HARRISON'S BASED GENERAL MEDICINE

PART - 2

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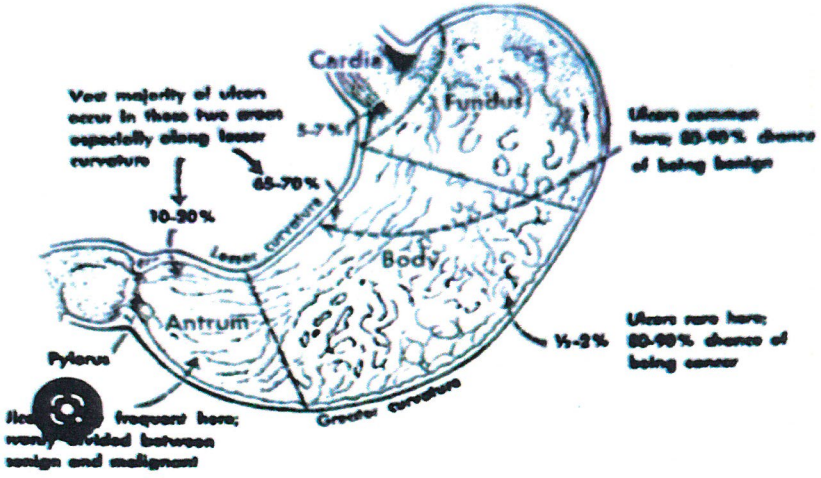
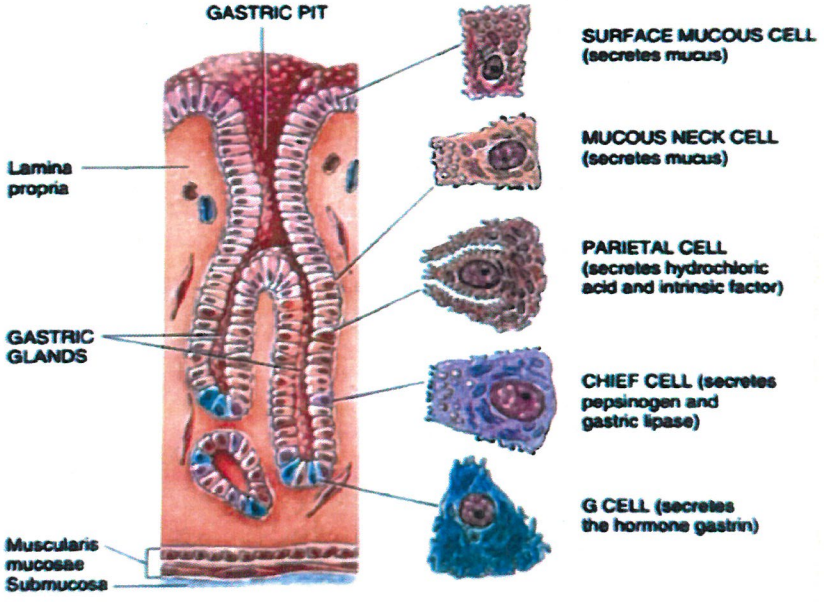
GASTROINTESTINAL
&
HEPATOBILIATY SYSTEM

GASTRIC ANATOMY / GASTRITIS

Anatomy

00:01:10





Fundus :

- Contains mucous and endocrine cells.
- ECL (enterochromaffin like cells) produces histamine.

Body :

- Less number of mucous and endocrine cells.
- Oxyntic/parietal cells at the level of neck/isthmus.

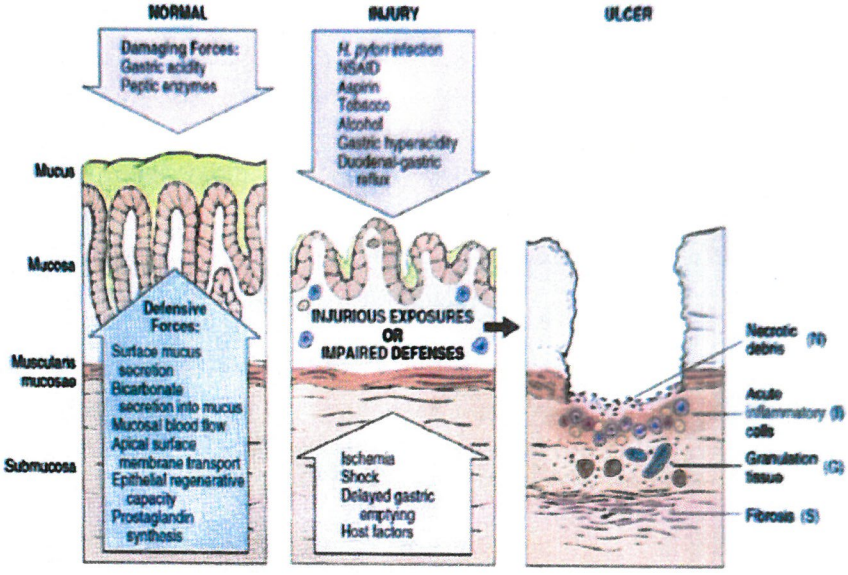
- Chief cells which produce pepsinogen are present in the base.

