GIT

Chapter - 1

INTRODUCTION

1) Innervation of GIT → Intrinsic – Enteric nervous system
Extrinsic – Autonomic

ANS:- ENTERIC NERVOUS SYSTEM

lies in the wall of gut beginning in the oesophagus extending all the way to anus.

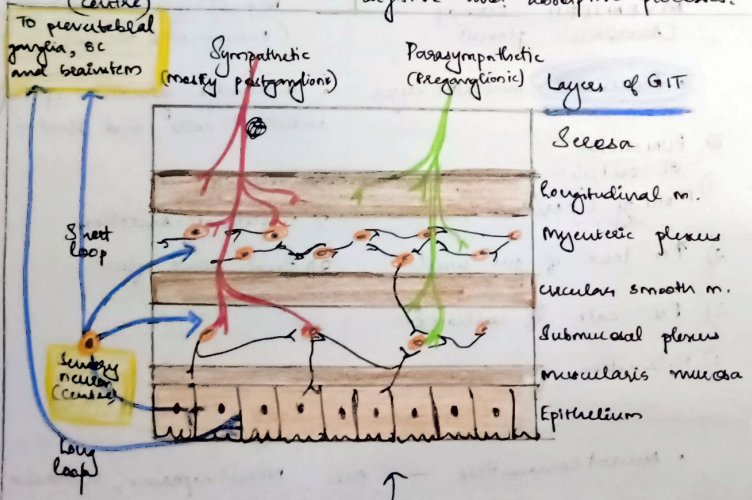
2 plexuses → Myenteric plexus
Meissner's plexus

MYENTERIC PLEXUS (Auerbach's plexus)	MEISSNER'S PLEXUS (Submucosal plexus)
• Innervates muscular layer	• Innervates glandular epithelium, intestinal cells and blood vessels
FUNCTIONS of control:-	It controls:-
1) Motility (Peristalsis)	1) Intestinal secretion
2) ↑es tone of gut wall	2) Local blood flow
3) ↑s rate of contraction	
4) Relaxation of sphincters	

- Neurotransmitters → Ach, Norepinephrine, serotonin, GABA, VIP, NO, dopamine etc
- The above 2 plexuses are interconnected
- 2 reflexes involved (look HCl)
  1) Long loop reflex – centre at CNS
  2) Short loop reflex – centre at GUT wall

Extrinsic innervation (ANS) ↔ Symp / Parasymp

SYMPATHETIC	PARASYMPATHETIC
• Fibres from $T_8 - L_2$	• From vagus (cranial outflow)
• NT → Norepinephrine	Also from sacrum (sacral outflow) of spinal cord
effect → NE: ↑ Contraction of sphincters; ↓↓ Motility and secretions	• NT → Ach, VIP, GIRP
	Ach: ↑ Motility, ↑ Secretion
	VIP: ↓ constriction
	GRP → G cell: ↑ Gastrin
∴ An increase in symp activity slows processes.	∴ ↑ in parasympathetic, promotes digestive and absorptive processes.



(Innervation diagram)

CHAPTER – 2

Salivary glands and Oesophagus

SE

1) SALIVA

I) Composition (pH 6 - 8)

- About 1500 mL / day is secreted
- 99% water, 1% solids
- Solids include both organic and inorganic

Inorganic substances	Organic substances
– Na^+, Cl^-, K^+, HCO_3^- (main)	lingual lipase, lingual amylase, lysozyme
– Ca^{2+}, PO_4^{3-} (small amts)	mucin, urea, uric acid (small amt)

II) Functions

1) **Buffering action** → ↓ in pH – mobilise Ca^{2+} from teeth; ↑ in pH – Ca^{2+} precipitation in teeth – Tartar

HCO_3^-, PO_4^{3-} and mucin are the buffering systems to maintain pH at about 7.

2) **Water balance**

When body fluid content decreases
↓
Decreased saliva secretion
↓
Dryness of mouth
↓
Sensation of thirst

3) Lubrication

- Keeps oral cavity moist
- Facilitates speech
- Helps in mastication and swallowing
- ~~Stimulates taste buds As solvent~~

4) Cleaning function

- Helps in oral hygiene and prevents dental caries.

5) Protective function

- Protective coating for soft tissues and hard tissues (eg: teeth)

6) Defense fn

- Presence of proteolytic enzymes like lysozymes (bactericidal)
- Abs. containing antibodies to destroy oral bacteria
- Saliva preps :-
  - Antibacterial, antiviral, antifungal and immunological

7) Digestive fns

- Enzymes : Amylase / Ptyalin → converts cooked starch to maltose
  lingual lipase → digest 30% of TAGs
- Formn of bolus
- Taste :- Act as a solvent for molecules to stimulate taste bud

8) Excretory fn

- Excretes → lead, Hg, thiocyanate
  → Alkaloids like morphine
  → Drugs like streptomycin
  → Viruses like rabies, mumps, poliomyelitis

III) Mechanism of salivary secretion → 1° from acinus → Modification

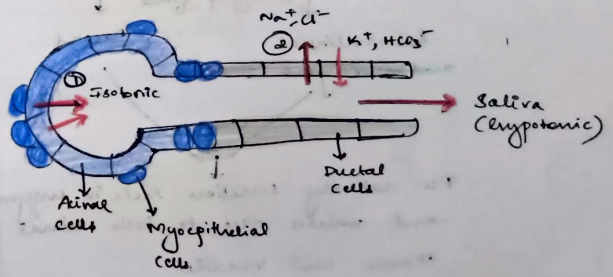
A Primary Secretion

- Acinar cells of salivary glands secrete the initial saliva into salivary duct.
- This is isotonic with plasma having same Na^+, Cl^-, K^+ and HCO_3^-.

B Modification of saliva

- In ducts, composition is modified by reabsorption of Na^+, Cl^- and secretion of K^+, HCO_3^-
- Ducts are relatively impermeable to water, so saliva becomes hypotonic and alkaline with low content of Na^+, Cl^- and high K^+, HCO_3^-
- Aldosterone ↑es K^+ and ↓es Na^+ conc in saliva

APPLIED : In Addison's disease, ↓high Na^+/Cl^- ratio.



IV) Regulation → Neural (Symp / Parasymp (↑es)) / Vascular

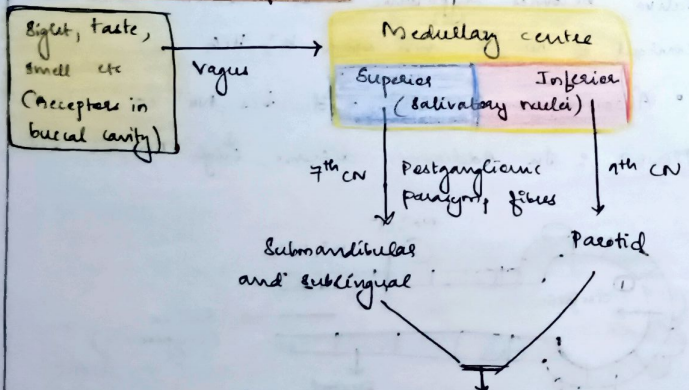
Neural

- Stimuli → taste, smell
- Parasymp stimln ↑es water content and ↓es organic constituents
- Food in mouth controls secretion by 2 reflexes:—

1) Conditioned reflex

- Sight, smell or even thought of food ↑es secretion
- Parasymp is stimulated here by impulses from higher centres

2) Unconditioned reflex



NOTE: Symp causes vasoconstriction and secretion of small amts of saliva rich in organic constituents.

Vascular

↑ed blood supply ↑es nutrition which ↑es secretion

V) Applied Physiology

1) Frey's syndrome

In case of trauma / surgery, chorda tympani n. injured during regeneration, this n. may join n. innervating sweat gland. This causes sweating during salivation.

