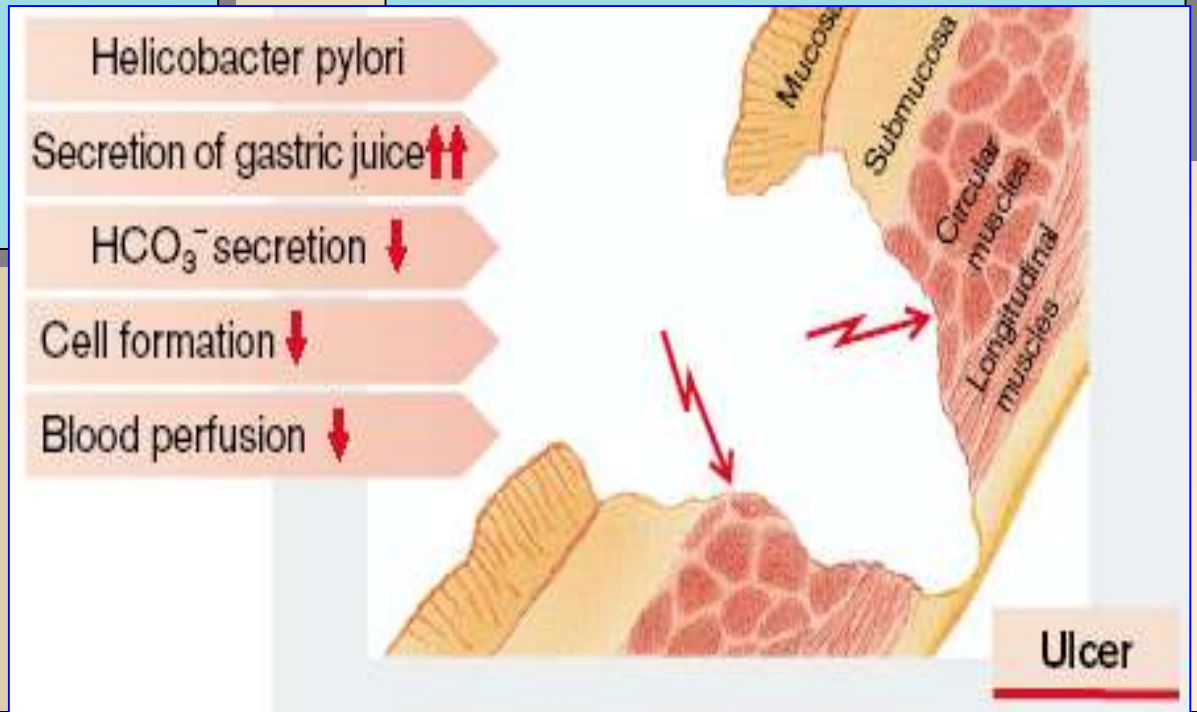
Faktor yang melindungi dari keasaman (protektif)



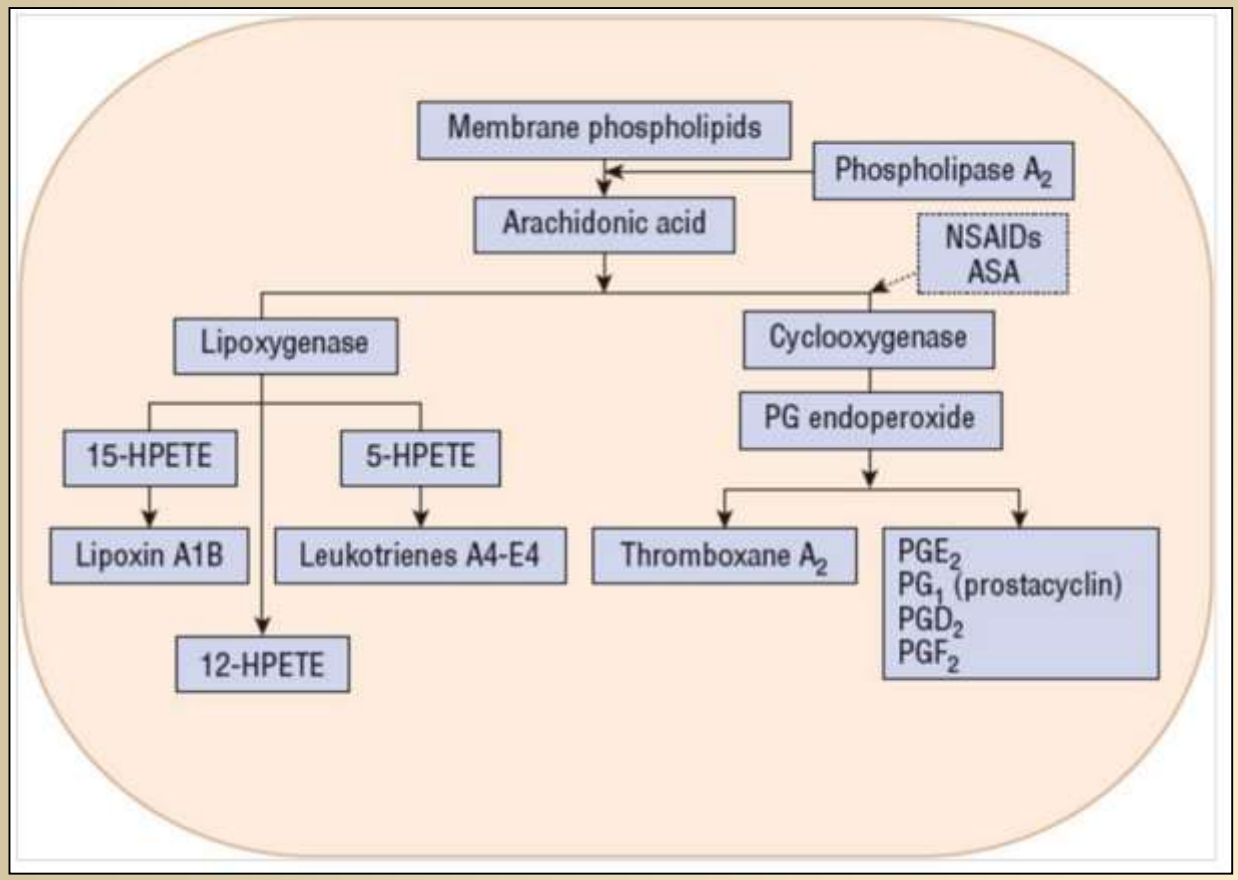
Lambung

- **Faktor Destruktif**
  - *Asam lambung*
  - Pepsin
  - *H. pylori*
  - NSAID, *Acidic agents,* Merokok (eksogen)

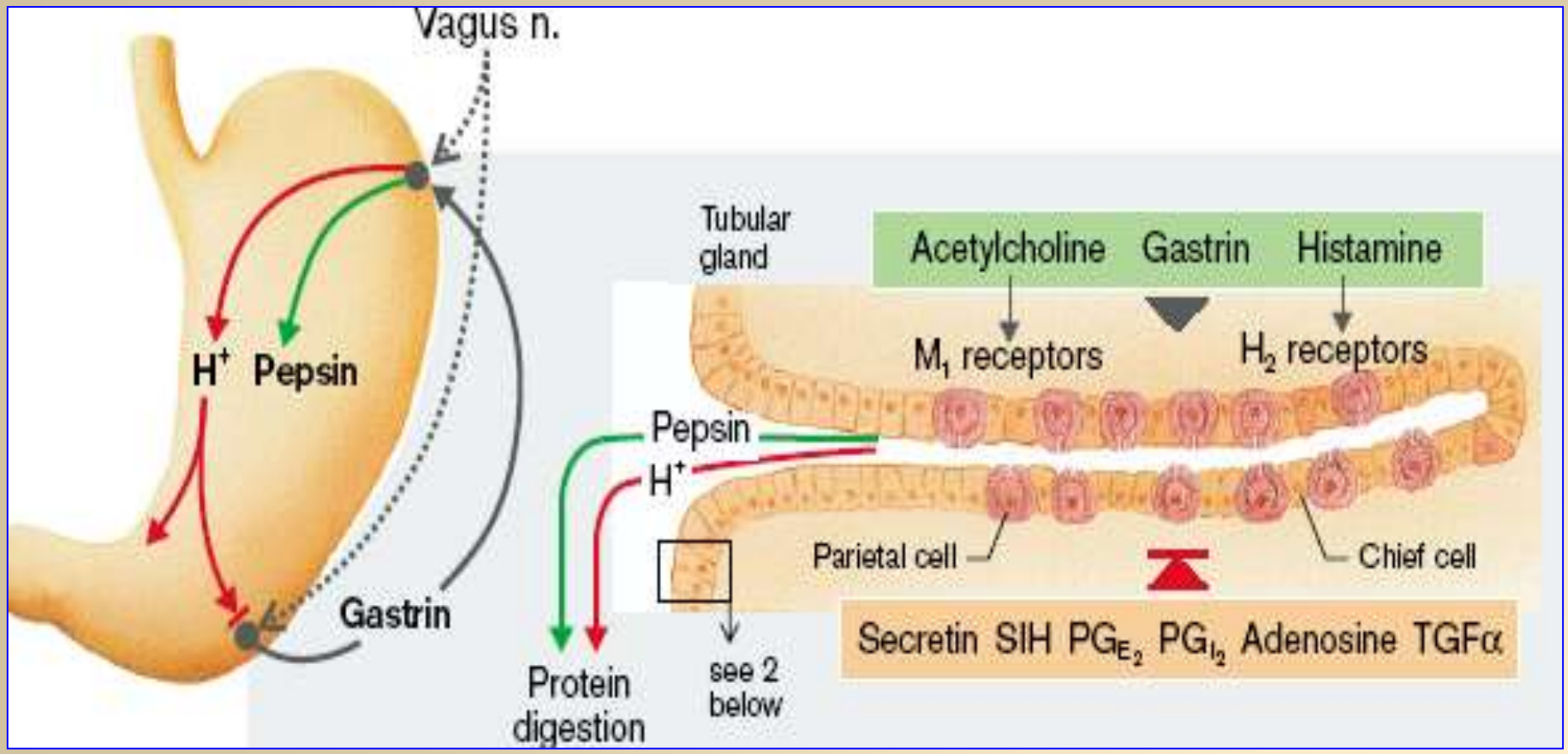
- **Faktor Protektif**
  - Produksi mukus
  - Buffer (HCO3-)
  - Prostaglandin
  - Aliran darah



NSAID-PG

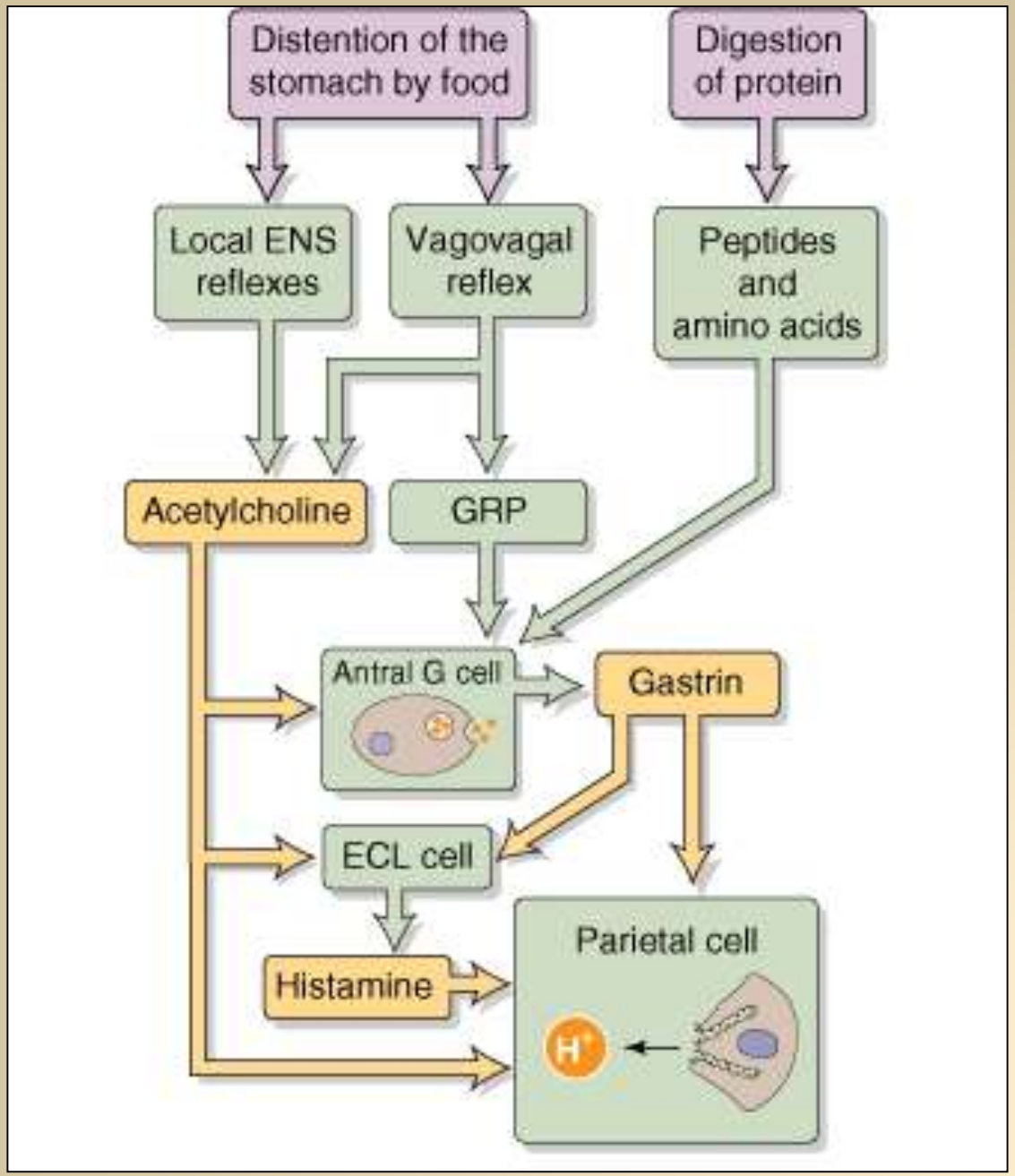

Membrane phospholipids
Phospholipase A_2
Arachidonic acid
NSAIDs
ASA
Lipoxygenase
Cyclooxygenase
PG endoperoxide
15-HPETE
5-HPETE
Lipoxin A1B
Leukotrienes A4-E4
Thromboxane A_2
PGE_2
PG_1 (prostacyclin)
PGD_2
PGF_2
12-HPETE

