

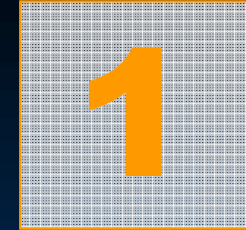
Summer Pathophysiology courses



GASTROINTESTINAL DISORDERS 1

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General symptomatology

Diarrhoea

- Mechanisms:

1) inactivation of pancreatic enzymes - low pH in duodenum, upper jejunum -> fat is in colon converted by bacterial enzymes to hydroxy fatty acids -> inhib. of absorption + stimulation of secretion

2) damage of the mucosa in upper small intestine (infections, toxins)

3) altering of bacterial luminal flora (low break down -osmotically active subst),

4) increase of intracellular cAMP (inhibition of phosphodiesterase)-At secretion

5) inhibition of particular ion absorption (bile acids, fatty acid prod. in colon) - abnormal amount of water(>) secreted by the intestine each day

1. Osmotic - poorly absorbed osmotically active compounds stops when the offending agent stopped., **loss of water bigger than loss of salts,**

Etio;

- Abusus of laxatives (magnesium sulphate), (which work to alleviate constipation

- excessive sugar (lactose), sugar alcohols - sorbitol (often found in sugar-free foods)

Diarrhoea

- **Maldigestion** (e.g. pancreatic disease **or coeliac disease**, (blind loop syndrome, --> formation of volatile acids by bacterial enzymatic breakdown in colon (lactate, isobutyrate, dihydroxybile acids, hydroxy fatty acids), **Lactose intolerance, fructose malabsorption**)

2. Secretory - little or no structural damage; increase in the active secretion, or there is an inhibition of absorption, intestinal fluid secretion is isotonic with plasma, **loss of water and salt is proportional**

Etio:

- Intestinal obstruction, inflammation, mesenteric ischemia,
- Chemicals: abuse of laxatives (phenolphthalein, senna), antibiotics (lincomycin, clindamycin, neomycin, tetracycline), theophylline, caffeine, alcohol (cAMP)
- Tumors: gastrinoma - Zollinger-Ellison syndrome --> gastrin (associated with adenomas of parathyroid, thyroid, adrenal - MEN I), Verner-Morrison syndrome (pancreatic cholera) tumor of the pancreas --> VIP, GIP
- Bacterial toxins: E.coli, Vibrio cholerae

Diarrhoea

3. **Exudative** - presence of blood and pus in the stool

- **Etio: inflammatory bowel diseases** (Crohn's disease, ulcerative colitis), E. coli

4. **Inflammatory**

- damage to the mucosal barrier **features of all three of the other types**
- passive loss of protein-rich fluids and a decreased ability to absorb (lost fluids)
- **Etio:** viral, bacterial, parasitic infections, autoimmune (**inflammatory bowel diseases**); tuberculosis, colon cancer, enteritis.

5. **Motor diarrhea** - abnormally intestinal or colon motility → transit of content, absorption (similar to secretory diarrhea)

- **Etio: Irritable bowel syndrome** (formerly: spastic colitis, mucus colitis) - (abnormal colonic contractility in response to stress, emotional tension grief, guilt); lost the ability to generate local segment waves motor abnormality of distal left colon)

Constipation

- Definition:

1. Objective: number of stools per day or per week (3-5 normally) problem: low/high residue diet (content of fibres)
2. Subjective: small, hard stools; difficulty with expulsion, incomplet evacuation or infrequency

- Mechanism: abnormal function of autonomic regulation, abnormal smooth muscle function

1. Systemic diseases& influences

A. Endocrine & metabolic disturbances

- **Diabetes** - neuropthy, gastropathy
- Porphyria, Amyloid neuropathy, Ureamia, Hypokalemia, Aging
- Panhypopituitarism, hypopituitarism, hypercalcaemia (hyperparathyroidism, milk-alkali syndrome), vit. D intoxication), Pheochromocytoma, Enteric glucagon excess (glucagonoma), Hypoadrenocorticism , Myxedema,

Constipation

A. Central nervous disturbances

- **Spinal cord.** sclerosis; central nervous disorders Sacral meningocele, Spinal cord injuries, Cauda equina tumor, Tabes dorsalis, Multiple sclerosis
- **Brain:** cerebral tumors, parkinsonism, cerebrovascular disease), paraplegia

2. Drugs

- Anticholinergics (propulsive + segmenting activity), Analgetics, Anesthetics
- Antacids (calcium and aluminium compounds),
- Anticonvulsants, Antidepressants (Phenothiazines), Barium sulphate, Bismuth, Diuretics, Drugs for Parkinsonism, Ganglionic blockers, Hypotensives, MAO Inhibitors, Myorelaxants,
- Metallic intoxication (As, Pb, Hg, P), Opiates (narcotic derivatives: heroin, morphine, meperidine, etc), Laxative addiction

Constipation

3. Diseases of intestine and colon

A. Neurogenic & neuromuscular disorders

- **Hirschsprung's disease** (congenital disorder <- absence of gangl. cells of myenteric plexus of the muscular layer proximal to the internal rectal sphincter)
- (absence of rectoanal inhibitory reflex, loss of rectosigmoid contraction, propulsion of faeces => dilated proximal colon),
- **Pseudo-obstruction** (familial disorder, episodes of ileus/obstipation <- lesions in myenteric plexus of the small, large bowel, esophagus), Chagas' disease (∅ ganglion cells of the colon, esophagus)
- **Smooth muscle atrophy** (Scleroderma, Dermatomyositis, Myotonic dystrophy, congenital myotonia)