2) Bell's palsy – paralysis of VII CN

3) Sialolithiasis – stone in salivary ducts

4) dry mouth seen in anxiety and dehydration

BA

CHAPTER - 3

STOMACH

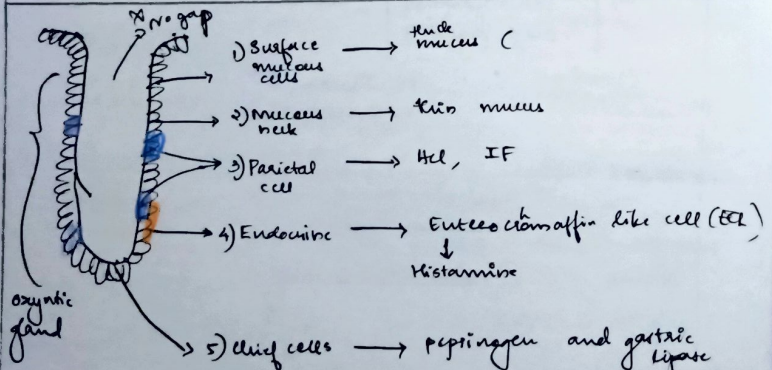
Essays

1) Gastric Juice Secretions

I) Composition (pH ~1)

- About 2-5 L secreted per day
- 99.5% water, 0.5% solids
- Solids → organic & inorganic

INORGANIC	ORGANIC
- Hcl, HCO_3^- - Na^+, K^+, SO_4^{2-}	1) Enzymes. Pepsinogen, gastric lipase, gelatinase 2) Mucus - thick → by surf epi cells - thin → by mucous neck cells of pyloric and cardiac glands 3) Intrinsic factor of Castle



Explanation of components

1) Hcl (Look Hcl secretion)
↳ Fns, secretion

2) Pepsinogen
- In pre. of Hcl, pepsin is active and digests protein (Acid-pepsin mixture)
APM

3) Gastric lipase
- Converts TAG → FA + glycerol

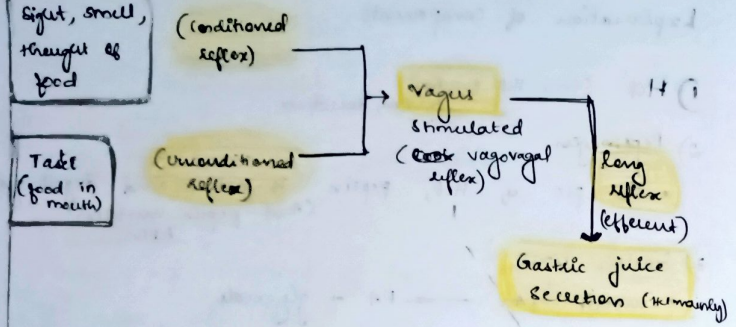
4) Gelatinase
- liquefies gelatin (protein in connective tissue)

5) Mucus
- Thick mucus → Protects gastric mucosa together with HCO_3^- form mucosal barrier, that prevents autodigestion of mucosa by APM
- Soluble mucus → lubrication of food

6) Intrinsic factor
- Req. for absorption of orally ingested Vit B_{12}.

II) Phases and Regulation

1) Cephalic phase
- Occurs before entry of food to stomach
- Secretion initiated by sight, smell or thought of food
- Under neural control (vagus n.)
- 24% of total secretion in this phase.

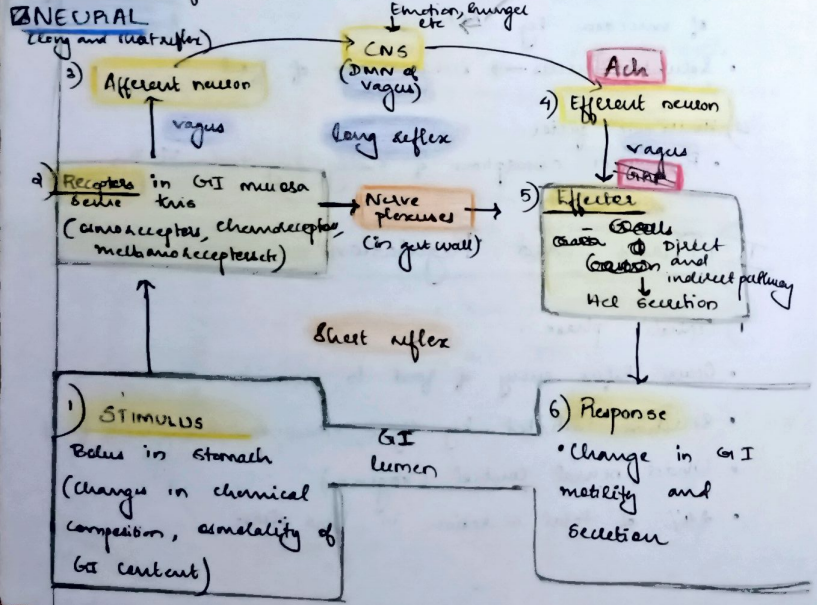


17 (1)

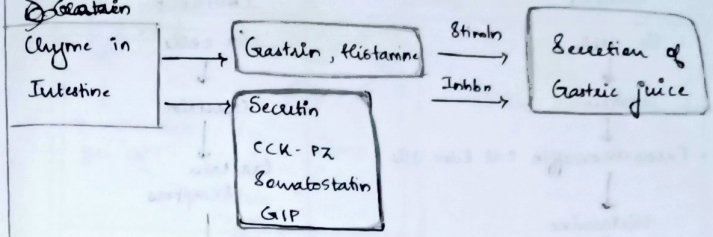
2) Gastric phase

- Occurs when food enters stomach
- Stimulus → bolus in stomach
- Mediated by both neural and hormonal mech
- 70% of total secretion occurs here

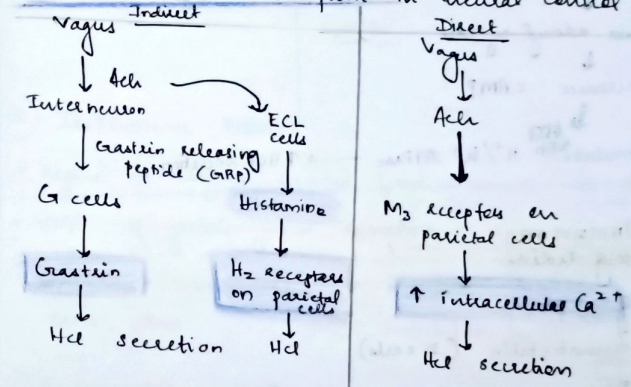
NEURAL



HORMONAL



Direct and indirect path in neural control



Role of each hormone

Stimulants / Inhibitors

(Write some few factors affecting HCl secretion)

1) GASTRIN and 2) HISTAMINE

- Most powerful stimulant
- From G cells in pyloric gland of stomach and 1st part of duodenum
- Products of protein digestion increase gastrin secretion

- ACTIONS → Direct / Indirect

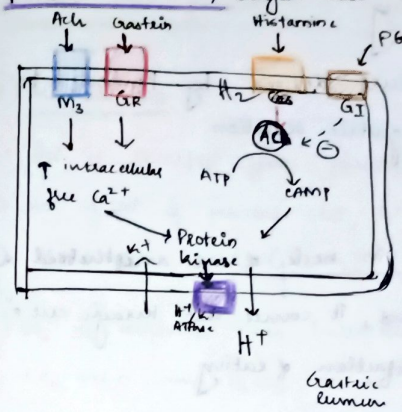
DIRECT	INDIRECT
G cells	G cells
↓	↓
Gastrin	Gastrin
↓	↓
Enterochromaffin cell like cells	Gastrin receptors
↓	↓
Histamine	↑es intracellular Ca^{2+}
↓	
H_2 receptors on parietal cell	
↓	
Activate adenyl cyclase	
↓	
Increased cAMP	
↓	
Stimulate H^+/K^+ ATPase ⟶ ↑ HCl secretion	

INHIBITORS

3) ~~Acetylcholine~~

- Somatostatin (D cells)
- PGE_2 – decrease adenyl cyclase activity and intracellular cAMP
- Low $pH_{(<3)}$ – inhibits H^+ secretion (-ve feedback),
- Intestinal influences – Fats, carbo and acid inhibit secretion
- Emotional responses – Anger ↑es secretion and motility; depression ↓es secretion

PARIETAL CELL / Oxyntic cell



AC → adenyl cyclase

3) INTESTINAL PHASE

- Begins as chyme emptied from stomach into duodenum
- 10% of gastric juice secretion
- Initially (early phase) ⟶ secretion is ↑ed
  later phase ⟶ inhibited by → Enterogastric reflex; Hormonal mechanism

1) Enterogastric reflex

- Mediated through myenteric nervous system, extrinsic and vagus
- Initiated by distention of SI in pres. of acids or protein breakdown products in upper intestine.