Pembentukan Asam Lambung

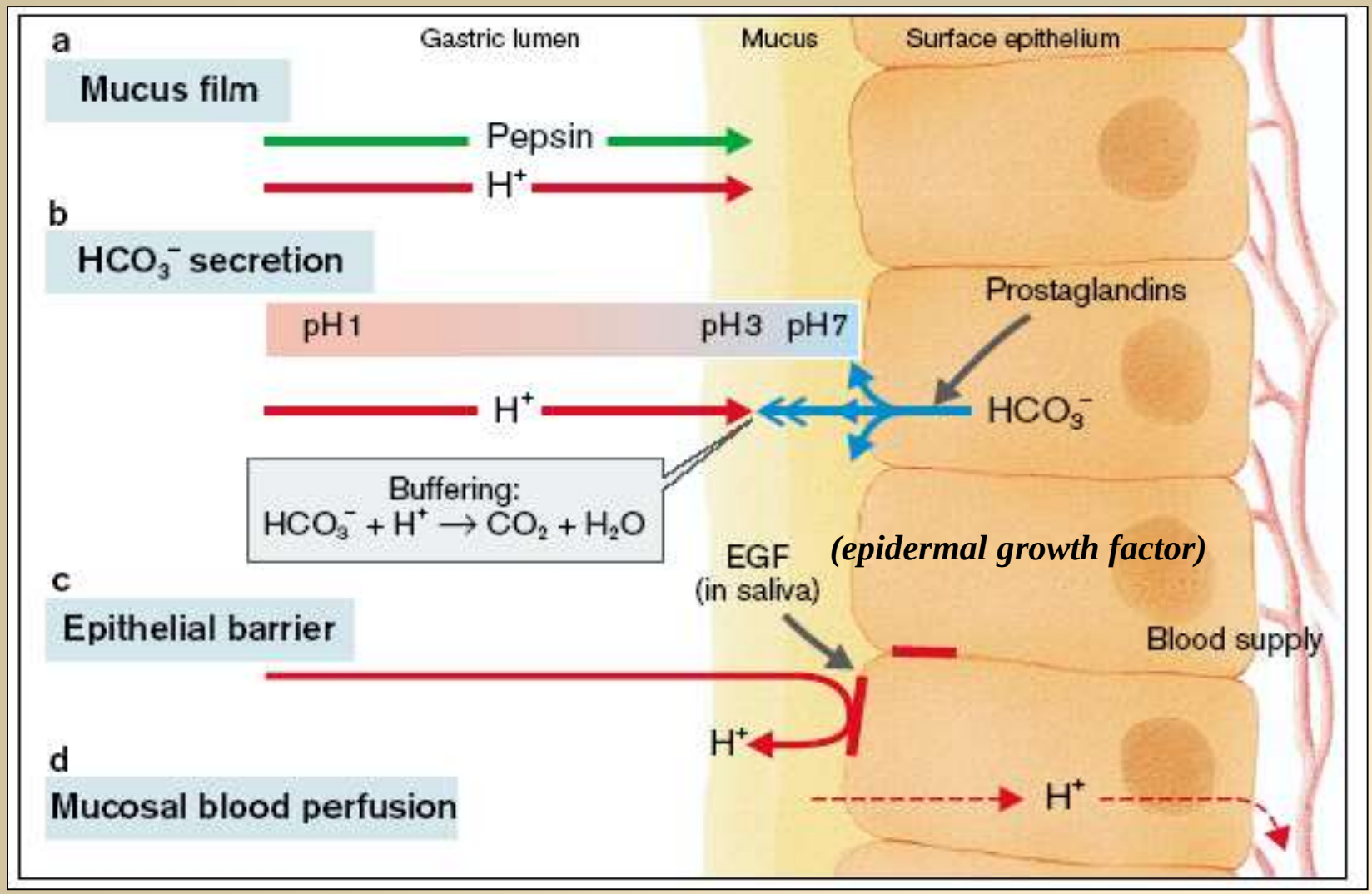


- The **regulation of gastric secretion** is achieved through neural, endocrine, paracrine, and autocrine mechanisms.
- **Stimulation** is provided by ***acetylcholine***, the postganglionic transmitter of vagal parasympathetic fibers (muscarinic M1 receptors and via neurons stimulating gastrin release by gastrin-releasing peptide [GRP]), ***gastrin*** (endocrine) originating from the G cells of the antrum, and ***histamine*** (paracrine, H2 receptor), secreted by the ECL cells and mast cells of the gastric wall.
- **Inhibitors** are ***secretin*** (endocrine) from the small intestine, ***somatostatin*** (SIH; paracrine) as well as ***prostaglandins*** (especially E2 and I2), transforming growth factor " (**TGFα**") and ***adenosine*** (all paracrines and autocrines). The inhibition of gastric secretion by a *high concentration of H+* ions in the gastric lumen is also an important regulatory mechanism (*negative feedback)*

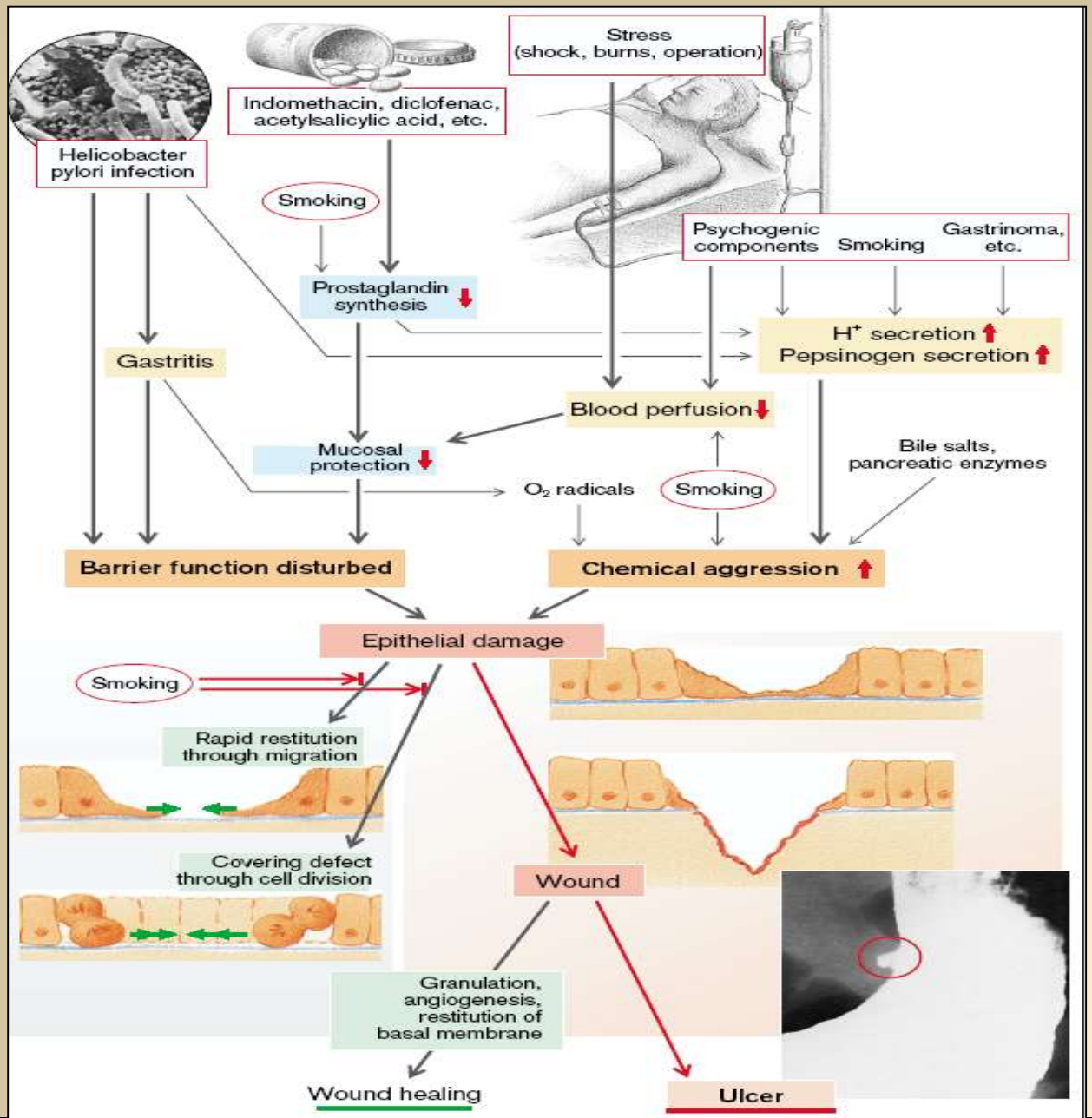
Gastric phase of gastric-acid secretion



Faktor Protektif



Pe↑ fakt destruktif → Pembentukan Ulkus



Acute stress ulcer

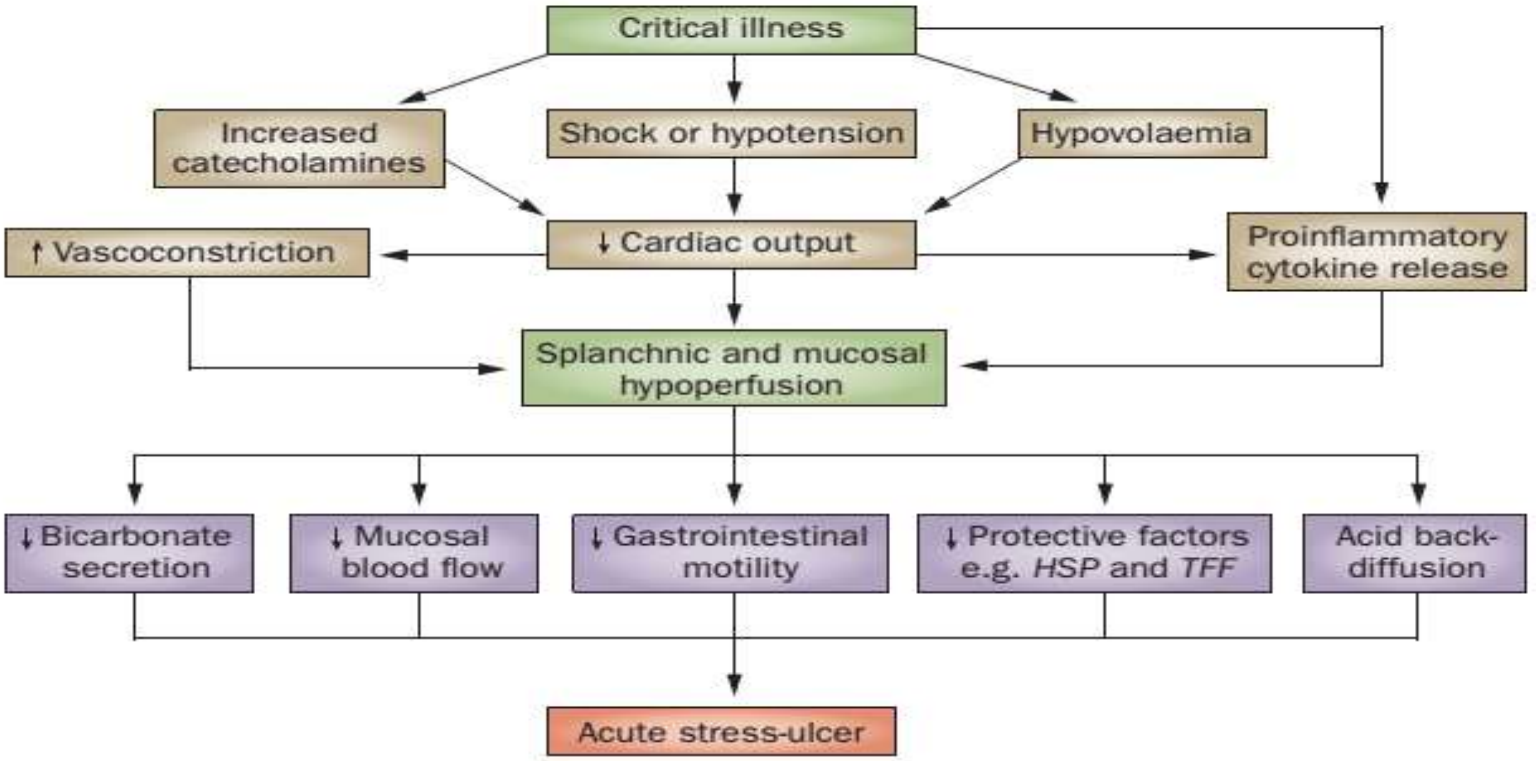
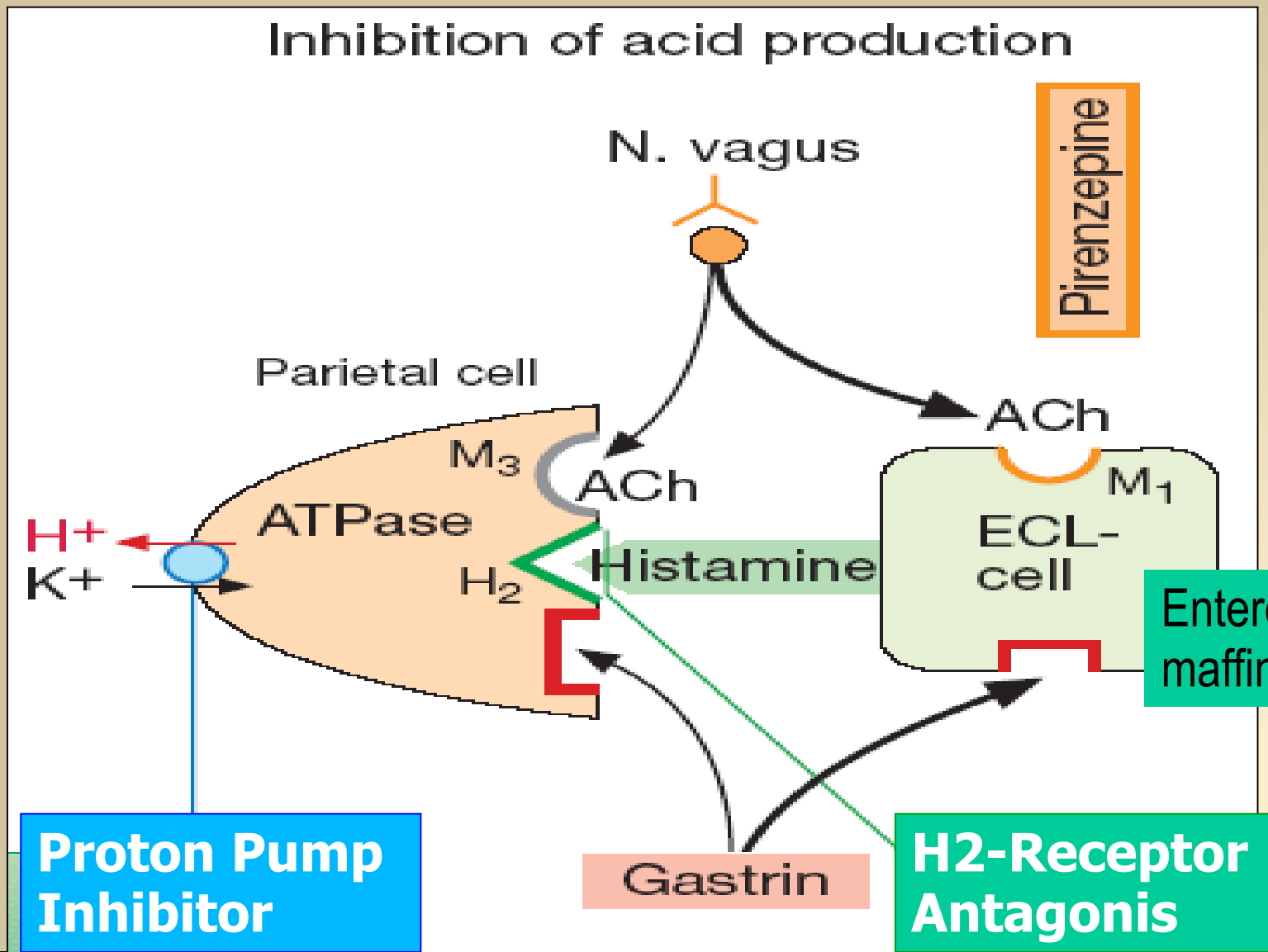


Figure 1 | Pathophysiology of stress-ulcer bleeding. Abbreviations: HSP, heat shock proteins; TFF, trefoil factor family peptides. Adapted with permission from Elsevier © Stollman, N. & Metz, D, *J. Crit. Care* **20**, 35–45 (2005).