B. Organic obstructive lesions in gut

- carcinoma, inflammatory strictures, ulcerative colitis, Crohn's disease)
- extracolonic compressions (tumors- kidney, uterus, ovaries, prostate), lymphogranuloma, venereum,

Constipation

4. Psychogenic constipation

- likely established in infancy (paternal authority-> withholding the stool, increased intervals between stools -> child's bowel habit) -> fully developed in the adults - => Irritation bowel
- **Megacolon** - obstipation leading to progressive dilatation of colon <-1. Agangliosis (Hirschprung's disease in children, adolescents, 2. Congenital (unknown origin), 3. Acquired (psychogenic megacolon, 4. Toxic megacolon [ulcerative & granulomatose colitis, amebias], pseudo-obstruction)

Disorders of motility

- **Dysphagia** = difficulty swallowing due to obstruction of esophagus, distension impair-
- **Causes** **a) mechanical** : intrinsic obstruction (tumors, strictures, diverticular herniations (outpouchings), extrinsic (tumors of mediastinum, lung, bronchi, thyroid gland, thymus, etc.) , **(b) functional dysphagia**: neural, muscular disorders affecting striated musculature of upper esophagus (dermatomyositis, Parkinsonism, extrapyramidal syndromes)
- **Achalasia** = form of dysphagic malfunction afflicting smooth muscles of middle and
- **Causes:** increased number of ganglionic cells in myenteric and submucosal plexuses atrophy of muscle, impaired vagus nerve → loss of normal muscle tone and peristalsis → accumulation of food and distension of upper esophagus
- **Hiatal hernia** = protrusion (herniation) of upper part of the stomach through the diaphragm into the thorax; (a) sliding (direct) hiatal hernia (b) paraesophageal (rolling) hiatal hernia

Disorders of motility

- **Gastroesophageal reflux** = reverse movement (reflux) of digested chyme and also gastric juice or duodenal content (bile acids, enzymes) from stomach to esophagus.
- **Causes**; (a) weakness of lower esophageal sphincter (b) delayed gastric emptying (gastric, duodenal ulcers → pyloric edema; strictures, hiatal hernia, etc.

- **Pyloric obstruction** = narrowing or blocking between stomach and duodenum (pyloric sphincter)

Causes (a) congenital, (b) acquired (gastric peptic ulcer, carcinoma → inflammation, edema, spasm, fibrosis); epigastric fullness, anorexia, weight loss, gastric distension, atony copious vomiting → **hypokalemic, hypochloremic alkalosis+ dehydration, malnutrition**

- **Intestinal obstruction (ileus) =**

(a) Mechanical ileus (rectal, colonic atresia, postinflammatory strictures, (b) Strangulation ileus (c) Functional ileus (failure of motility)

- **Symptoms**; 1. Pain - intermittent colicky-character; if strangulation constant, perforation peritonitis → cramps, abdominal pain; 2. Vomiting + Distension of bowels:

Disorders of motility

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Disorders of motility

- **Intestinal obstruction (ileus)**

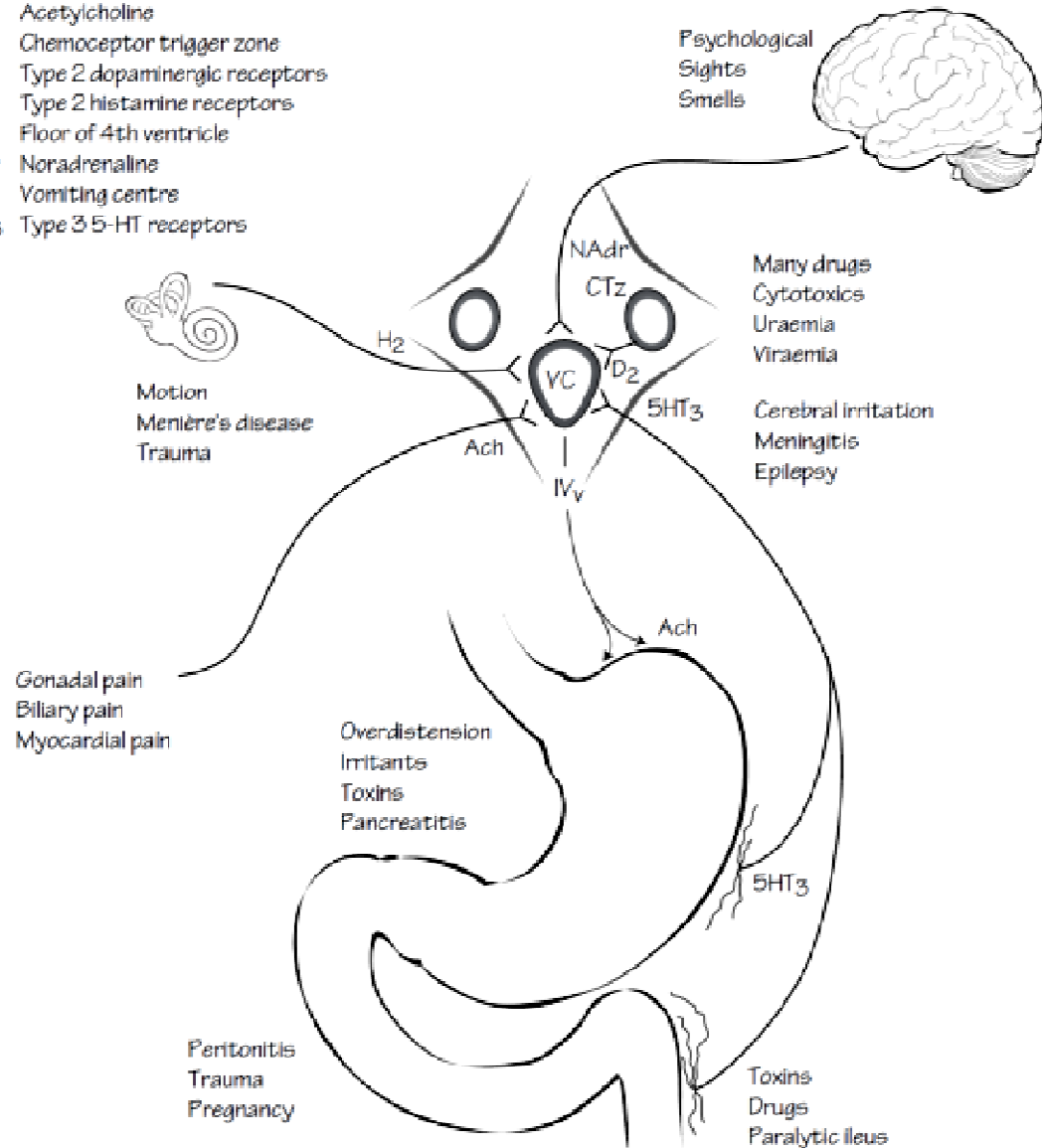
1. **Mechanical ileus** (rectal, colonic atresia, postinflammatory strictures,
2. **Strangulation ileus** (inguinal, diaphragmatic)
3. **Functional ileus** (failure of motility)

- **Symptoms.**

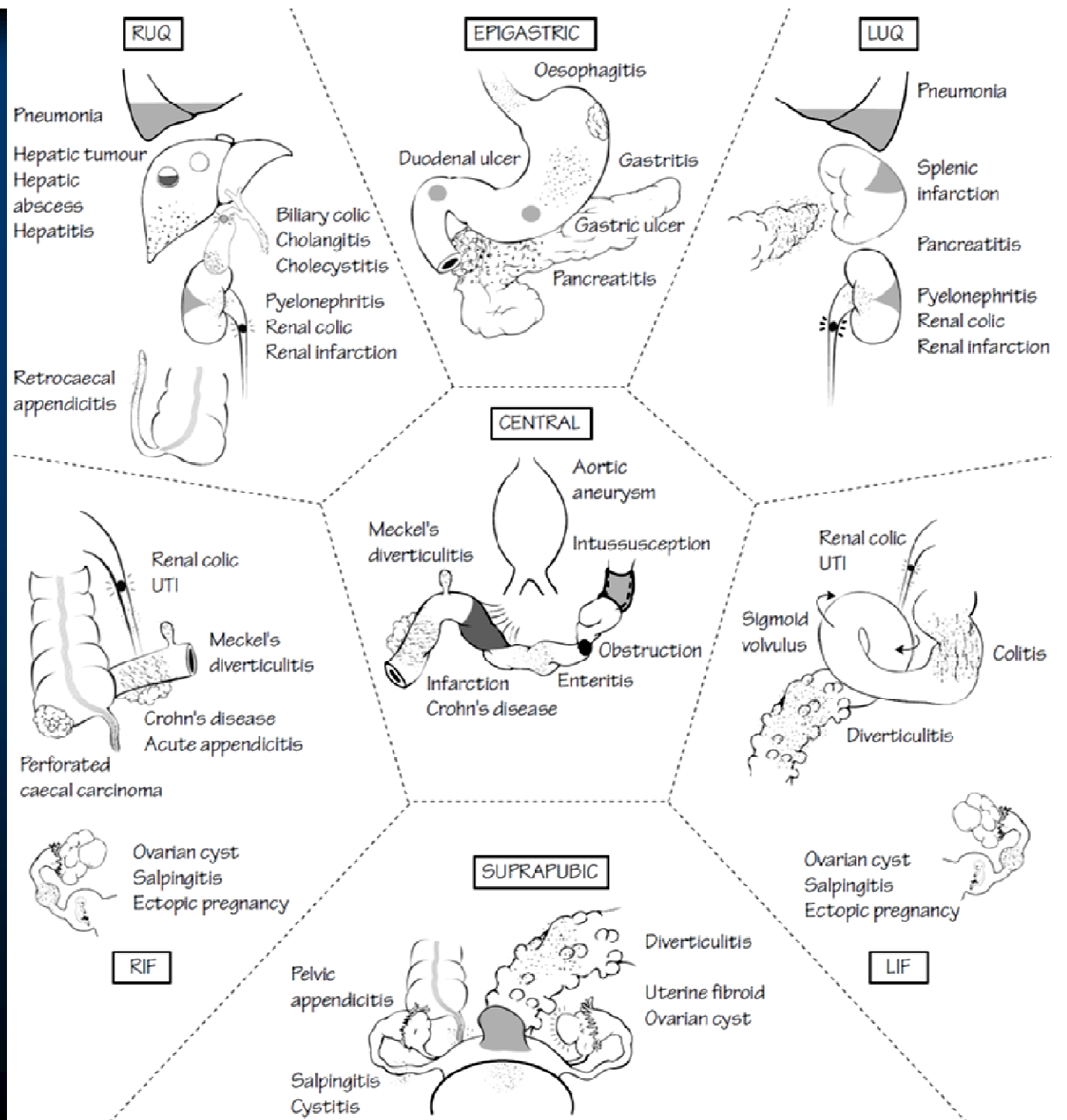
1. **Pain** - intermittent colicky-character; if strangulation constant, perforation peritonitis -> cramps, abdominal pain;
2. **Vomiting** + Distension of bowels: early profuse (pylorus), bile-stained (upper small intestine), large distension, no vomiting (lower intestine);
3. **Diarrhea**