2) Hormonal mechanism

- Pres. of acid, fats etc in upper small intestine cause release of hormones ⟶ CCK, GIP, somatostatin
  ↓
  Inhibit gastric secretion

IV) Sham feeding

Experimental procedure devised by Pavlov to demonstrate cephalic phase of gastric secretion.

PROCEDURE

- A hole is made in neck of an anesthetised dog
- When dog eats food, it comes out through cut end
- But dog has satisfaction of eating
- This procedure is supported by preparation of Pavlov's pouch with fistula from stomach. The fistula opens to external and is used to observe gastric juice during cephalic phase.
- After vagotomy, sham feeding does not induce gastric secretion. This proves role of vagus n. during cephalic phase.

V) ABNORMALITIES (Applied)

- Hyposecretion - occurs in
  1) Pernicious anemia
  2) Gastric atrophy etc
  3) Carcinoma
- Hypersecretion - in :
  1) Gastric / duodenal ulcer
  2) ~~Carcinoma~~
  3) Zollinger - Ellison syndrome

2) Gastric HCl Secretion

I) Mechanism

- HCl is secreted from parietal cells (fundus and body of stomach)
- In cytosol of parietal cell, H^+ derived from breakdown of carbonic acid (H_2CO_3).

STEPS

1) CO_2 is derived from intracellular metabolism.
2) $CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow H^+ + HCO_3^-$
3) HCO_3^- is exchanged with Cl^- on basolateral membrane of HCO_3^-/Cl^- exchanger.
4) Cl^- that enters parietal cell, passively transported into gastric lumen.
5) In lumen, $Cl^- + H \longrightarrow HCl$ (by H^+/K^+ pump active pumping - H^+ enters cell)

∴ For each H^+ secreted into lumen, one HCO_3^- is reabsorbed into plasma.

- After a heavy meal

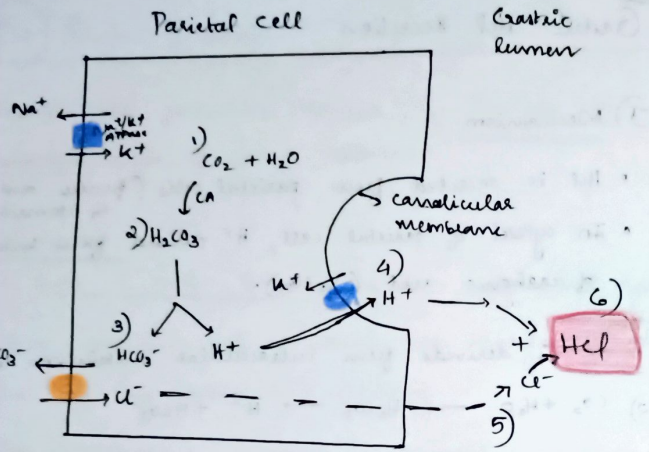
↓

Increase HCl secretion

↓

Increase HCO_3^- diffuse to blood

↳ Excreted to urine → Post prandial alkaline tide



CA → carbonic anhydrase

II) Functions of Hcl

1) Conversion of pepsinogen → pepsin
2) Bacteriostatic
3) Stimulate flow of bile
4) Stimulate secretion of some GI hormones
5) Preventive role against carcinoma stomach.

III) Factors affecting secretion

(Same as gastric juice secretion → Stimulants, Inhibitors)

IV) Applied Physiology

1) Gastric mucosal barrier

This barrier protects mucosa from damage by intraluminal Hcl (autodigestion) by :-

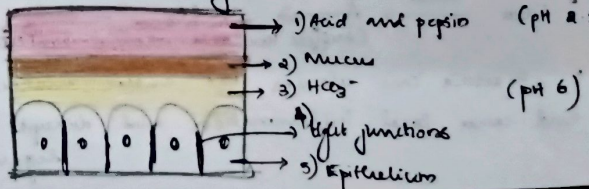
1) Mucus secretion
- Gastric mucosal epithelium is covered by mucus
- Mucus is of thick insoluble variety and doesn't flow. It is called "unstirred layer."

2) Bicarbonate secretion
- Blue mucus and epi, HCO_3^- rich fluid helps in maintaining pH.

3) Tight junctions
- Provide a barrier to back diffusion of H^+

4) Prostaglandins
- Maintains mucosal barrier by stimulating secretion of mucus and HCO_3^- and blood flow.

5) Mucosal blood flow (Enjoy)
- Rapidly carries away any acid that penetrates the cellular lining. Also O_2, HCO_3^-, nutrients to cells.



Brief A → Functions of Stomach

1) Reception of food
2) Temporary storage of food
3) Mechanical and chemical digestion
4) Abs of alcohol and drugs
5) IF helps in abs of vit B_{12} → matur of RBCs

Essay

3) PEPTIC ULCER

It is an excoriated area of stomach or intestinal mucosa caused by (Pathophysiology)

1) Helicobacter pylori infection
2) Decreased mucosal defence
3) Hypersecretion of acid
4) Smoking, alcohol.
5) Genetic predisposition → O blood group more prone to duodenal ulcers

I) CAUSES

A) Helicobacter pylori infection

- Major cause of peptic ulcer
- It is Gram -ve Bacillus secrete urease
- Urea $\xrightarrow{\text{Urease}}$ Ammonia + CO_2 (Buffers the acid around bacteria)
- ∴ Bacteria can colonise the antral mucosa and cause local inflammation and disrupt immune defences.
- The bacteria also inhibits somatostatin (from D cells) hence causing ↑ HCl → Gastritis → ulcer

B) Decreased mucosal defence

- Mucus is a viscous gel containing mucin, phospholipids, electrolytes (mainly HCO_3^-), water secreted by mucous cells.
- Separates HCO_3^- rich layer from acid content of stomach
- Protects mucosal epithelium from injury by acidic chyme
- Use of NSAIDS → inhibit mucous and HCO_3^-
- Catecholamines (released during stress) → inhibit mucous → Stress ulcer

C) Hypersecretion of acid (Hyperchlorhydria)

- In chronic anxiety → secretion ↑es
- Intake of spicy food → " "
- Zollinger-Ellison syn → Gastrin secreting tumor of Pancreas

II) FEATURES

1) Upper abdominal pain (Epigastric)
2) Hemetemesis
3) Vomiting
4) Melena

III) Complications

- Perforations – in mucosal coat results in communication of gastric / duodenal lumen with peritoneal cavity
- Hemorrhage from ulcer
- Gastric obstruction
- Steatorrhea and weight loss

IV) Investigations

1) Barium meal study
2) Endoscopy and biopsy
3) Basal acid estimation
4) Pentagastrin test
5) Serum gastrin antibodies

V) Treatment

~ Antibiotics to kill bacteria (specific)

Specific	Non-Specific	Surgical
1) H_2 receptor antagonist - Ranitidine - Cimetidine	1) Antacids (Alkali Gelusil) 2) Yoga 3) Diet regulation 4) Avoid spicy food 5) NSAID withdrawn 6) Use of cold milk	Vagotomy Gastrectomy
2) Proton pump blockers - Omeprazole		
3) Muscarinic blockers - Atropine - Pirenzepine		
4) Gastrin blockers		
5) Antibodies		

VI) Differences b/w gastric and duodenal ulcer

GASTRIC ULCER	DUODENAL ULCER
1) Seen along curvature of stomach, esp at incisura angularis	Seen in 1st part of duodenum
2) Less common	More common
3) More in old age group	More in young age group
4) Equal in both sexes	More common in males
5) Chronic gastric ulcer are associated with malignancy	CDA - Not associated with malignancy
6) Normal levels of gastric acid secretion	High levels of gastric acid secretion Easy of back diffusion of H^+
7) No relief, food aggravate pain	Pain relieved by food and antacids Complication less
8) More severe	
9) Deep seated and large in size	Superficial and small in size