Obat yang menghambat produksi asam



H_2 - Receptor Antagonist

- FD= blok sec kompetitif R/ H2 (tidak pada R/ H1) ➔hambat sekresi asam lambung (60%)
- Indikasi : ulkus Peptik, GERD,
- Golongan H2 Reseptor Antagonis :
  - ★cimetidine : inhibitor enzim P450
  - ★ranitidine
  - ★famotidine
  - ★nizatidine

	Cimetidine	Ranitidine	Famotidine	Nizatidine
Bioavailability	80	50	40	>90
Relative Potency	1	5 -10	32	5 -10
Half life (hrs)	1.5 - 2.3	1.6 - 2.4	2.5 - 4	1.1 -1.6
Duration of action (hrs)	6	8	12	8
Inhibition of CYP 450	1	0.1	0	0
Dose mg(bd)	400	150	20	150

Proton Pump Inhibitors (PPI)

- prodrug ➔ Saat lingkungan lambung asam➔ terbent metabolit aktif sulfenamid ➔berikatan secara kovalen (irreversibel) dg enzim K^+H^+ATPase yang berperan pd Proton Pump ➔hamb pertukaran H^+/K^+ ➔ sekresi H+ ↓↓(>90%)
- Kemampuan hamb sekresi HCL >> H2 antagonis & long duration
- Golongan obat :
  - ♣ omeprazole : inhibitor enz P450
  - ♣ lansoprazole

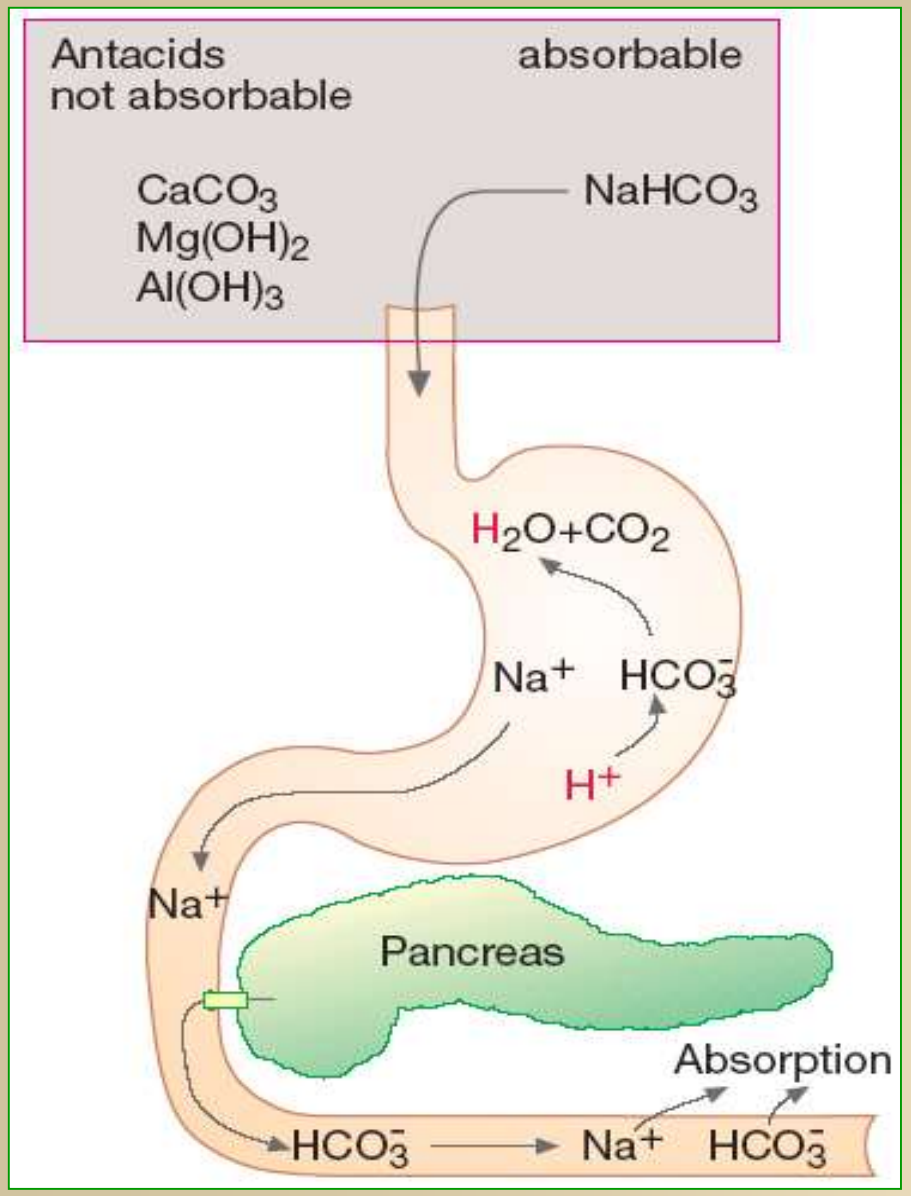
Antikolinergik

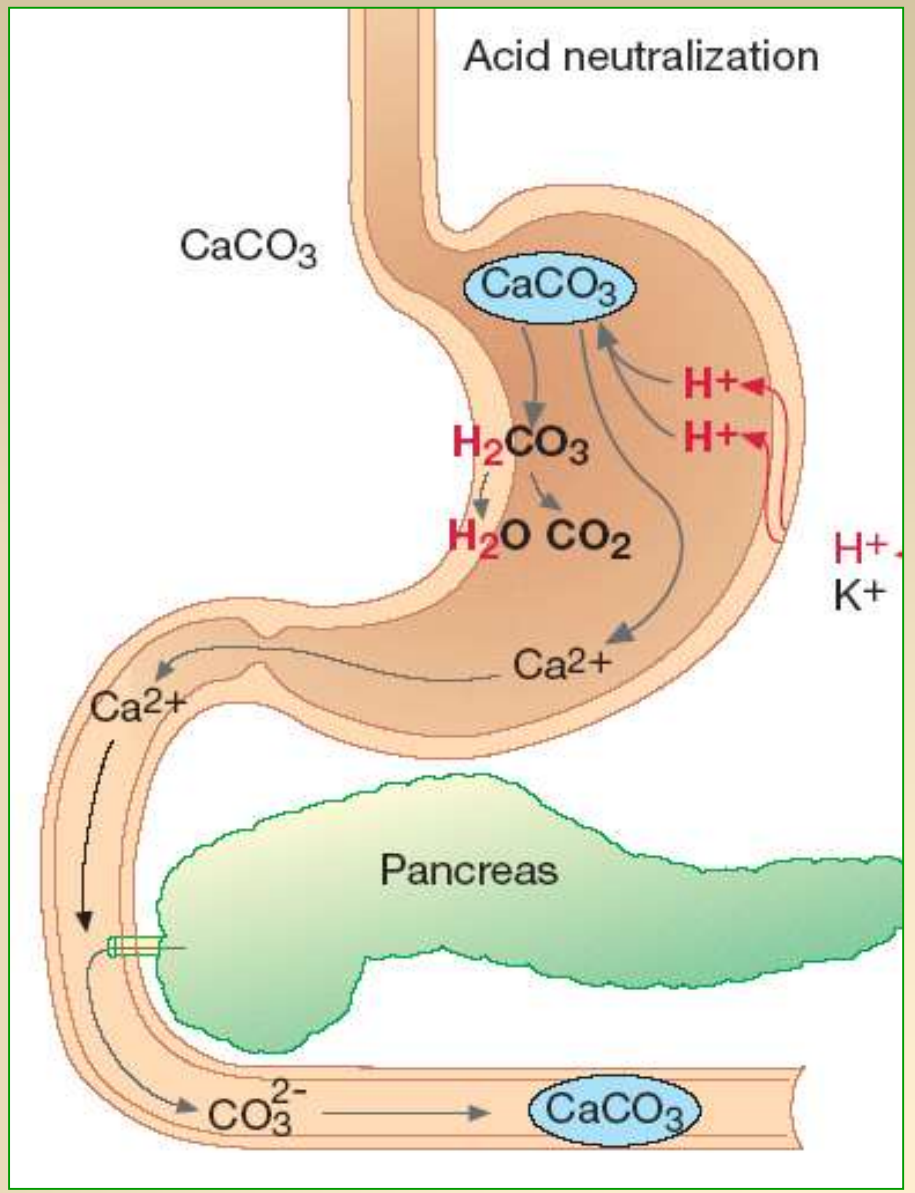
- Bekerja sebagai antagonis R/ M1 ➔hambat sekresi asam dan pepsin
- Contoh : pirenzepine
- Bukan DOC karena ES >>>

Antasida

- Bekerja dg menetralisir keasaman lambung dengan cara me ↑ pH lambung
- H+ akan berikatan dg CO_3^{2-}, HCO_3^- atau OH^- (komponen antasid)
- Indikasi : ulkus peptik, GERD, dispepsia non ulkus
- Menyembuhkan ulkus lebih lama dp H2 antagonis

- Makanan ➔buffering effect, mk antasid diberikan di antara makan (mis 1j stl mkn)
- Antasida nonabsorbable lbh dipilih (ES sistemik <<<) dp antasid absorbable


Antacids
not absorbable
absorbable
$CaCO_3$
$Mg(OH)_2$
$Al(OH)_3$
$NaHCO_3$
H_2O+CO_2
Na^+
HCO_3^-
H^+
Na^+
Pancreas
Absorption
HCO_3^-
Na^+
HCO_3^-


Acid neutralization
$CaCO_3$
$CaCO_3$
H^+
H^+
H_2CO_3
H_2O CO_2
H^+
K^+
Ca^{2+}
Ca^{2+}
Pancreas
CO_3^{2-}
$CaCO_3$

Antasida

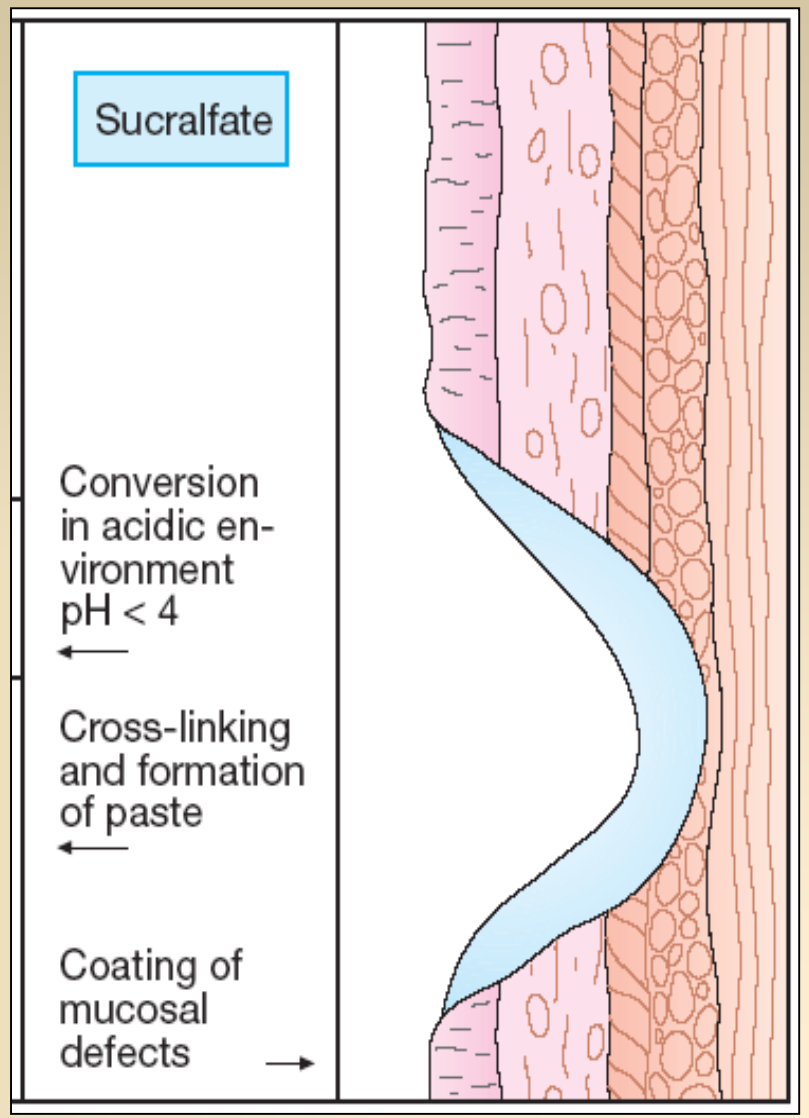
ANTASIDA	GARAM	ES	KET
Alumunium	Hidroksida	konstipasi	Al & Mg mengikat pepsin → pepsin inaktif → sekresi asam ↓
Magnesium	Hidroksida / Trisilikat	diare	
Al/ Mg dan Ca/Mg kompleks	Hidroksida / Karbonat		
Sodium	Bikarbonat	Alkalosis (jgk panjang)	
Alginic acid preparation	Al/ Mg kompleks + alginic acid		Utk GERD, me↓ refluk
Kalsium	Karbonat	Hiperkalsemia (dosis >>>)	