Vomitus

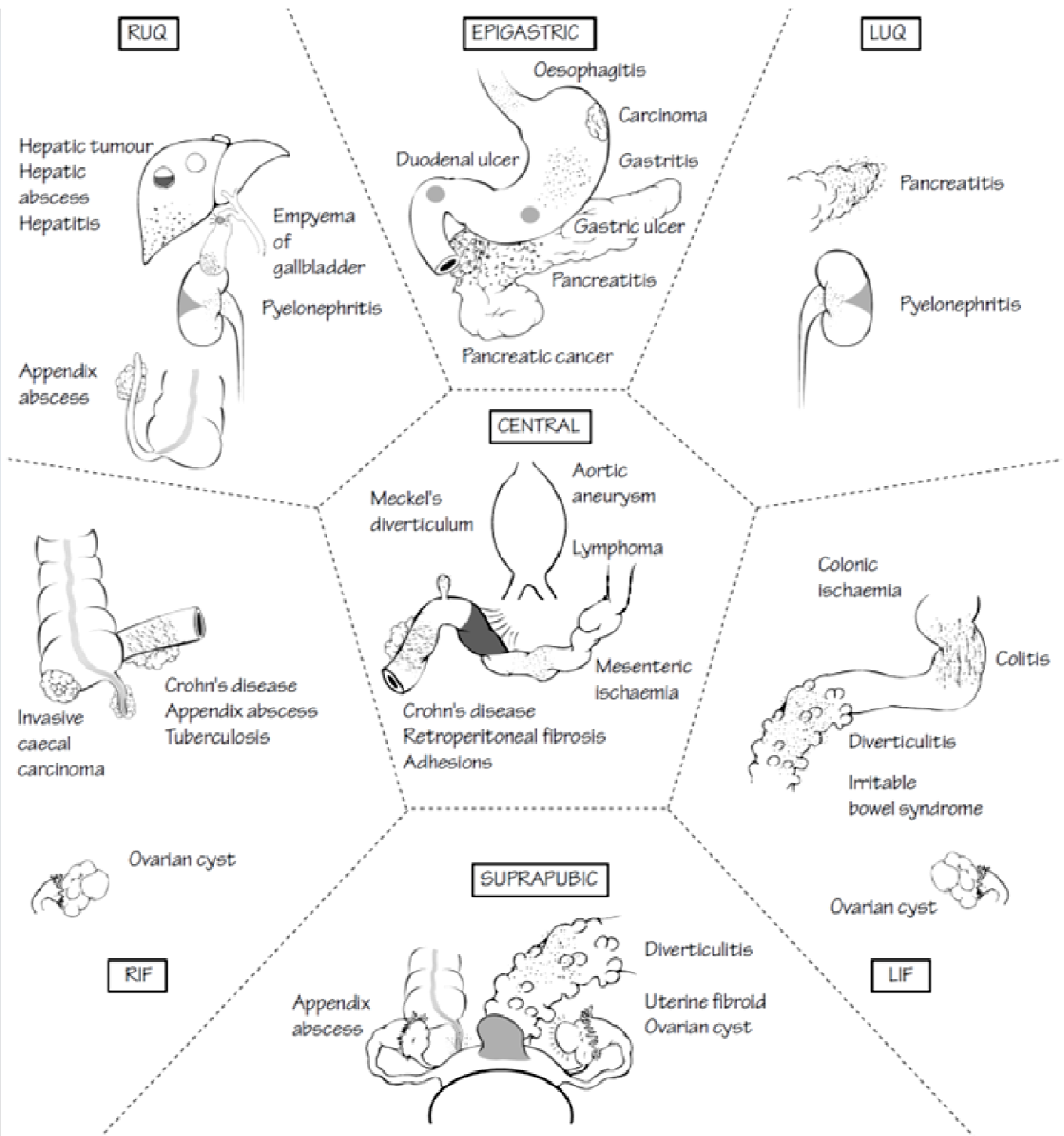
- Ach Acetylcholine
- CTz Chemoceptor trigger zone
- D₂ Type 2 dopaminergic receptors
- H₂ Type 2 histamine receptors
- IV_v Floor of 4th ventricle
- NAdr Noradrenaline
- VC Vomiting centre
- 5HT₃ Type 3 5-HT receptors