CHAPTER-4

Pancreas, Liver and Biliary System

1.) **Pancreatic juice** (Ecoqy)

ANS:- I) **Composition** (pH - alkaline and high HCO_3^-)

- About 1500 mL / day
- 99.5% water and 0.5% solid
- Solids → Organic, Inorganic

Inorganic	Organic
1) Cations → Na^+, K^+, Ca^{2+}, Mg^{2+}	1) Enzymes (digestive)
2) Anions → HCO_3^-, Cl^-, SO_4^{2-}	2) Trypsin inhibitor
3) H_2O — helps in neutralising acidity of chyme	3) Albumin, globulin, kallikrein, mucoproteins, alkaline phosphatase

II) **Functions**

1) **Digestive enzymes**

A) Proteases → trypsinogen, chymotrypsinogen, Proelastase, carboxypeptidase A and B

B) Starch splitting → α - Amylase (Activator Cl^-)

C) Lipolytic → Pancreatic lipase
Procolipase
Cholesteryl ester hydrolase
Phospholipase $-A_2$

A) **PROTEASES** → Endo, Exo

(i) **Endopeptidases**

- Break peptide bond in interior of peptide chain
- Eg:- Pepsin, trypsin, chymotrypsin, elastase

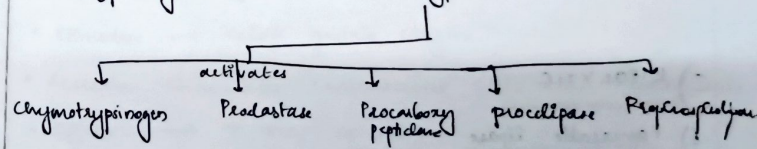
(ii) **Exopeptidase**

- Break terminal peptide bond
- Eg:- Carboxypeptidases

- Proteases are inactive in pancreatic duct
- Active only after entering duodenum otherwise pancreas will be digested.

i) **Trypsin**

- Most imp proteolytic enzyme
- Trypsinogen —enterokinase→ trypsin



- End product of protein digestion → peptides
- Trypsin inhibitor is present in pancreatic juice.

ii) **Chymotrypsin**

- Action similar to trypsin
- Diff → trypsin can clot blood, chymotrypsin cannot

iii) Procarboxypeptidase – A and B

- Split off AA from polypeptide
- End product → AA

iv) Elastase

- Breakdown elastin
- End p → oligopeptide, dipeptide, aa

B) AMYLOLYTIC ENZYMES

- α- Amylase
- Act on cooked and uncooked starch
- Split α-1,4 linkage
- Products → Maltose, maltriose, α-limit dextrin
  → Glucose not formed

NOTE → In acute pancreatitis, serum α-amylase ↑es

C) LIPOLYTIC

i) Pancreatic lipase

- Triglycerides → Mono + FA

ii) Procolipase

- Activated → trypsin
- Substrate → fat droplet
- Facilitates exposure of active site of pancreatic lipase

iii) Cholesteryl ester hydrolase

- cholesteryl ester → cholesterol

iv) Phospholipase A_2

- Phospholipids → FA + lysophospholipids

2) Role of bicarbonate

- Neutralise acidic chyme → only then pancreatic enzymes can act
- In alkaline pH pepsin is inactive. Otherwise pepsin will digest all pancreatic enzymes
- In diarrhoea → loss of bicarbonate → acidosis

3) Role of secretin

- From S cells of duodenal mucosa

III) Regulation of secretion and phases

- Role of secretin
- From S cells of duodenal mucosa
- Stimulus → acidic gastric chyme
- Secretin stimulates centroacinar cells and ductal cells
- Effect → ↑ HCO_3^- secretion
  ↑ volume of pancreatic juice
  (via cAMP)

- Role of CCK-PZ and vagal stimln
- Stimulate acinal cells
- Release enzymes

PHASES

- No food → small volume of basal secretion from pancreas
- Intake of food → ↑ secretion

1) Cephalic phase

- Food in oral cavity, smell, sight (conditioned and unconditioned vagal reflex) → Neural control
- Secretion rich in enzymes, poor in HCO_3^-

2) Gastric phase

- Distention of stomach by food
- Control → Neural → vagovagal reflex ~~Enzyme rich~~
  → Hormonal → gastrin
- Enzyme rich juice

3) Intestinal phase

- When chyme enters duodenum and jejunum
- Hormonal control → Secretin and CCK-PZ
- HCO_3^- rich juice
- Enzyme rich secretion (stimulated if there is partially digested protein and fat)
- Also, acidic gastric chyme (due to products of protein digestion) come in contact with duodenal mucosa;

↓

Vagovagal reflex

↓

Enzyme rich secretion

Regulation

Gastric phase

Peptides and amino acids → G cells → Gastrin

Gastric distention → Vagovagal reflex

Cephalic phase

Sight, smell and taste of food, chewing etc → Vagal stimln

Gastrin (+) and Vagovagal reflex (+) → Pancreatic secretion - rich in enzymes

Pancreatic secretion - rich in enzymes → Digestion of food → FA, peptides, AA absorbed from intestine → ↓ FA and AA in intestine

Intestinal phase

Acidic chyme in duodenum → S cells → Secretin → Pancreatic secretion rich in HCO_3^- and water → Neutralisation of acid

Fatty acids & peptides in duodenum → I cells → CCK → Pancreatic secretion - rich in enzymes

↓ FA and AA in intestine (−) → I cells

Acidic chyme in duodenum (−) → S cells

IV) Applied physiology

1) **Steatorrhea** occurs in pancreatic insufficiency

- Fat digestion impaired

2) Acute Pancreatitis

- Normally pancreatic enzymes are active only in duodenum. Here, it becomes active in pancreas itself → widespread digestion of Pancreases

Causes → idiopathic, alcoholism, gall bladder stones

Investigation → S. amylase, S lipase, USG, CT

3) Chronic pancreatitis

- Seen in chronic alcoholism, gall stones
- Degeneration of acini, pancreatic ↓ deficiency

Brief answers

1) Resp Functions of liver

I) Synthetic functions

- Plasma proteins, esp → albumin
- Clotting factors → 5, 7, 9, 10, fibrinogen, prothrombin
- Enzymes → ALP, AST, ALT
- Urea
- 25-OH cholecalciferol

II) Metabolic functions

Carbohydrates → glycogenolysis, gluconeogenesis, glycogen synthesis

Proteins → Syn of urea
→ Syn of AA from FA
→ Deamination
→ Purine - pyrimidine metabolism

Lipids → Both degradation and syn of fat
→ β oxdn, lipoproteins syn, saturated FA, cholesterol, PPL

III) Bile secretion

- Components of bile (Bile salts, acids) formed by hepatocytes
- Conjugation of bilirubin

IV) Detoxification and protective fn

V) Miscellaneous

- Storage fn → Glycogen, protein, fat, vit B_{12} and A
- Site of erythropoiesis in IUL
- Destruction of RBC and reservoir of blood
- Hormonal inactivation → cortisol, aldosterone, insulin, glucagon, testosterone

2) Functions of Gall bladder

1) Storage of bile

- In b/w meals → sphincter of oddi closed
  ↓
  Bile diverted into gall bladder from hepatic duct (through cystic duct)

2) Concentration of bile

- Gall bladder mucosa absorbs water, Na, Cl and HCO_3^-
- (Bile salt, Pig, cholest, calcium, lecithin not absorbed)

3) Acidification of bile

- It is by reabsorption of HCO_3^- from bile and
- Secretion of H^+ into bile (in exchange for Na^+)

4) ↑es viscosity

- By secreting mucous → lubricant

5) Equalises pressure in biliary system

- By reabsorption of water

3) Bile

a) Composition

- 500 - 1000 ml / day
- 97% water and 3% solids → organic, inorganic

Inorganic	Organic
Na^+, K^+, Ca^{2+}	Bile salts and pigments
HCO_3^-, Cl^-	Cholesterol, lecithin
	FA, fats
	ALP

b) Mechanism of secretion

1) 1st stage → hepatocytes secrete bile with bile acids, cholesterol and organic constituents