Obat yang Melindungi Mukosa (Mukoprotektan)

- Sukralfat
- Prostaglandin analog

SUKRALFAT

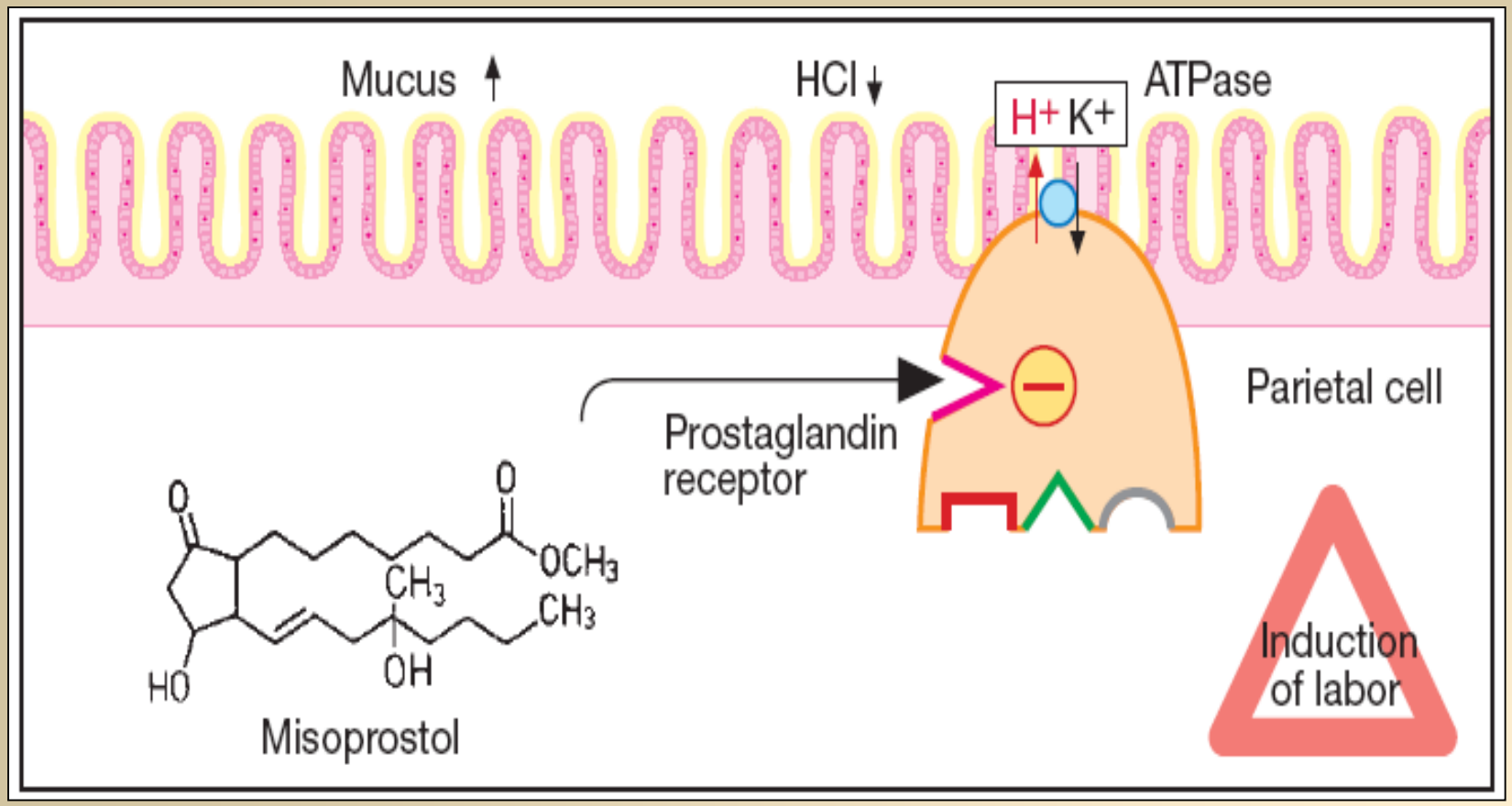
- Stl pemberian oral, molekul sukralfat mengalami cross-linking dengan gastric juice, membentuk suatu pasta yg melekat pd defek mukosa & melindungi lapisan yg lebih dalam.
- Sucralfate menghambat H+ ➔protektif thd asam & juga thd pepsin, trypsin & bile acids ➔ defek mukosa dpt sembuh lebih cepat
- Diminum saat lambung kosong (1 jam sblm makan dan sebelum tidur)
- Well tolerated, tapi mengand sejml residu Al(OH) shg dpt menyebabkan konstipasi

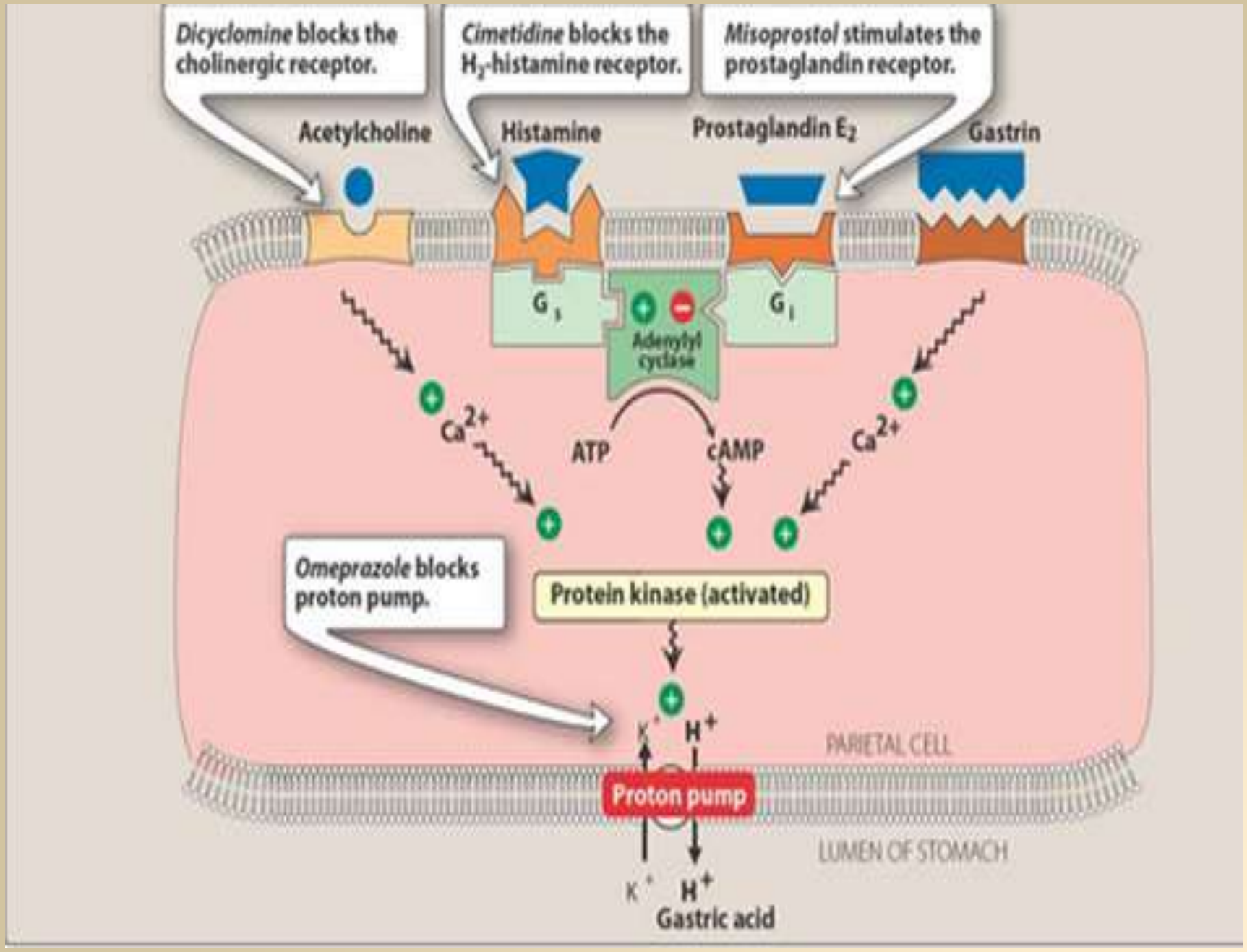


Prostaglandin Analog

- Bekerja sebagai analog PG E1, lebih stabil dp PG endogen
- PG E1 dan PG I2 endogen ➔ menstimuli prod mukus & menghamb sekresi asam ➔ penting utk memelihara integritas barier mukosa gastroduodenal
- Sintesa PG melalui jalur yang melibatkan enzim COX1
- NSAID spt Aspirin ➔hamb COX 1 ➔sintesa PG oleh sel parietal ↓ ➔sekresi asam ↑ & erosi ➔ ulkus
- misoprostol
  - Terbukti dpt mencegah dan menyembuhkan ulkus peptik akibat pemakaian NSAID jangka panjang
  - Lebih efektif dp H2 antagonis utk ulkus peptik akibat NSAID
  - ES : diare, kontraksi uterus pd ibu hamil

Prostaglandin Analog




Dicyclomine blocks the cholinergic receptor.
Cimetidine blocks the H2-histamine receptor.
Misoprostol stimulates the prostaglandin receptor.
Acetylcholine
Histamine
Prostaglandin E2
Gastrin
G1
G1
Adenylyl cyclase
Ca2+
ATP
cAMP
Ca2+
Omeprazole blocks proton pump.
Protein kinase (activated)
K+
H+
PARIETAL CELL
Proton pump
LUMEN OF STOMACH
K+
H+
Gastric acid

Anti Helicobacter pylori

Type	Duration	Efficiency
First line		
Standard triple therapy:		
PPI + two antibiotics (clarithromycin + metronidazile or amoxicilin)	7–14 days	70–85%
Second line		
Bismuth-containing quadruple therapy:		
PPI + bismuth salt + tetracycline + metronidazole	14 days	77–93%
Non-bismuth based concomitant therapy:		
PPI + clarithromycin + amoxicillin + metronidazole	14 days	75–90%
Levofloxacin triple therapy:		
PPI + amoxicillin + levofloxacin	14 days	74–81%
Salvage regimens		
Rifabutin-based triple therapy:		
PPI + rifabutin + amoxicillin	10 days	66–70%

Kuna, 2019

OBAT MEMPENGARUHI KONTRAKTILITAS GIT

Meningkatkan Kontraktilitas

- **Anti konstipasi**
- **Prokinetik Agent**
- **Anti muntah**

Menurunkan kontraktilitas

- **Anti diare**

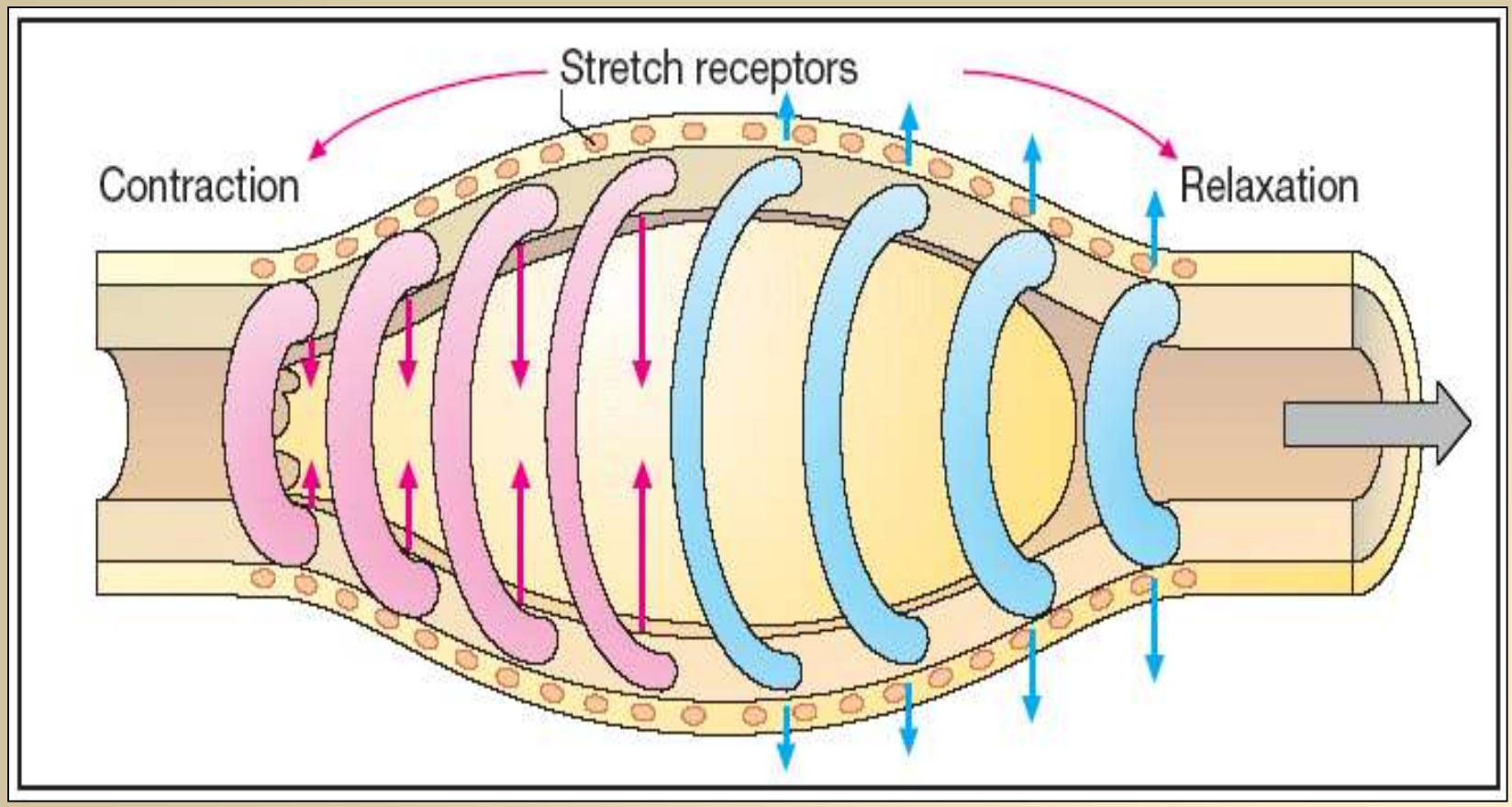
ANTIKONSTIPASI
= LAKSATIF =

Stool Formation

Kolon : absorbsi air ~90%

- Absorbsi berlebihan
  - Konstipasi : keras, *dehydrated stool*
  - Perlu usaha keras untuk defekasi (mengejan)
  - Berbahaya utk pasien dengan :
    - *Recent episiotomy, colostomy, hemorrhoids, cardiovascular disease*
- Absorbsi Inadekuat
  - Diare: lunak, tidak berbentuk, cair

Peristaltik : Aktivasi intramural mekanoreceptor



Definisi

Laxative	Production of soft, formed stool over 1 or more days
Cathartic	Rapid, intense fluid evacuation of bowel.