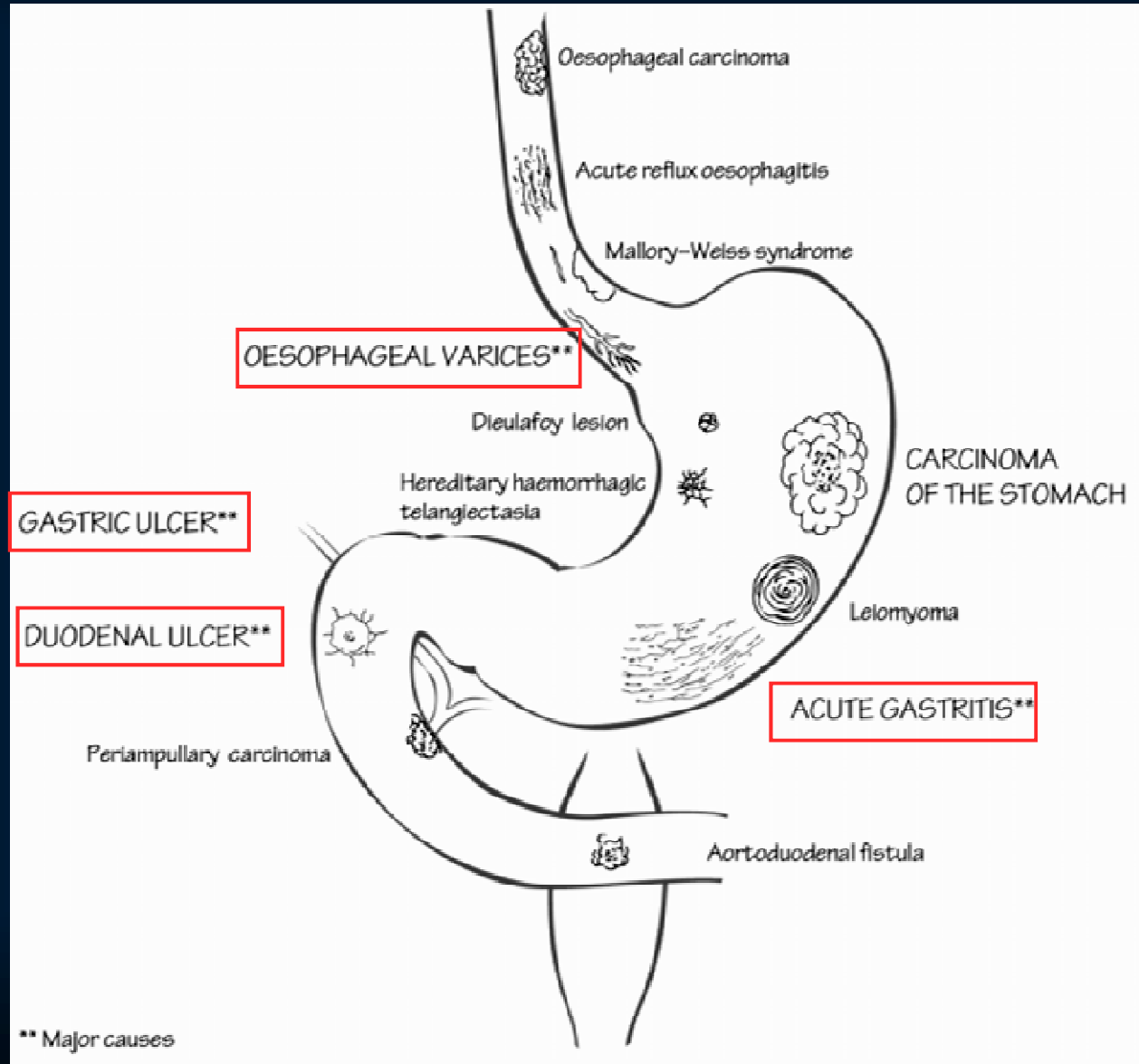
Acute abdominal pain



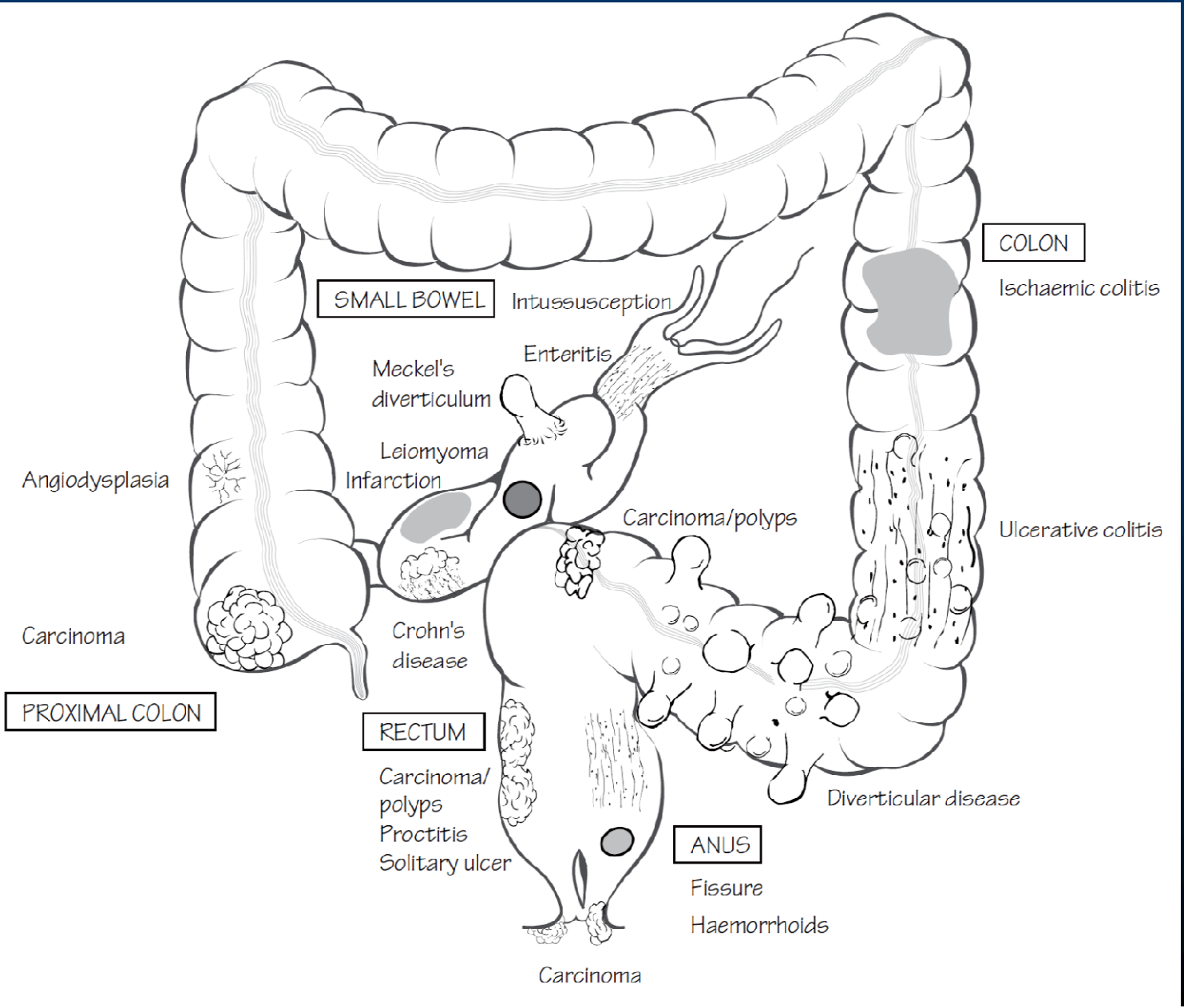
Chronic abdominal pain



Hematemesis



Rectal bleeding



Disorders of nutrient intake

- **Maldigestion** = impaired ability to digest (chemical and mechanical breakdown) large molecules of proteins, lipids and sugars to smaller components (amino acids, monosaccharides, fatty acids, TAG, DAG etc)
 - **Pancreatic insufficiency (fat)** - Chronic pancreatitis, Pancreatic carcinoma, Pancreatic resection, Cystic fibrosis
 - **Bile salt deficiency** (fat, vit. A,D,E,K) Acute hepatitis, Liver cirrhosis, Chronic intrahepatic cholestasis, Intestinal stasis (bacterial enzymatic deconjugation)
 - **Post-resection syndromes** of stomach, pancreas, intestine
 - **Selective deficits of enzymes** - Lactase deficiency
- **Malsecretion** = exudative gastroenteropathy
- **Disorders of intestinal motility** – Ileus
- **Malnutrition** – kwashiorkor

Disorders of nutrient intake

- **Malabsorption** = impaired absorption from the bowels to blood
 1. **Primary malabsorption syndrome** - Cellakia, Tropical sprue, Selective malabsorption, Malabsorption of mono-and disaccharids -
 2. **Inflammation of small intestine** - Enteritis (TBC), Enterocolitis (Crohn disease), Ulcerative colitis
 3. **Systemic disorders afflicting intestine** - Collagenosis, Amyloidosis,-Whipple disease, Lymphoblastomas
 4. **Alteration of intestinal flora-** Enterocolitis, Drugs (cytostatics, ATB)
 5. **Infections** - parasites, bacterias, fungi, viruses, protzoa
 6. **Intestinal damage** - physical (radiation) , chemical (cytostatics)
 7. **Endocrine disorders** - Diabetes mellitus, Zollinger-Ellison syndrome, Carcinoid, Hypothyreosis
 8. **Cardiovascular disorders-** Heart failure
 9. **Reduction of absorption surface** - Resection of intestine, Intestinal shunts