2) 2nd stage → Secretory epithelial cells of bile duct secrete Na^+ and HCO_3^- to bile
→ Under influence of secretin

c) Differences b/w hepatic and gall bladder bile

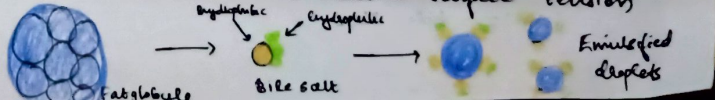
	In Gall bladder bile
1) Water content	less
2) pH	less
3) Solids	More
4) Bile salts	
5) Viscosity	

4) Properties and functions of Bile salts (HAD C^2 LEMP)

micelle

1) Emulsification
Hydrotropic effect

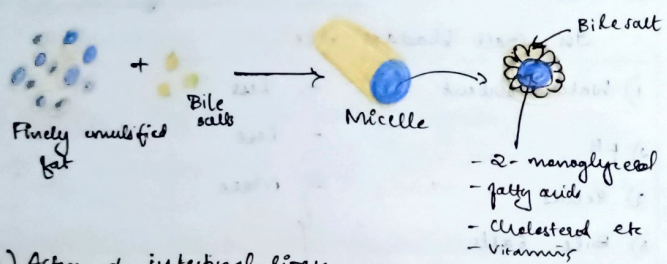
- Helps in digestion of fat
- Emulsification is process by which fat globules are broken to minute droplets and form emulsion in SI.
- Mech → Bile salts reduce surface tension



2) Hydrotropic effect

- Helps in absorption of fats
- Bile salts combine with fats and make complexes of fat called micelles.
- Hydrotropic – micelle formn allows fats to make action. water soluble hence helps for absorption of fats

(fat soluble vitamins A, D, E and K)



3) Actn of intestinal lipase

4) Detergent action → inhibn of bacterial growth

5) Choleretic effect

- Substances which stimulate secretion of bile from hepatocytes.

Eg:- Bile salts, secretin, CCK-PZ

Cholagogue action

- Cholagogues are substances that stimulate ~~secretion~~ release of bile from gall bladder (contraction) into intestine

Eg:- CCK-PZ, bile salts

6) Laxative action

- Agent which induces defecation by stimulating peristaltic movements of intestine.

7) Prevention of ~~Maintenance~~ gall stone formn

- BS keep cholesterol and lecithin in soln
- In absence of BS, cholesterol precipitates along with lecithins and forms gall stone.

5) Enterohepatic circulation ↔ of bile salts, of " pigments

It is the circuln of a substance from intestine to liver.

- Substances involved → Bile salts (mainly), drugs and bilirubin
- More than 90% of bile salts secreted in bile are reabsorbed from SI.
- In this, 50% diffuse through mucosa of duodenum and early part of jejunum, whereas remainder is absorbed by active process in distal ileum.
- These then enter portal circln and to liver hepatocytes. As a result, there is recycling.

Liver — 1° Bile acids: Cholic acid, Chenodeoxycholic acid

Intestine — 2° Bile acids: Cholic acid → Deoxycholic acid; Chenodeoxycholic acid → Lithocholic acid

Liver:

Conjugation with glycine and taurine

Glycine: Glycholic acid → Combination Na^+ and K^+ → Na^+ - Glycocholate, K^+ - "

Taurine: Taurocholic acid → Sodium taurocholate, K^+ "

Bile salts

(Enterohepatic circle of Bile salts)

On an average, these salts make the entire circuit around 17 times before being thrown out in the feces.

IMPORTANCE

1) Decreases workload of liver — as it recycles bile salts ~~and vitamins~~

- Conserves cholesterol (used to syn bile acids)
- Reduce the need for denovo bile acid synthesis

2) Conservation of metabolic resources

- Minimise loss of bilirubin, hormones (Eg: estrogen) and certain drugs maintaining plasma level.

3) Detoxification

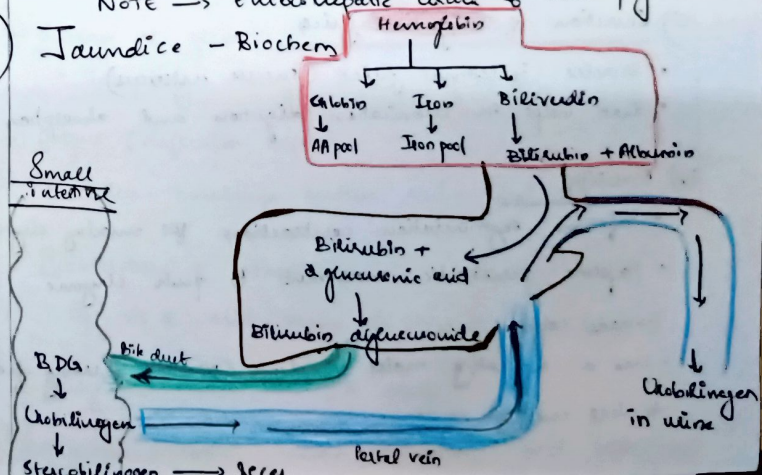
- Some xenobiotics and conjugated toxins secreted into bile may be reabsorbed; thus process prolongs their half-life unless interrupted.

4) Clinical relevance

- Disruption of enterohepatic circulation (Eg:- ileal resection of diseases like Crohn's) can cause:-
  - i) Fat malabsorption
  - ii) def of fat-soluble vitamins
  - iii) cholesterol gallstones
- Certain drugs rely on enterohepatic circle for prolonged action (Eg:- oral contraceptives).
- Interfering with circle (Eg:- using BA sequestrants) can reduce serum cholesterol levels.

6) Jaundice - Biochem

NOTE → Enterohepatic circle of bile pigments



CHAPTER-5

SMALL AND LARGE INTESTINE

1) Function of SI

ANS: i) Digestion of nutrients

- Breakdown of carbohydrates, proteins and fats by disaccharidases, peptidases and lipases.
- Digestion is completed in duodenum and jejunum.

ii) Absorption of nutrients (mostly jejunum)

- Absorbs → monosaccharides
  - AA and small peptides
  - FA and monoglycerides (via micelle formn)
  - water and electrolytes
  - vitamins (Eg :- B_{12} with help of intrinsic factor)
- Iron from duodenum
  B_{12} and bile salts from ileum

iii) Secretion of digestive juices

- Secretes intestinal juice (succus entericus)
- that helps in lubrication, digestion and absorption

iv) Motility

- Performs segmentation contractions for mixing chyme
- Performs peristaltic movements to push chyme towards colon
- has a migrating motor complex (MMC) during fasting to clear residual content.

v) Hormonal function

- Enteroendocrine cells in mucosa release :-
  - Secretin → stimulates pancreatic HCO_3^- secretion
  - CCK → " bile and enzyme release
  - GIP, GLP-1 → involved in insulin regln

vi) Immune fn

- Peyer's patches and mucosal immune system protects against pathogens.
- secretory IgA maintains gut immunity.