Laxatif

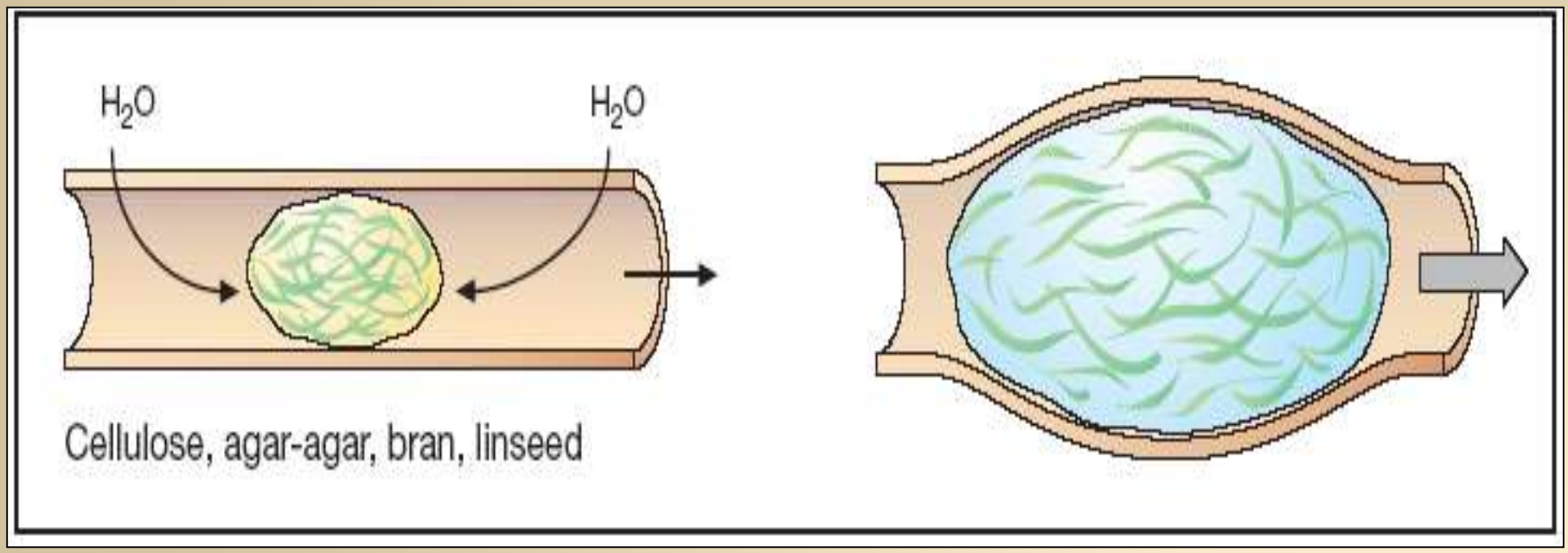
- Bulk forming (Pembentuk massa)
- Surfactants (Pelicin & Pelunak)
- Stimulants / Irritant (Perangsang)
- Osmotics (Menambah volume cairan)

Bulk Forming Laxatives

- Meresorbsi air
- Melunakkan dan menambah besar ukuran faeces
- Ukuran faecal yang menggembung ➔distensi dind usus ➔ menstimuli peristalsis

- Uncleaned rice (brown rice)
- Bran
- Seaweed (tangle)
- Methylcellulose
- Psyllium
- Polycarbophil
- Makanan kaya serat lain

Bulk Forming Laxatives



Surfactant Laxatives

- Menurunkan tegangan permukaan (spt detergen)
- Fecal softener
  - Memfasilitasi penetrasi cairan

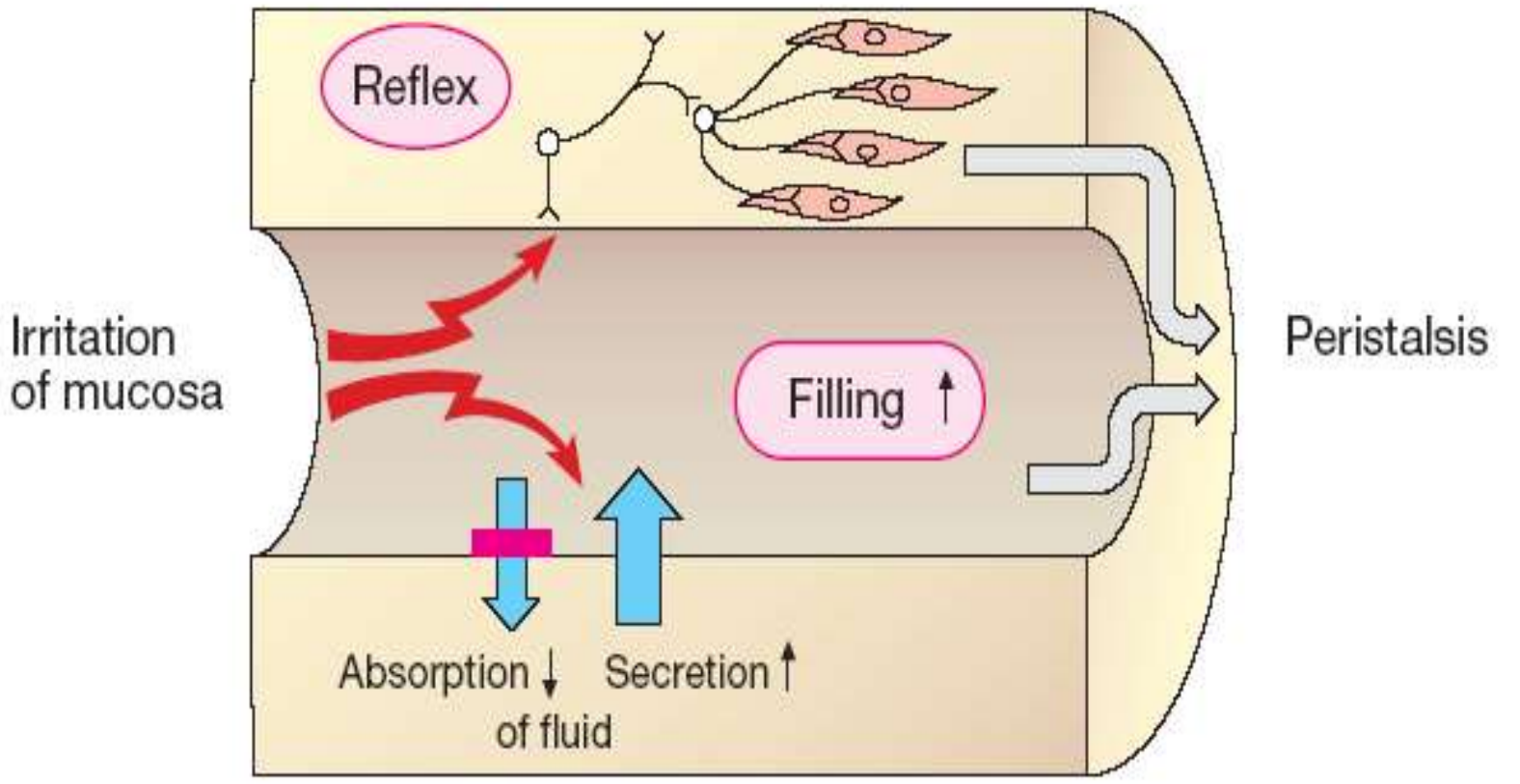
- Docusate salts
- Castor oil
- Mineral oil
- Dehydrocholic acid

Stimulant Laxatives

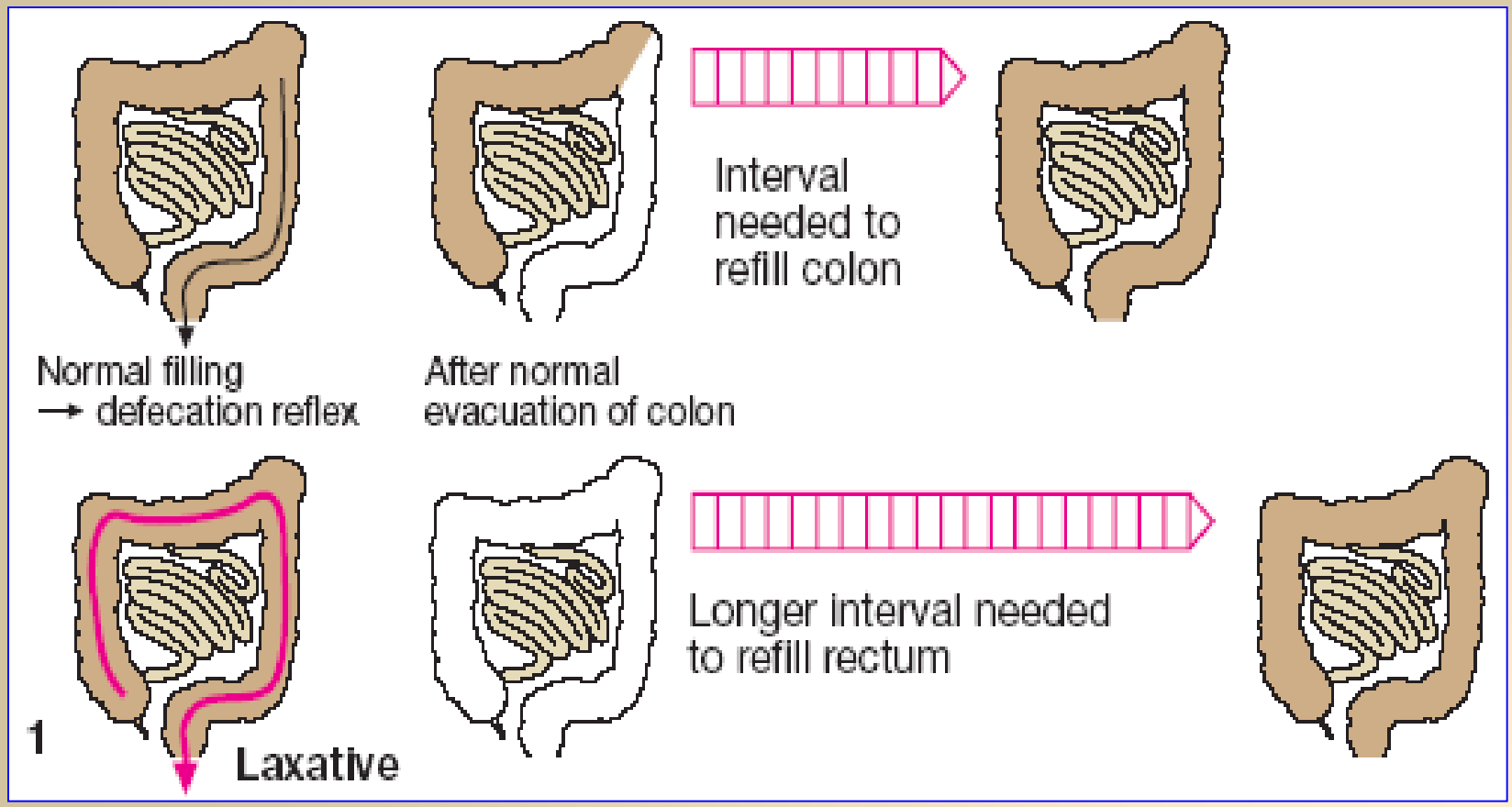
- Menstimuli peristalsis
- Me↑ sekresi air dan elektrolit ke lumen usus.
- Me ↓ reabsorbsi air dan elektrolit

- Polyphenol or diphenylmethane
  - Phenolpthalein
  - Bisacodyl
- Anthroqiunon
  - Senna, Cascara
  - Aloe, Casanthranol

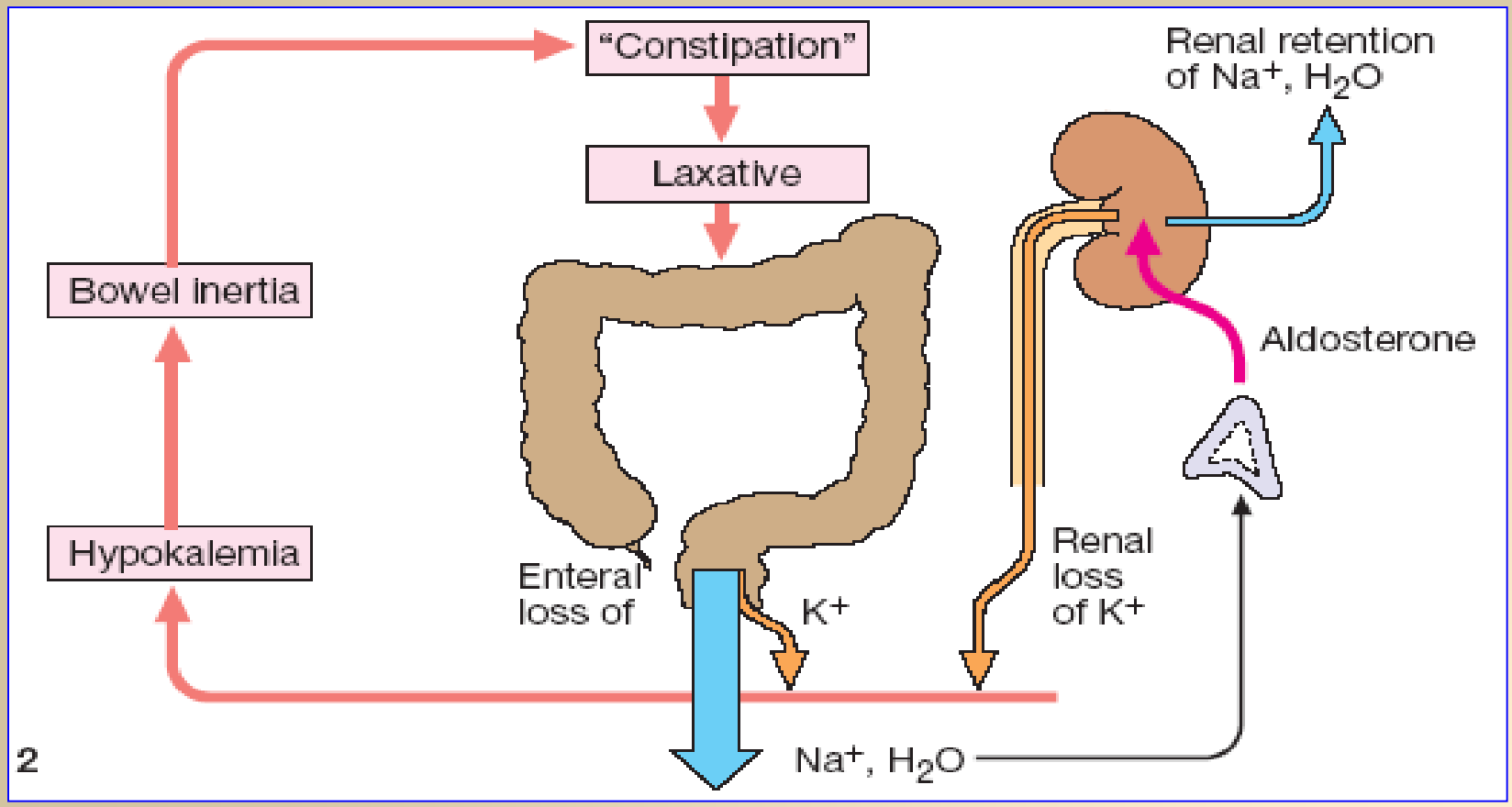
Stimulant / irritant Laxatives



Misuse Laxatives



Misuse Laxatives



Osmotic Laxatives

- Berupa garam / glukosa yang tidak / sulit diabsorbsi, sehingga tetap berada sebagai salah satu komponen faekal
- me↑ volume cairan di lumen usus kecil dan usus besar secara osmotik ➔me ↑ peristaltik
- Mg ➔me ↑ sintesa kolesistokinin ➔me ↑ motilitas kolon