Oesophagus pathophysiology

- Gastro-oesophageal reflux disease (GERD)
- Barret oesophagus

Gastroesophageal Reflux Disease - GERD

Definitions

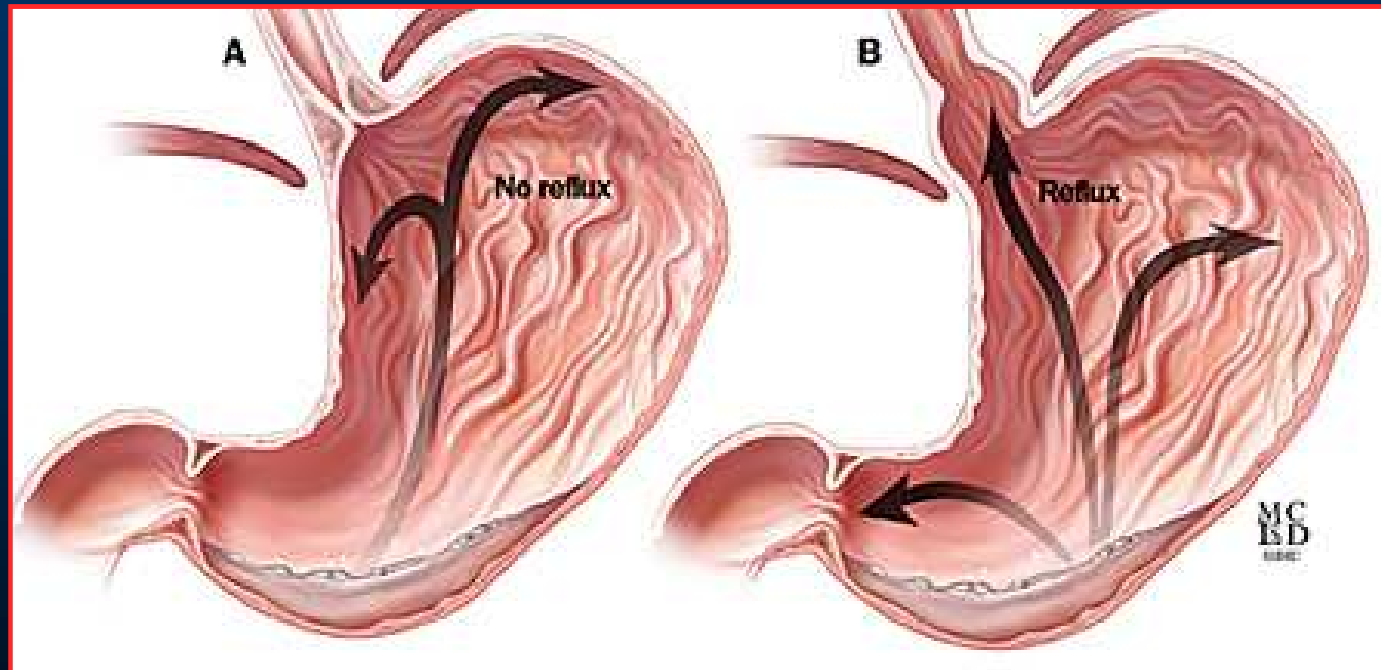
- **Gastroesophageal reflux** - involuntary movement of gastric contents to the esophagus; normal physiological process that occurs several times a day without symptoms or damage
- **Gastroesophageal reflux disease (GERD)** - reflux of gastric contents into the esophagus produces damage to esophagus, pharynx, or larynx