2) Functions of large intestine (ABSORB M V D)

1) Absorption of water and electrolytes
2) Bacterial fermentation
   - Gut flora ferment undigested carbs and proteins
3) Storage of feces
   - Temporary storage before defecation
4) Output (defecation reflex)
   - Reflex involving rectum and anal sphincters
5) Reabsorption of vitamins
   - Eg vit K and some B vitamins produced
6) Butyrate and SC FA prodn
7) Mucus secretion → lubrication and protection

8) Vitamin B12

9) dehydration of contents
- Converts chyme to solid ~~contents~~ feces

3) Dietary fiber → biochem

4) Composition of intestinal juice (pH ~ 7.5–8)
- Volume 1–2 L/day
- Water, electrolyte, mucus, SPLEEN
- Intestinal enzymes (WERME) — secreted by Brunner's (duodenum) & goblet cells

- Sucrase	Sucrose →	Glu + Fru
- Peptidase	Small pep →	amino acids
- Lactase	Lactose →	glu + gal
- Enterokinase	activates	trypsinogen → trypsin
- Nucleotidase	DNA/RNA →	Nucleotides → Nbase + Sug_1 + PO_4^{2-}

CHAPTER – 6
Gastrointestinal movements

SE

1) Deglutition → is swallowing is an active process by which ingested food bolus enters stomach

Ans:- I) Stages → Oral, Pharyngeal, Esophageal

ORAL STAGE (voluntary)
- chewed food rolled into bolus by movements of cheek and tongue
- Contraction of front part of tongue press bolus against hard palate
- Movements of middle parts pushes it back
- By strong contraction of hyoglossus, enter into esophagus
- Afferent and efferent → 5, 9, 10 CN

PHARYNGEAL STAGE (involuntary)
- less than 2 seconds
- Initiated when food comes in contact with posterior aspect of tongue, palate, tonsils, post pharyngeal wall

↓

Automatic pharyngeal muscle contraction

↓

Oesophagus

▷ 4 outlets

1) Back to mouth : Prevented by approximation of tongue against roof of mouth

2) Into nasopharynx :- prevented by pressing against soft palate against post pharyngeal wall.

3) Into larynx : Prevented by

- deglutition apnea
  - Rec, swallowing center inhibits medullary respiratory centre.
- tight approximation of vocal cord
- Horizontal deflection of epiglottis → it covers laryngeal opening
- Contraction of sup constrictor of pharynx

4) Pharynx → Oesophagus

- By relaxing upper oesophageal sphincter

OESOPHAGEAL STAGE (involuntary)

- Transport bolus from pharynx → stomach
- 2 types of movements
  - 1st degree peristalsis (1° P)
    - A ring of contraction proximal to bolus
    - Portion distal to bolus relaxes (receptive relaxation)
  - 2nd degree peristalsis
    - When 1° peristalsis fails to empty bolus into stomach the retained food initiates 2° waves due to distention of oesophagus.
    - Initiated by ENS and long vagovagal reflex
- When peristaltic wave reaches LES, it relaxes and allows food to enter stomach. This relaxation is mediated by neurons that release NO and VIP.

II) Disorders

1) Dysphagia → difficulty in swallowing

2) Achalasia cardia / Cardiospasm

- It is a motility disorder of oesophagus caused by failure of LES to relax and loss of coordinated peristalsis of oesophageal body.

Pathophysiology

1) Loss of inhibitory neurons in myenteric plexus (particularly NO and VIP)

2) Impaired relaxn of LES during swallowing

3) Absence of coordinated peristaltic contractions of oesophagus

4) LES remains tonically contracted causing obstn.

5) Leads to oesophageal dilatation above LES and retention of food.

FEATURES

1) Dysphagia
2) Regurgitation
3) Chest discomfort
4) Weight loss

Management

- Pneumatic dilation of sphincter or incision of oesophageal muscle (myotomy)
- Inhibition of Ach release by injection of botulinum toxin into LES produces relief for several months.

3) Gastro-oesophageal reflex disease (GORD)

- Condition in which there is reflux of gastric contents into oesophagus
- due to incompetence of LES
- This reflux causes heart burn and oesophagitis and can lead to ulceration of oesophagus

4) Aerophagia

- Some people (esp nervous people), swallow large amts of air.
- Some air is regurgitated, some absorbed and rest reaches colon and expelled as flatus.
- Gas in intestine can cause cramps, borborygmi (rumbling noises) and abdominal discomfort

IV) Deglutition reflex (Pharyngeal stage)

1) Receptors – around pharynx
2) Afferent – carried by V, IX, X
3) Deglutition centre – lower pons and medulla (NTS and NA)
4) Efferent – V, IX, X, XII
5) Effector organ – pharyngeal muscle contraction

↓

Peristaltic movements occur leads to relaxation of UES

SE

2) Gastric movements

Peristaltic activity of the gastric musculature

A) Motility of the empty stomach

1) Migrating motor complex (MMC)

2) Hunger contractions

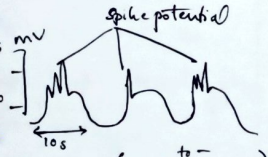
B) Motility related to meals

1) Receptive relaxation / gastric filling movements

2) Mixing peristaltic movement

3) Gastric emptying movement

A) Motility of empty stomach



(−65 to −45 mV)

- Spontaneous rhythmic fluctuations occurs in membrane potential of smooth muscles of GIT (except in oesophagus and proxi of stomach)
- This is the Basic Electrical Rhythm (BER) and is initiated by interstitial cells of Cajal
  - They act as pacemaker cells in stomach and SI → located near myenteric plexus.
- Rate of BER → Stomach : 4/min
  Duodenum : 12/min
  Distal ileum : 8/min
- Function of BER is to coordinate peristaltic and other motor activity

1) Migrating motor complex

- Cycles of peristaltic waves, migrate from oesophagus to distal ileum, during fasting (interdigestive period)
- Phase I → Quiscent period
  Phase II → Irregular electrical activity
  Phase III → burst of regular activity
- MMC migrates aborally (5cm/min) at an interval of 90 min
- FN → It clears stomach and SI and in preparation for next meal. MMC stops with intake (interdigestive housekeeper) of food.

2) Hunger contractions

- Mild peristaltic contraction occurs in empty stomach, which over a period of hours ↑ in intensity and are called "hunger contractions"
- MMC are responsible for this
- When they become strong, they fuse to cause tetanic contractions.
- Lasts for 2-3 min, may be painful
- Are associated with sensation of hunger.

B) Motility related to meal

1) Receptive relaxation / Gastric filling

- When food enters stomach, the fundus and greater curvature relaxes to accomodate food.
- It is a vagovagal reflex initiated by distention of stomach
- Its significance is to accomodate food easily without much ↑ in pressure (1-2 L)

2) Peristalsis / Mixing waves

- Begins in mid stomach (body) when stomach wall stretched by gastric contents, and moves towards antrum
- ENS → Mix gastric contents with enzymes and acid and form chyme
- Controlled by BER and peristalsis becomes more intense near pylorus to help grind food
- Occurs at 3-4 times/min.

RETROPULSION

- When chyme hits a closed pyloric sphincter, it is pushed backward into stomach → further mixing
- Important in grinding solid particles into smaller ones.

NOTE: Peristalsis Due to ENS, independent of extrinsic innervation

- local stretch releases secretonin, which activates myenteric plexus

3) Gastric emptying

- The duration the chyme remains in stomach and empties itself into SI is called gastric emptying time.
- Takes 3-4 hrs

Factors influencing

1) Consistency of food

- liquid food empties faster than solids because solids depends on mixing movements to form semi-solid chyme.

2) Gastric factors (promotes emptying)

- Volume of gastric content
- greater the volume, greater peristaltic waves and greater the emptying
- Gastrin → promotes
- Type of food → Rate of emptying: Carb > Proteins > fats

3) Duodenal factors (inhibit gastric emptying)

- Enterogastric reflex (reflex initiated in duodenum)

Stimulated by :-	Mechanism
- acidity of chyme	→ ↑ Secretin → ↓ gastric motility
- Hyperosmolar food	→ Reflex via enteric neuves
- Partially digested proteins (acidic)	
- fatty chyme	→ CCK → inhibits motility
- Distention of duodenum	→ enterogastric reflex

DA

APPLIED ASPECTS

Movement of small intestine

Vomiting (Abnormal movement of stomach)

1) ~~Swallowing Syndrome~~

- Reverse peristalsis
- Vomit centre → Reticular formn of medulla oblongata near vagal nucleus location