- Salts laxatives
  - Magnesium hydroxid
  - Sodium phosphate
- Hyperosmolar laxatives
  - Laktulosa
  - Sorbitol, Glycerin
  - Lactitol
  - PEG

Lactulose

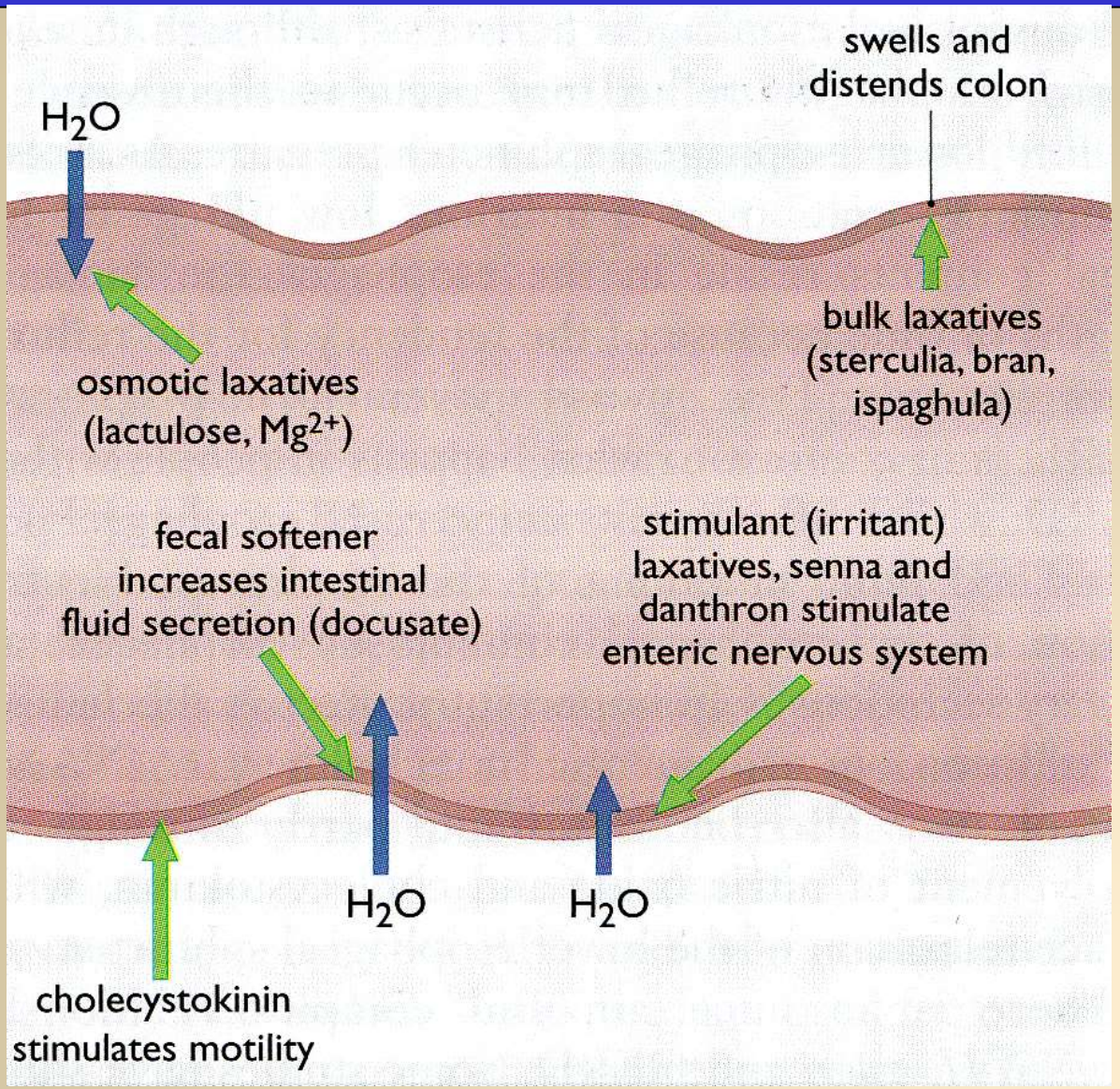
FD

- Bakteri usus mendegradasi laktulosa → pH asam → menghambat difusi NH3 ke sirkulasi (krn dikonversi menjadi NH4 +), & meningkatkan difusi NH3 dari darah ke usus utk dikonversi menj NH4+

Indikasi

- Konstipasi pd lansia
- Mencegah ensefalohepatik portal sistemik

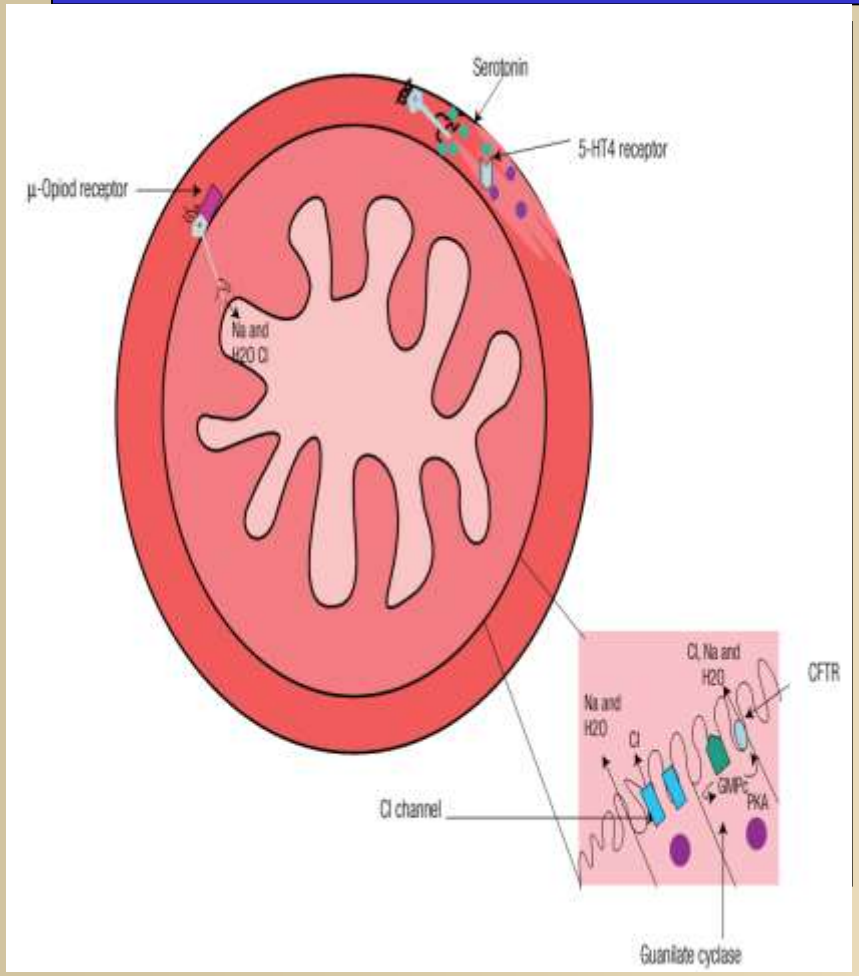
Mechanism of Action Laxative



RESUME ANTI KONSTIPASI

Laxative type	Examples	Proposed mode of action	Potential limitations
Dietary fiber/bulking agents	Wheat bran Psyllium seed husk Methylcellulose	Luminal water binding increases stool bulk and reduces consistency	Flatulence and abdominal distension Stool impaction (rarely) Not recommended in frail, immobile, or palliative care patients
Osmotic laxatives			
Undigestible disaccharides and sugar alcohols	Lactulose Sorbitol	Luminal water binding by creating an osmotic gradient	Bloating, flatulence
Synthetic macromolecules	PEG Polycarbophil	Luminal water binding	Bloating
Salinic laxatives	Magnesium hydroxide (e.g., milk of magnesia) Magnesium citrate Magnesium sulfate Sodium phosfate	Luminal water binding Increases fluid excretion	Electrolyte imbalance (must be used with caution in patients with compromised renal or cardiac function)
Stimulant laxatives			
Diphenylmethane derivatives	Bisacodyl, sodium picosulfate	Act locally to stimulate colonic motility, decrease water absorption from large intestine	Abdominal discomfort and cramps
Anthraquinones	Senna, aloe, cascara	Act locally to stimulate colonic motility, decrease water absorption from large intestine	Abdominal discomfort and cramps

Obat baru Antikonstipasi



- Chloride channel activators
- Guanylate cyclase C activators
- Opioid Antagonists
- Serotonergic agonist

Chloride channel activators

- FD =

1. Secara selektif mengaktivasi kanal Cl-2 (ClC2) mel PKA→ me↑ sekresi cairan di usus → distensi massa
2. Menginduksi peristaltic tanpa berefek langsung pd otot polos intestin

Guanylate cyclase C activator

- FD = menstimulasi peningkatan cGMP intraseluler dan selanjutnya mengaktivasi ClC

Opioid antagonist

- Methyl naltrexone (MTNX)= Alvimopan
- N-metyl –menurunkan lipid solubility-efek SSP (-)
- Antagonis reseptor μ, meningkatkan motilitas usus

Serotonin agonist

- 5-HT4 agonis reseptor
- Prokinetic agent

NEW DRUG

Mechanism of action	Agent	Dose	Indication
Cloride Channel Activator	Lubiprostone	24 ug/BID	Chronic constipation, IBS-C
Guanilate-Cyclase C Activator	Linaclotide	75-600 ug/d	Chronic constipation, IBS-C
Opioid Receptors antagonists	Alvimopan Methilnaltrexone	6-16 mg 30-300 min before surgery then BID for 7 days 8-12 mg Subcutaneously every other day as needed	Opiate-induced constipation, postope ileus and chronic methadone use
Serotoninergic agonist	Prucalopride * Tegaserod # Cisapride$ Mosapride$ Renzapride$	2 mg/d 2-6 mg/BID	* Chronic Constipation and IBS- # Not widely available in all countr $ No conclusive evidence

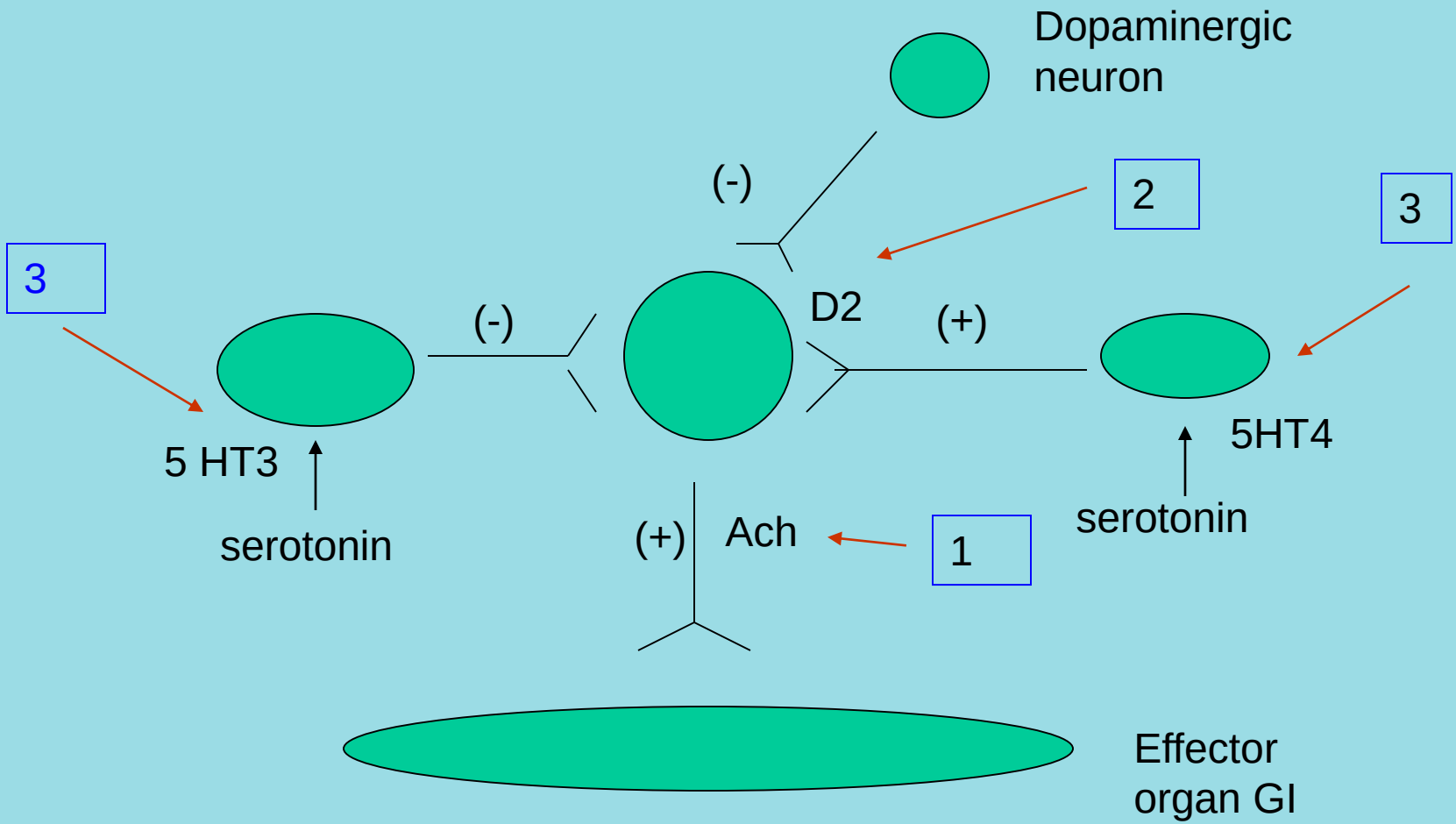
Agent	*Typical dosage**	*Time of onset*	*Adverse effects*
Bulking agents			
Methylcellulose powder	19 g per day	12 to 72 hours	None compared with placebo[17]
Polycarbophil (Fibercon) tablets	1,250 mg, one to four times per day	12 to 72 hours	None recorded[18]
Psyllium (Metamucil) powder	1 tsp or 1 packet one to three times per day	12 to 24 hours	Bloating, abdominal distension in 4% to 18%[16,17]
Osmotic laxatives			
Lactulose solution	15 to 30 mL per day	24 to 48 hours	Bloating and cramping; nausea in up to 20%[19]
Magnesium citrate solution	150 to 300 mL, single dose or short-term daily dose	30 minutes to 6 hours	Increase in magnesium, causing lethargy, hypotension, respiratory depression[20]
Magnesium hydroxide suspension	30 to 60 mL per day	30 minutes to 6 hours	Increase in magnesium, causing lethargy, hypotension, respiratory depression[20]
Polyethylene glycol (Miralax) powder	17 g per day	24 to 48 hours	Minimal adverse effects of cramping and gas[18]
Sorbitol solution	2 to 3 tbsp, single dose or short-term daily dose	24 to 48 hours	Bloating, cramping, and nausea[19]
Stool softeners			
Docusate sodium (Colace) capsules	100 mg twice per day	24 to 48 hours	None reported[16]
Stimulant laxatives			
Bisacodyl (Dulcolax) tablets	5 to 15 mg per day	6 to 10 hours	Diarrhea and abdominal pain in 56% in week 1 and 5% in week 4[21]
Senna tablets	15 mg per day	6 to 12 hours	Abdominal pain in up to 12%[16]
Chloride channel activators			
Lubiprostone (Amitiza)† capsules	24 mcg twice per day	Within 24 hours	Nausea in 18%[22]
Peripherally acting mu-opioid antagonists			
Methylnaltrexone (Relistor)‡ solution	Weight-based subcutaneous injection, once or twice per day	30 to 60 minutes	Diarrhea in 8% Abdominal pain in 13%[23]
Other			
Linaclotide (Linzess)† capsules	145 mcg per day	—	Diarrhea in 16%, which led to treatment cessation in 4%[24]