Symptoms

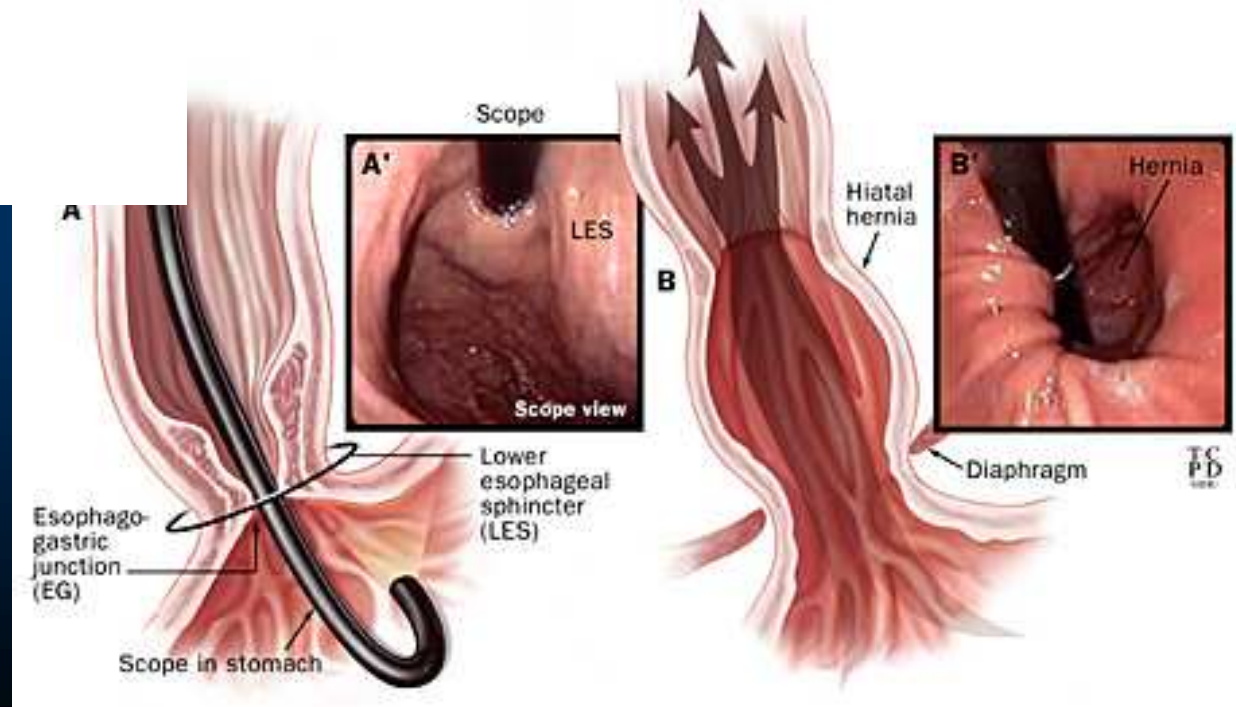
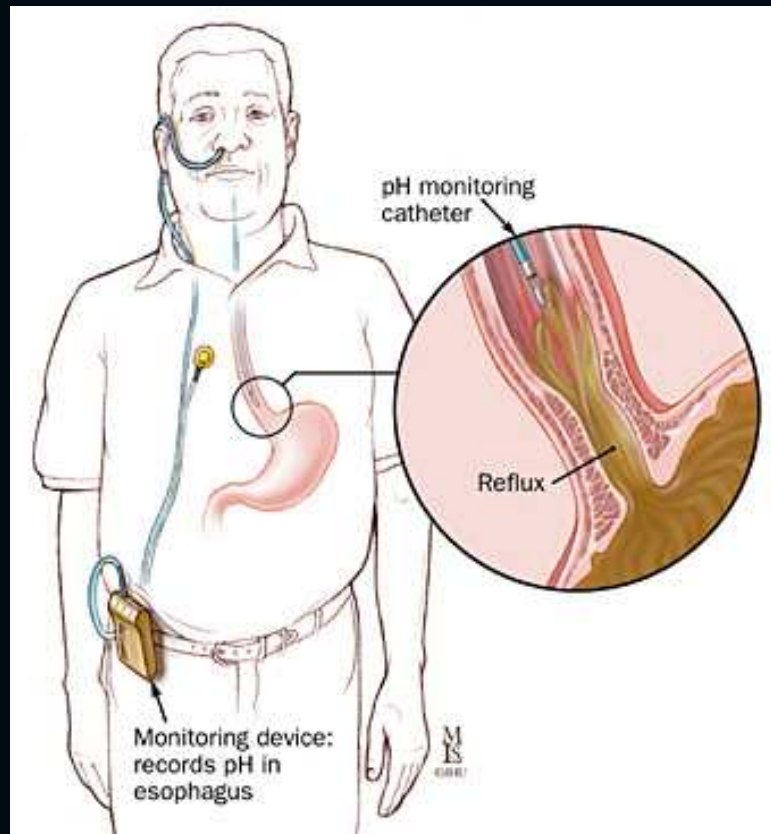
- **burning middle - chest pain** - radiate through to the back; non-burning chest pain exist too
- **regurgitation even vomiting** of sour or bitter-tasting food or liquid
- **difficulty swallowing (dysphagia)** - abnormal esophageal motility or due to esophageal stricture
- **extra-esophageal manifestations** = **sore throat**, coughing, increased salivation, and shortness of breath can occur without esophageal symptoms

Gastroesophageal Reflux Disease - GERD

Physiologic reflux - brief in duration, relatively infrequent, and occurs almost exclusively **after meals** and is caused by a sudden relaxation of the LES that is not induced by swallowing.



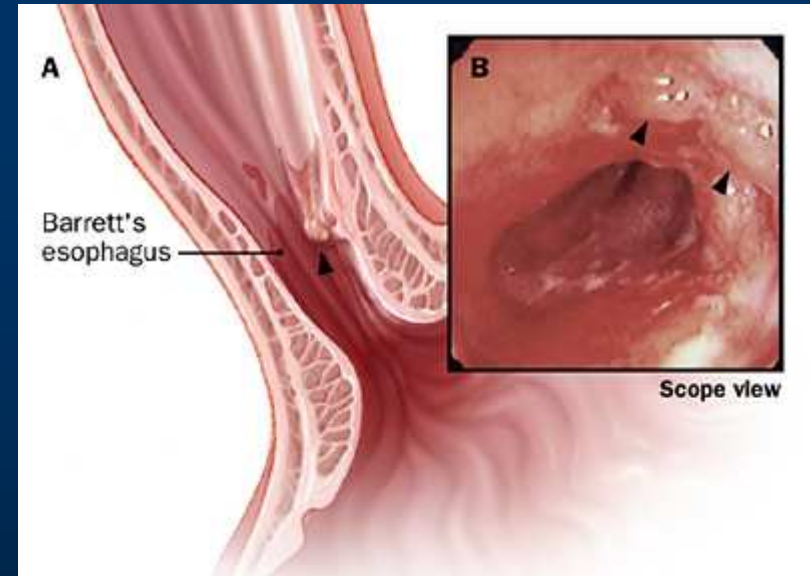
Mechanism of gastroesophageal reflux disease.



A, Normal esophagogastric (EG) junction; B, hiatus hernia

Barrett's Esophagus (Barrett syndrome)

- Barrett syndrome (columnar epithelium lined lower oesophagus (CELLO), refers to an abnormal change (metaplasia) in the cells of the lower portion of the esophagus
- Metaplasia - replacement of squamous epithelium by simple epithelium with goblet cells and a villiform surface configuration that resembles intestinal mucosa
- Forms: **Long-segment vs. short-segment type Barrett's esophagus**
- Premalignant condition & risk factor for adenocarcinoma of the esophagus (30–45 x higher than in normal), 3 times higher in white than black, M-to-F ratio is 7-6:1



A, Short segment Barrett's esophagus
B, Long segment Barrett's esophagus