I) Actvn through ↔ direct actvn / afferent impulses

DIRECT ACTVN of vomiting centre

- an injury to area
- Raised intracranial pressure

Afferent impulses actvng vomit centre

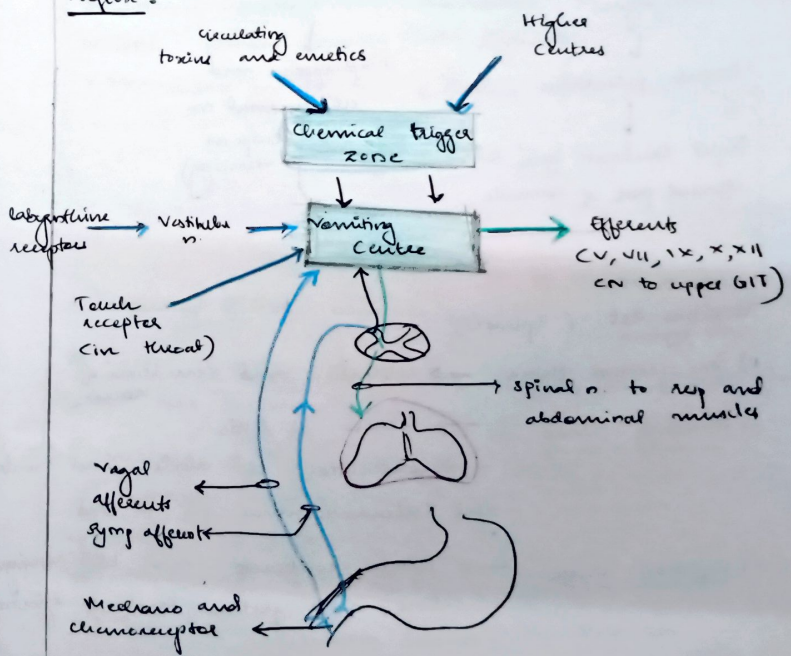
1) Visceral efferent pathway in the sympathetic and vagi
   - relay impulses arising due to irritation of mucosa of upper GIT
2) Afferent impulses from vestibular nuclei
   - Mediate nausea and vomiting → motion sickness
3) Afferent from higher centres (diencephalon and limbic system)
   - Mediate emetic response to stimuli such as nauseating smell, sickening sights and memory etc

II) Actvn of Chemoreceptor trigger zone (CTZ)

- CTZ in area postrema on lateral walls of 4th ventricle
- More permeable to many substances as it lies outside the blood-brain barrier
- Chemoreceptor cells initiate vomiting by :-

1) circulating emetic drugs in patients with uraemia and radiation sickness
2) Circulating emetic substances such as emetin, apomorphine, digitalis and glucosides.

Reflex :-



Vomiting reflex

Irritation of GIT mucosa

↓

Stimln of mucosal receptors

↓

Afferents → by vagus and symp fibers

↓

Reach vomit center

↓

Efferents → V, VII, IX, X, XII CN

- Back to irritated organ → Reverse peristalsis → Propel contents from irritated part of stomach → Vomit expelled out
- Spinal nerve → Diaphragm and abdominal m. (Help in vomiting) → Vomit expelled out

Vomiting act (3 phases)

1) Pre-ejection phase → salivation and sensation of nausea

2) Retching phase → Closure of glottis
→ Contraction of abdominal muscles and intraabdominal p. is ↑ed

3) Ejection phase → Pylorus contracts and LES, esophagus relax and gastric contents ejected (Reverse peristalsis)

3) Movement of small intestine

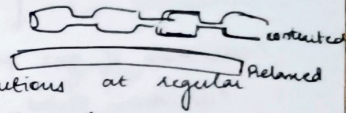
I) Motility of SI during interdigestive period

- Migrating motor complex (MMC)
  - = Fasting
  - = It sweeps out chyme remaining in intestine
  - - Control hormone → Motilin

II) Motility of SI during digestive period

- They are mixing movement and include :-

- SEGMENTAL CONTRACTIONS



- Concentric ring like contractions at regular intervals divides lumen into segments.
- Mechanism :- Distention of portion of SI with chyme
  ↓
  Stretching of wall
  ↓
  Stretch receptor
  ↓
  Concentric contraction of circular muscles
- Frequency of BER = 10-12/min

- TONIC CONTRACTIONS are prolonged contractions that isolate one segment of intestine from another

⇒ Functions of segmental and tonic contractions
i) Thorough mixing
ii) Active absorption
iii) Massaging effect on blood vessels
iv) ↑es transit time and favours absorption

(vi) PERISTALSIS (By Bayliss and Starling)

- Reflex propulsive movement initiated when gut wall stretched with contents.
- From oesophagus to rectum
- Mechanism :- Stretch releases serotonin

↓

Stimulate sensory fibres of myenteric plexus (cholinergic neurons which pass in 2 directions)

↓

Antegrade ↔ Retrograde

Contraction of gut proximal to stimulus and relaxation distal to stimulus (receptive relaxation)

- Rate → 2-25 cm/s
- Proximal contraction : Ach and substance P
  Distal contraction : NO, VIP etc
- The peristaltic waves always travel from oral end towards aboral end of intestine → Starling's law of gut / "Law of intestine"

(vii) Movement of villi

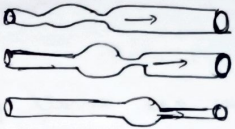
- Consists of all alternate shortening and elongation
- Lashing movement

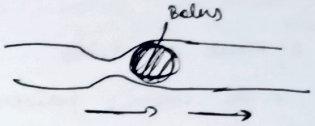
FUNCTIONS:

- ↑es mucosal lymph and blood flow
- Stir luminal contents and ↑es absorption

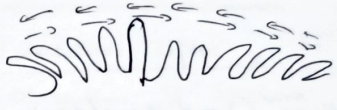
Diagrams:-

1) Segmental contraction





2) Peristalsis — Receptive relaxation



3) lashing movement of villi

4) Movements of large intestine (3 types of movements)

1) Haustral shuttling (similar to segmentation contractions)
2) Mass Peristalsis
3) Mass action contraction

1) Haustral shuttling

- Contraction of circular muscle produces constrictions rings at regular intervals
- Contraction of longitudinal m. (taenia coli) causes portion btw rings to bulge in bag-like sacs called haustrations.

(2) • Contraction disappears within 60s and are initiated in a nearby area.

⇒ FUNCTIONS

- Vigorously mix contents of colon
- Expose mass contents to mucosa and facilitate absorption.

2) Mass peristalsis

- In colon, peristaltic waves are small pressure waves of prolonged dwell and propel contents towards rectum

3) Mass action contractions (3 to 4 times/day)

- Special type of peristaltic contractions observed only in colon.
- They move material into rectum and cause rectal distention initiate defecation reflex.
- A mass movement can be initiated by:-
  1) Gastrocolic / duodenocolic reflex
  2) Intense stimuli of parasymp nerves
  3) Overdistention of a segment of colon

(2) GASTROCOLIC REFLEX

- Contraction of colon induced by entry of food into stomach
- Results in an urge to defecate after meal. Because of this, defecation after meal is a rule in children
- In adults, the bowel training suppresses the reflex
- The reflex contains 2 phases:-
  1) Early / Rapid → initiated by distention of stomach
  2) Late / slow → mediated by Gastrin and CCK, which are secreted into blood after meal

5) Defecation reflexes and abnormalities

1) Intrinsic reflex

- Distention of rectum with faeces initiates afferent signal via myenteric plexus
- Initiates peristaltic waves in descending, sigmoid colon and rectum causing active contraction of smooth m.
- Forces faeces towards anus
- Since this reflex is weak on its own, it is facilitated by parasympathetic defecation reflex.