PROKINETIK AGENT

Indikasi

- me↑motilitas gaster→ mengosongkan lambung lbh cepat →Tx Gatroparesis
- me↑ tonus spinkter bawah esofagus →spinkter bisa menutup sempurna → Tx GERD

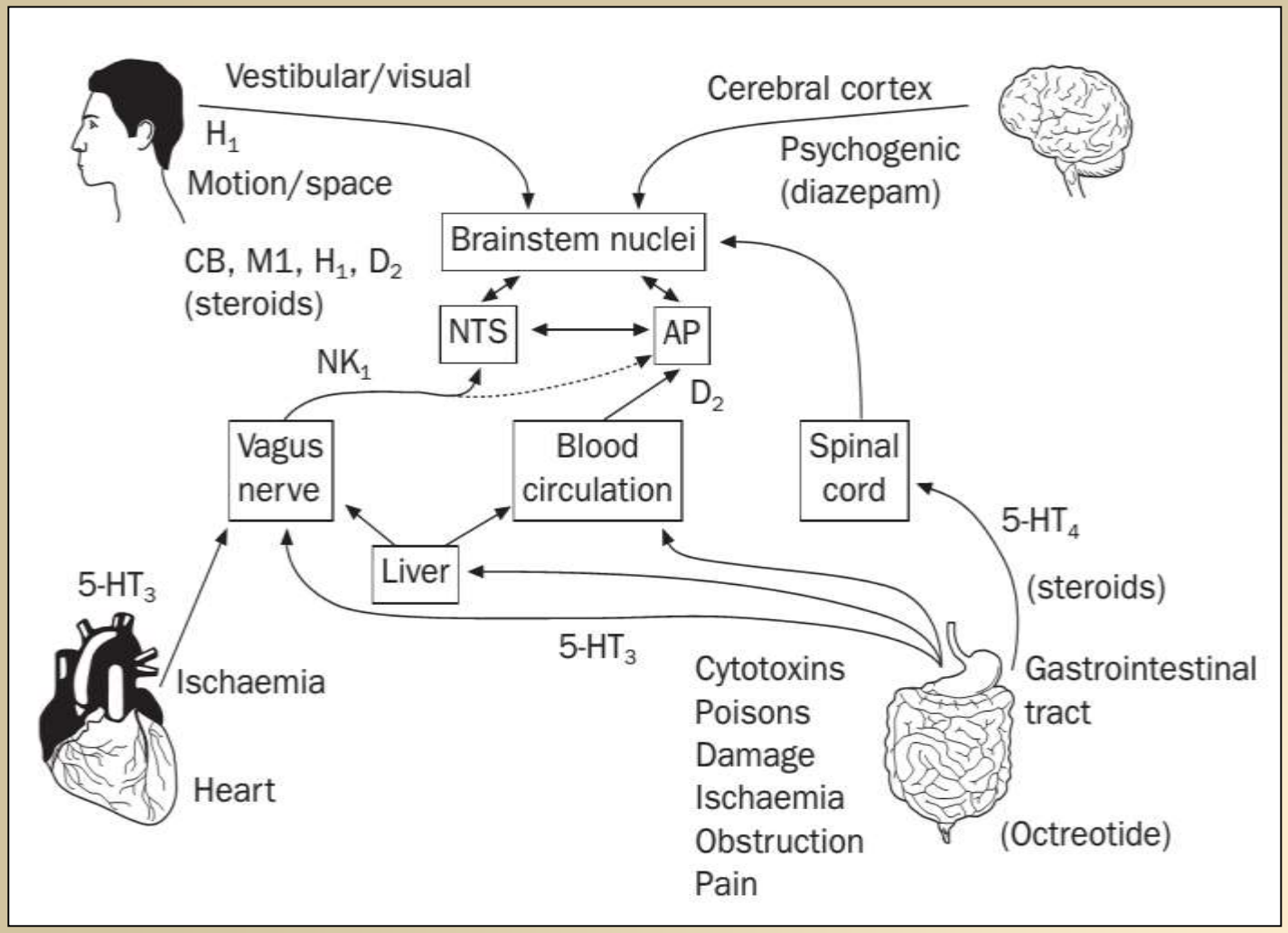
Conceptual model of prokinetic agents



Classification of prokinetic agents

Mech. Of action	General pharm. class	Example of drug	Used medications
Aktivasi R/ Musc.	Cholinergic agents	Betanechol neostigmin	Costipation pseudoobstruction
Inhibisi R/D2	Antagonis R/Dopamin	Metoclopramide Domperidone	GERD
Aktivasi R/5HT4 Inhibisi R/5HT3	Agonis R/Serotonin Antagonis R/ Serotn	Cisapride Metoclopramide	Gastroparesis
Aktivasi R/Motilin	Motilin like agents	Erytromycin	Gastroparesis

EMETIC PATHWAY



NTS, nucleus tractus solitarius; AP, area postrema;
CB, cannabinoid;
NK1, neurokinin-1 receptor; D2, dopamine;
M 1, muscarinic-1 receptor; H1, histamine

ANTI EMETIC

From: **Management of Intractable Nausea and Vomiting in Patients at the End of Life: "I Was Feeling Nauseous All of the Time . . . Nothing Was Working"**

JAMA. 2007;298(10):1196-1207. doi:10.1001/jama.298.10.1196

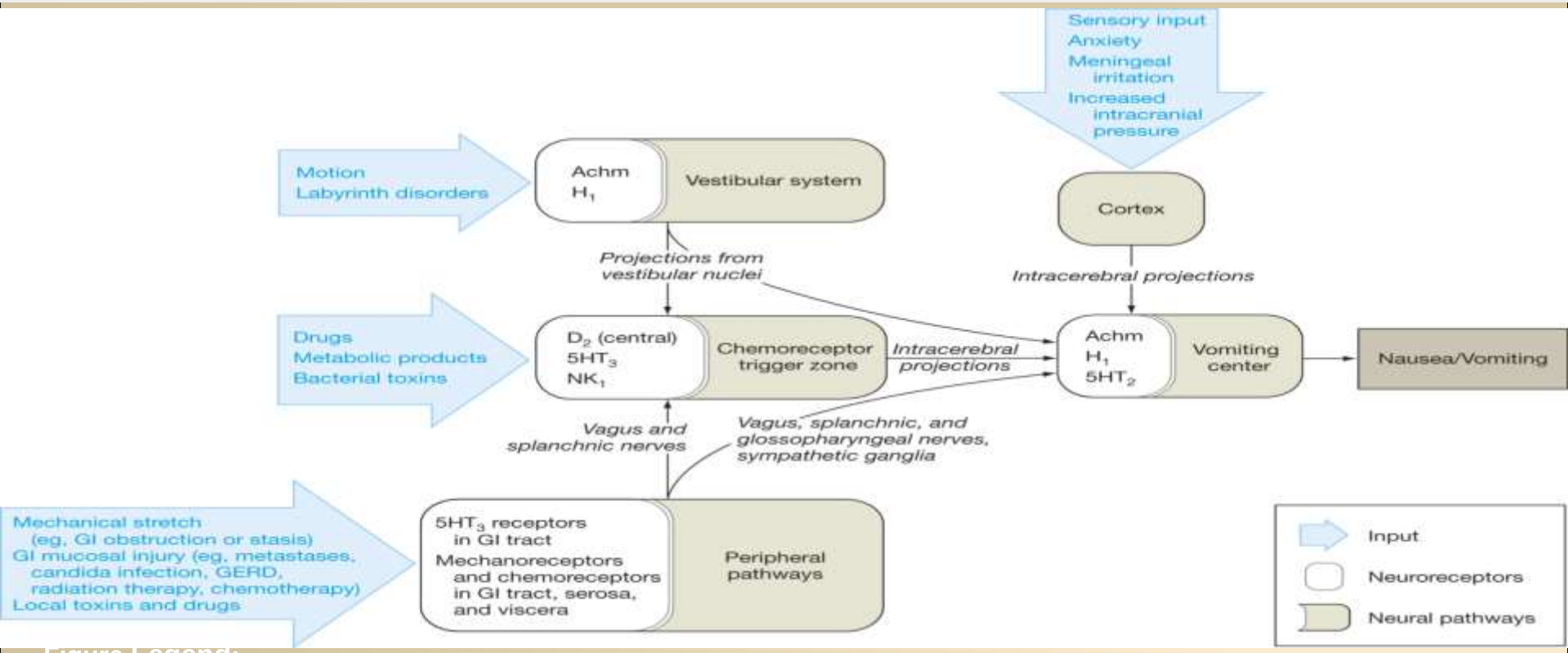
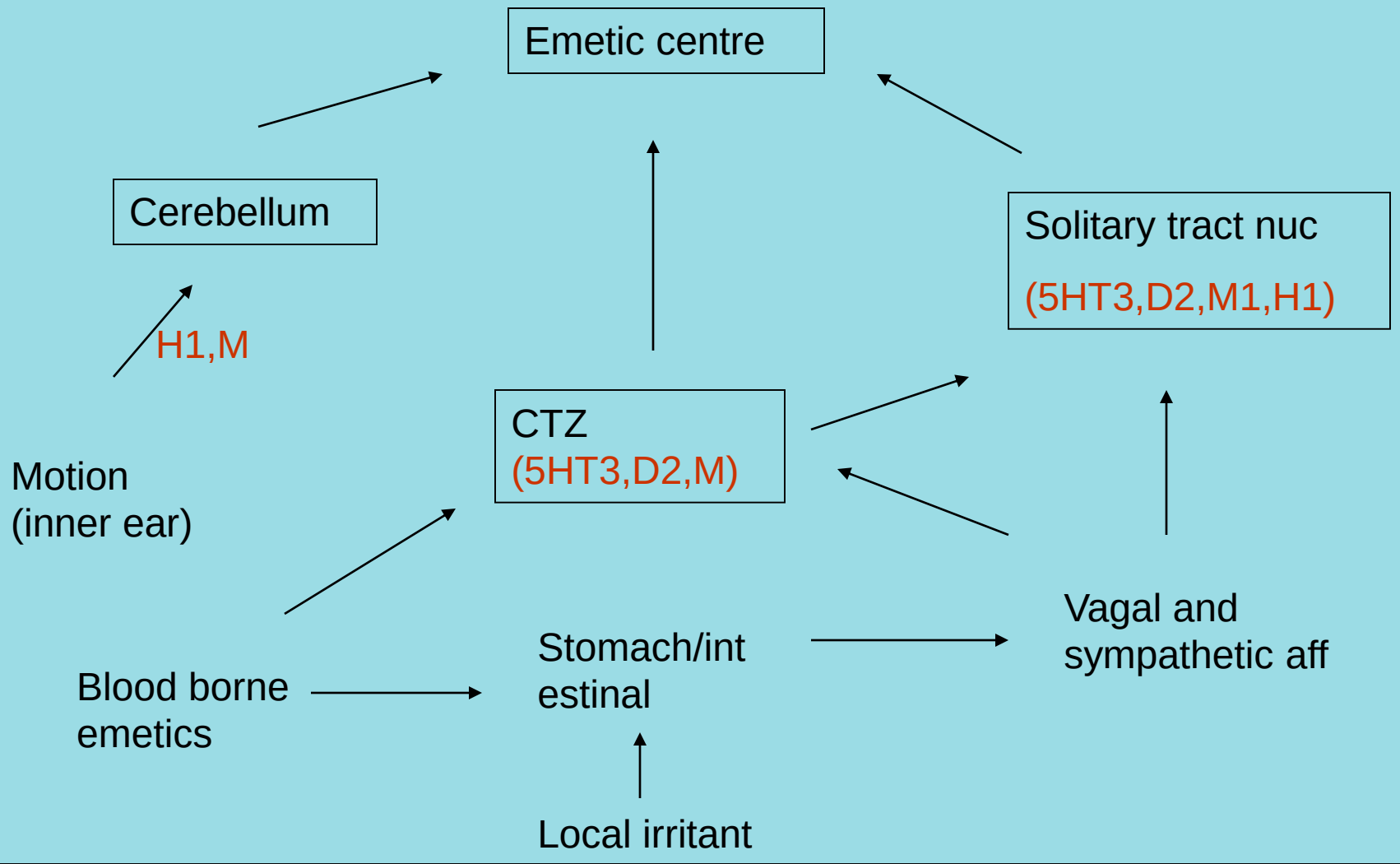


Figure Legend:

Achm indicates muscarinic acetylcholine receptor; D2, dopamine type 2 receptor; GERD, gastroesophageal reflux; GI, gastrointestinal; H1, histamine type 1 receptor; NK1, neurokinin type 1 receptor; 5HT2, 5-hydroxytryptamine type 2 receptor; and 5HT3, 5-hydroxytryptamine type 3 receptor.

Conseptual model of antiemetic agents



Mis : Chemotherapeutic drugs can trigger emesis by two ways:

- **Direct activation of the medullary chemoreceptor trigger zone**. 5-HT3, D2 (dopamine) and NK-1 receptors play a critical role as neurotransmitters.
- **Cell damage of the GI tract.** This causes serotonin release from the enterochromaffin cells, this molecule activates 5-HT3 receptors on vagal and splanchnic afferent fibers that send impulses to the medulla, activating the CTZ which stimulates the vomiting center.

Antiemetik

- Serotonin (5HT) Antagonists
- Dopamine (DA) Antagonists
- Anticholinergics (muscarinic blockers)
- Cannabinoids

General classification of antiemetic agents

Antiemetic class	**Examples**	**Type vomiting most effective**
5 HT3-antagonist	Ondansetron	Cytotoxic drug
Centrally acting dopamine antagonist	Metoclopramide(5HT 3) Promethazine(antim usc&antihist)	Cytotoxic drug
H1- antagonist	Cyclizine	Vestibular(motion sickness)
Muscarinic antagonist	Scopolamine	Motion sickness
Neurokinin rec	Investigational	Cytotoxic drug
Cannabinoid rec antag	Drobabinol	Cytotoxic drug

Serotonin Antagonists

- Indikasi : mengatasi ES penggunaan kemoterapi yg menginduksi muntah
- Ondansetron (Zofran®)
- Tidak mempengaruhi R/ dopamine ➔ tdk ada efek ekstrapiramidal
- Granisetron (Kytril®)

Dopamine Antagonists

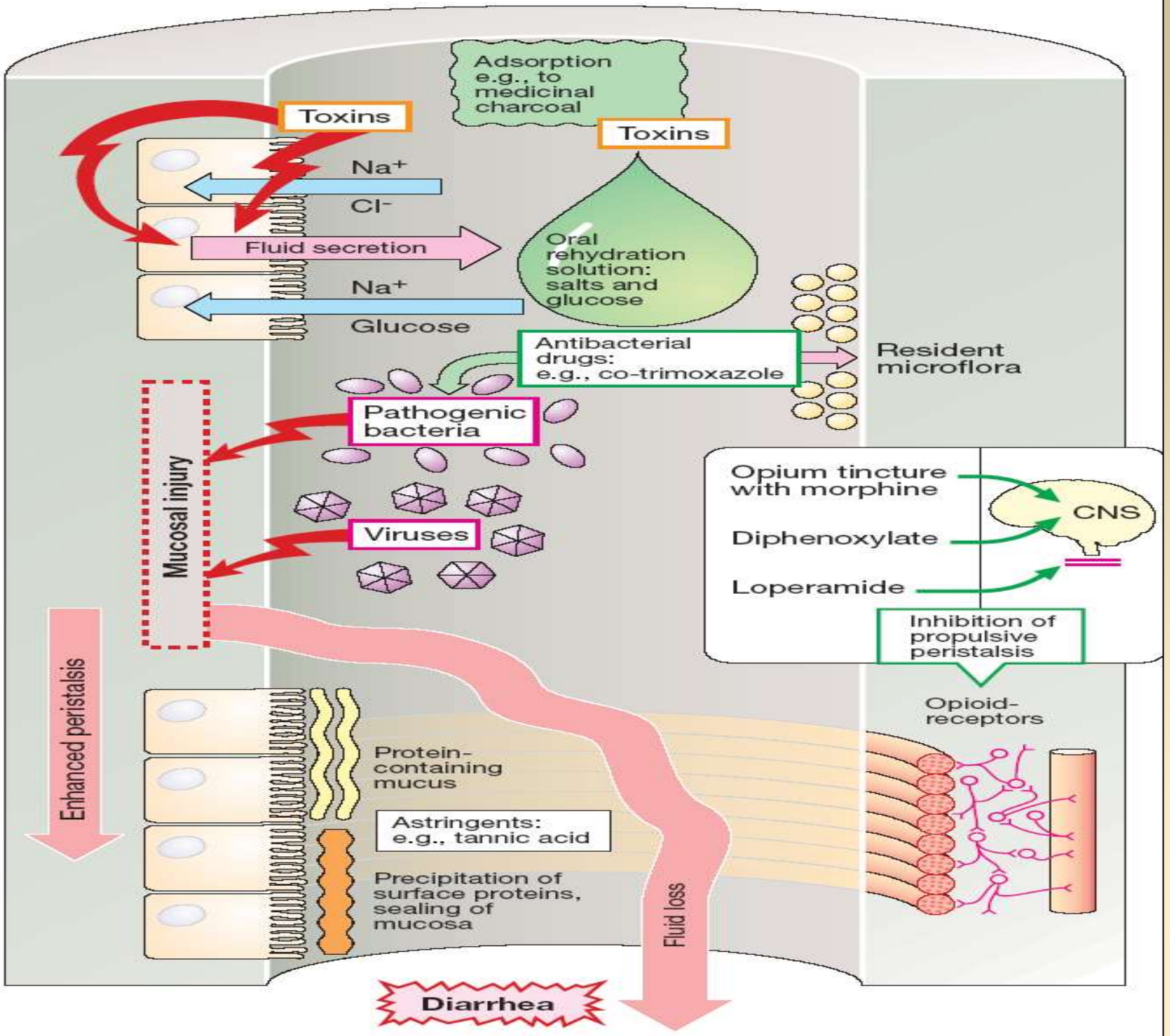
- Phenothiazines
  - prochloraperazine
  - promethazine
- Butyrophenones
  - haloperidol
  - droperidol
- metoclopramide

ANTIDIARE

Anti Peristaltik / Antimotility
Suplemen : Pre-b iotik & Pro-biotik, Zink

Antidiare

- Diare sering merupakan suatu akibat / kompensasi dari ….
  - Terapinya lebih ditujukan bagaimana mengatasi dehidrasi dan causa diare, bukan gejalanya.
- Reseptor opioid di GIT berperan dlm me↓ motilitas usus
  - Memperpanjang wkt reabsorbsi cairan


Adsorption e.g., to medicinal charcoal
Toxins
Toxins
Na+
Cl-
Fluid secretion
Oral rehydration solution: salts and glucose
Na+
Glucose
Antibacterial drugs: e.g., co-trimoxazole
Resident microflora
Pathogenic bacteria
Mucosal injury
Viruses
Opium tincture with morphine
CNS
Diphenoxylate
Loperamide
Inhibition of propulsive peristalsis
Opioid-receptors
Enhanced peristalsis
Protein-containing mucus
Astringents: e.g., tannic acid
Precipitation of surface proteins, sealing of mucosa
Fluid loss
Diarrhea

Treatment

1. Rehidrasi : Oral Rehydration Solution (ORS)
2. For child : Supplemental zinc therapy, multivitamins, and minerals : folate, vit A, zinc, magnesium, and copper (WHO 2005).

   - For all children with diarrhea: child > 6 mo : 20 mg zinc/day ; child <6 month 10mg zink /day. For 14 days
3. Diet (dimulai stl 4 j rehidrasi)

   - sesuai umur, ASI lanjutkan

   - porsi kecil tp sering, kaya energi & mikronutrien,

   - jus buah kaleng hindari (hiperosmoler)

   - Probiotik t.u utk diare ok rotavirus
3. Sering diresepkan tp manfaat ?? Anti-diarrhea non spesific ; antimotility, antisecretory, adsorbent

ORS

	mmol/L
Sodium	75
Chloride	65
Glucose, anhydrous	75
Potassium	20
Citrate	10
Total osmolarity	245

RDA for a child aged 1 year

Folate	50 µg
Zinc	20 mg
Vitamin A	400 µg
Copper	1 mg
Magnesium	80 mg

ZINK

- Zinc sbg ko-faktor enzim yg berperan di dalam sintesa DNA & RNA, dan protein → berperan penting dlm pembelahan sel, pertumbuhan dan perbaikan jaringan.
- Pd keadaan diare, zinc menstimulasi pembelahan sel → reepithelisasi (perbaikan mukosa) lebih cepat
- mempengaruhi system imun (pertahanan tubuh) spesifik humoral ataupun selular dan mempengaruhi proses penyerapan intestinal dan/atau proses transport sekretorik. (meningkatkan absorpsi Na+ dan menurunkan sekresi Cl-)
- efek penghambatan mikroba (antimikroba), seperti Salmonella thypi, Salmonella parathypi A, Shigella flexneri, Shogella sonnei.
- Hasil penelitian : mempersingkat durasi diare s.d 25%, menurunkan angka kegagalan terapi dan kematian sebesar 40% pada diare persisten, serta mempunyai efek profilaksis untuk 2-3 bulan ke depan setelah pemberian zink selama 10 hari.

ANTIMOTILITY : opiate-like antidiarrheal agent

- FD = Inhibits intestinal peristalsis and has mild antisecretory properties.
- Indikasi : mild to moderate traveler's diarrhea
- KI utk enteroinvasive diarrhea, bloody or suspected inflammatory diarrhea (febris, significant abdominal pain), children < 2 y.
- paregoric/opium tincture, diphenoxylate , defenoxin, loperamide , codein
- Loperamide is the agent of choice for adults (4–6 mg/day; 2–4 mg /day for children > 8 y)

STOOL MODIFIERS = ADSORBENT

- bulking action, hanya perbaiki konsistensi faeces,
- Inadequate proof of efficacy in acute adult diarrhea
- Contoh : Kaolin-pectin, activated charcoal, attapulgite, Wheat bran
- ES kaolin= terkumpulnya tinja beserta racun2nya di usus besar (toxic megacolon)
- KI= diare krn E. coli, salmonella, shigella

Antisecretory agents

- Bismuth subsalicylate can alleviate stool output in children or symptoms of diarrhea, nausea, and abdominal pain in traveler's diarrhea.
- Racecadotril is an enkephalinase inhibitor (nonopiate) with antisecretory activity, and is now licensed in many countries in the world for use in children. It has been found useful in children with diarrhea, but not in adults with cholera.

Probiotik & Prebiotik

Probiotics	Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host
Prebiotics	Nondigestible substances that provide a beneficial physiological effect for the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria
Synbiotics	Products that contain both probiotics and prebiotics

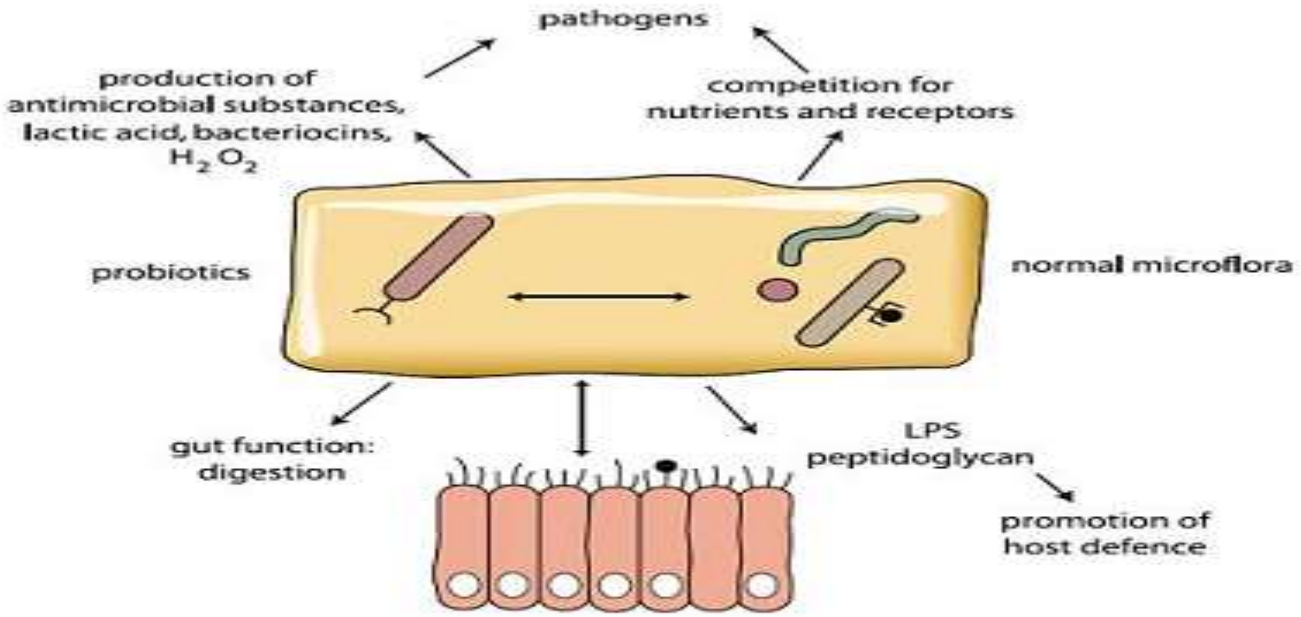


Fig. 3 The normal microbiota and probiotics interact with the host in metabolic activities and immune function and prevent colonization of opportunistic and pathogenic microorganisms (Reproduced with permission from Sullivan and Nord [2005].)

Probiotik & Prebiotik

- Probiotics (live m.o) affect the intestinal ecosystem by stimulating mucosal immune mechanisms and by stimulating nonimmune mechanisms through antagonism/competition with potential pathogens.
- Prebiotics (non-digestable subs) affect intestinal bacteria by increasing the numbers of beneficial anaerobic bacteria and decreasing the population of potentially pathogenic microorganisms

Probiotics

Immunologic benefits	• Activate local macrophages to increase antigen presentation to B lymphocytes and increase secretory immunoglobulin A (IgA) production both locally and systemically • Modulate cytokine profiles • Induce hyporesponsiveness to food antigens
Nonimmunologic benefits	• Digest food and compete for nutrients with pathogens • Alter local pH to create an unfavorable local environment for pathogens • Produce bacteriocins to inhibit pathogens • Scavenge superoxide radicals • Stimulate epithelial mucin production • Enhance intestinal barrier function • Compete for adhesion with pathogens • Modify pathogen-derived toxins

Prebiotics

- Metabolic effects: production of short-chain fatty acids, fat metabolism, absorption of ions (Ca, Fe, Mg)
- Enhancing host immunity (IgA production, cytokine modulation, etc.)

TERIMA KASIH....