2) Parasympathetic defecation reflex (spinal cord reflex)

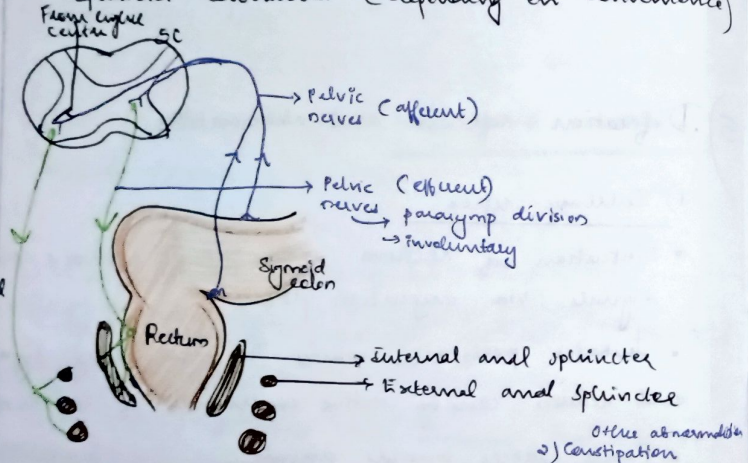
Distention of rectum
↓ Pelvic n. (Afferent)
Sacral segments (S2 & S3)
↓
Reflex parasymp discharge (mainly from S2)
↓ Pelvic nerves (Efferent)

- Inhibition of internal anal sphincter (relaxation)
- When rectal pressure above 50mmHg, discharge in pudendal n. inhibited
- This relaxes external anal sphincter and facial expulsion

NOTE :- Gastrocolic and duodenocolic reflexes aid in defecation

9) Voluntary defecation

- It can be initiated by straining
- Can also be inhibited by keep external anal sphincter contracted (depending on convenience)



Other abnormalities
2) Constipation
3) Diarrhoea

1) Hirschsprung's disease / aganglionic megacolon

- Congenital absence of ganglion cells in both myenteric and submucosal plexus
- Site of involvement is distal colon
- Leads to blockage of both peristalsis and mass action contractions at the aganglionic segment
- ∴ Feces pass the aganglionic region with great difficulty and accumulate in large intestine.
- Can be treated by cutting the aganglionic portion of colon and anastomosing the cut ends.

CHAPTER- 7

Digestion and absorption of food

Essays

1) Digestion and absorption of carbohydrates, proteins and fats.

Ans:-

I) Digestion of carbohydrates

- Sources :- Cereals (starch), meat (glycogen), milk (lactose), table sugar (sucrose), fruits (monosach)

A) In mouth

- By salivary α- amylase (Ptyalin)
- Digests cooked starch ⟶ Maltose

B) In stomach

- Minimal carbohydrate digestive activity and α- amylase action continues

C) In small intestine

- Polysaccharides —(Pancreatic α-amylase)→ Oligosaccharides (Eg:- Starch, glycogen) (Eg: maltose, dextrin)
- Dextrin —(α-limit dextrinase)→ Glucose
- Sucrose —(Sucrase)→ Glucose + Fructose

II) Absorption of carbohydrates (Jejunum and upper ileum)

- Glucose and galactose by a common Na^+ dependent active transport. (using SGLT1)

- Fructose by facilitated diffusion
- Pentose by simple diffusion

ABNORMALITIES

1) Congenital lactose intolerance
   - due to congenital def of enzyme lactase

I) Digestion of proteins (by exopeptidases and endopeptidases)

A) In stomach

- Pepsinogen to pepsin
- Pepsin splits protein into proteoses, peptones and polypeptides.

B) In small intestine

- Pancreatic proteases
- Brush border proteases

Reactions:- Nucleoproteins —HCl→ Proteins + Free NA

Free NA (RNA and DNA) —Ribonuclease / deoxyribonuclease→ Nucleotides + Nucleosides

Nucleotides and nucleosides —Nuclease, Nucleotidase, Nucleosidase→ Pentoses (purine and pyrimidine)

II) Absorption of proteins

- end products of protein digestion — AA, dipeptides, tripeptide are absorbed through epithelial surfaces
- Mechanism :-
  - Na^+ dependent active transport
  - Simple diffusion
  - Endocytosis

Abnormalities

1) Def of trypsin — inadequate absorption of proteins
   - occurs in pancreatic diseases

2) Malabsorption of AA due to lack of transporters

- HARTNUP's disease
  - due to congenital defect in transporters for neutral amino acids in intestine and renal tubules.
- Cystinuria
  - congenital defect in transporters for basic amino acid.

III) Digestion of fats

Types of fat

- Simple / neutral fats → triglycerides and cholesterol
- Compound fat → phospholipids
- Associated fats → steroids and fat-soluble vitamins

Site of digestion

- by lipolytic enzymes in mouth (lingual lipase) and stomach (gastric lipase)
- Occurs mainly in small intestine

Mechanism of digestion

1) Emulsification of fats by bile salts
2) Hydrolysis of fat by pancreatic and intestinal lipolytic enzymes (Pancreatic lipase, cholesteryl ester hydrolase etc)
3) Acceleration of fat digestion by micelle formn.

ABSORPTION of fat

→ from duodenum in micelles form (Absorptive form)

- These micelles on entering enterocytes release TAG, cholesterol ester and phospholipids
- These are then associated with apo B48 and A1 to form chylomicron which is absorbed in lacteals

Abnormalities

1) Lipid malabsorption

Causes :-

- def of pancreatic lipase in pancreatic diseases
- Bile def in disorders of liver and gall bladder

Eg: Steatorrhoea → an ↑ed amt of fat in stools

Essay

Q) Gastrointestinal hormones and their actions

Ans:

Based on their physicoanatomical similarities GIT hormones can be classified into 3 types :-

1) Gastrin family
2) Secretin "
3) Other GI hormones

1) Gastrin fam	Secretin fam	Others
- Gastrin	- Secretin	- Motilin
- CCK-PZ	- Gastric inhibitory peptide (GIP)	- Somatostatin (GIP)
	- Vasoactive intestinal peptide (VIP)	- GRP
	- Glucagon	
	- GLP (Glucagon like peptide)	

GASTRIN

- Stimulants for secretion
- Pre. of food (protein) in stomach
- Stimln of local nervous plexus in stomach and SI
- Vagovagal reflex during gastric phase of gastric secretion
  ∴ GRP released at vagal nerve ending which stimulates G cells

~~Inhibiting factors~~

- Inhibiting factors

- Acid in antrum → directly on G cells (-ve feedback regn) and
- Indirect by → release of somatostatin (potent inhibitor)

SECRETIN

- Stimulants

- Prosecretin is stimulated when acid chyme enters duodenum of stomach
- Products of protein digestion

FUNCTIONS (table)

- ↑ ↑ potency of CCK
- Constricts pyloric sphincter

CCK

- Stimulants

- Pre. of chyme - containing digestive products of fats and proteins ie → fatty acids, peptides and amino acids in upper part of SI.

- Actions :-

1) Pancreatic secretion ↑
   - ↑ secretin secretion
   - ↑ enterokinase "
2) Gall bladder contraction ↑
3) SI motility ↑
4) Inhibits gastric motility
5) Augments contraction of pyloric sphincter
6) Suppress hunger
7) Induces drug tolerance to opioids

HORMONE	STIMULI	SITE OF SECRETION	Actions: GASTRIC SECRETION	GASTRIC MOTILITY	Pancreatic Secretion	Bile secretion	Gall bladder contraction	SI secretion	SI motility
1) Gastrin	- Small peptides, aa - Gastric distention - Vagal stimulation	G cells of gastric antrum	+	+	+	0	0	0	0
2) CCK	- Small peptides, aa - FA	I cells of duodenum and jejunum	0	−	+	0	+	0	+
3) Secretin	- Acid - Fatty acids	S cells of duodenum	−	0	+	+	0	0	0
4) GIP	- FA - AA - oral glucose	Duodenum and jejunum	−	−	0	0	0	+	—
5) VIP	- FA	Jejunum	−	−	0	0	0	0	0
6) Somatostatin	- Acid in stomach	D cells of islets of Langerhans	−	−	−	0	−	0	0

7) MOTILIN

- Source & secretion → Mo cells in stomach and intestine
  Enterochromaffin cells in intestine
- Stimulant Actions :- → When chyme from stomach enters duodenum
- Functions

1) Accelerates gastric emptying
2) ↑ mixing and propulsive movements of GI
3) ↑es peristalsis in colon

8) Gut-brain axis

- It is a bidirectional communication b/w central and ENS, linking emotional and cognitive centres & peripheral fns of intestine.
- Gut flora plays an imp role in signalling as it is involved in prodn of chemicals like Ach, catecholamines etc
- These chemicals activate vagus n. that process info to brain about intestines.

CLINICAL APPLICATIONS

- Probiotics have been tried for treating central nervous disorders.