Antrum/pylorus :

- Contains pyloric glands.
- G cells produce gastrin.

Layers of gastroduodenal mucosal defence :

Luminal pH is 1-2.



Layers :

1. Mucosa : Epithelial cells.
    - Lamina propria.
    - Muscularis mucosa.
2. Submucosa : Meissner's plexus.
3. Muscularis propria : Outer longitudinal, inner circular.
    - Between them lies the myenteric plexus.
4. Serosa.

Protective factors :

- Mucous secretion.
- Bicarbonate secretion.
- Regenerative capacity.

3 layers of gastroduodenal mucosal defence are preepithelial, epithelial and subepithelial.

Single most important factor in defence is prostaglandins.
Pacemaker cells of GIT : Interstitial cells of Kajal.

Enteric nervous system :

- A.K.A. Little brain.
- Intrinsic innervation : Auerbach plexus (motility), meissner's plexus (intestinal secretion).
- Extrinsic innervation : ANS.

Cooperative synergism :

- ECL ⟶ histamine ⟶increases cAMP ⟶ increase acid production.
- GRP (bombesin) ⟶ G cells ⟶ Gastrin ⟶ CCKB receptor parietal epithelial cells ⟶ increase acid production.
- ACH ⟶ M3 (via Ca 2+) ⟶ increase acid production.

CCK/PGs/Somatostatin/GIP : Decrease acid production.
BAO/MAO > 0.6 : Indicates gastrinoma.

Acute Gastritis 00:14:03

- Inflammation of gastric mucosa.
- m/c cause is NSAIDS > infections.
- Histology : Infiltration by neutrophils.
- No correlation between endoscpy and histology.

Acute phlegmonous gastritis :

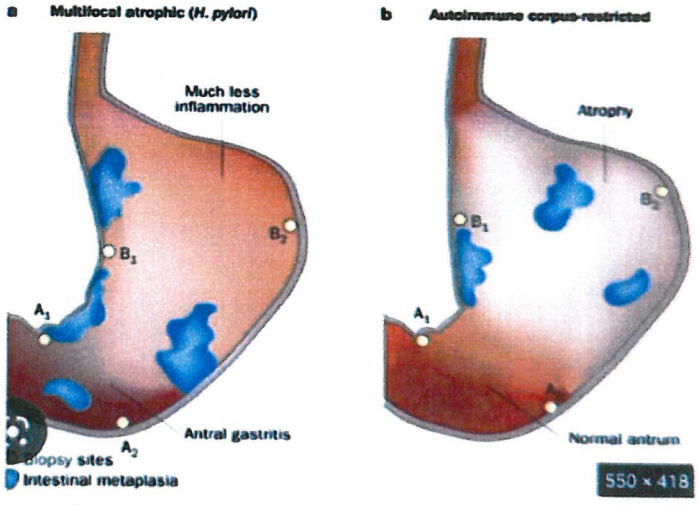
- Dangerous acute gastritis.
- Progressive inflammation with thickening of the wall, necrosis and gas formation.
- Seen only in immunocompromised.
- Caused by streptococci > E.coli.
- Characterised acute abdominal pain, vomiting and fever.
- High mortality.

Chronic gastritis :

Superficial involvement with lymphocytes and plasma cells.
Can progress to atrophic gastritis ⟶ Intestinal metaplasia ⟶ Dysplasia ⟶ Carcinoma.

Types :

1. Type A gastritis :
   - Autoimmune.
   - HLA B8 and DR3.
   - Associated with SLE, T1 DM, vitiligo.
   - AMAG : Autoimmune metaplastic atrophic gastritis.
   - Anti-parietal cell antibodies present.
   - Achlorhydria, megaloblastic anemia seen.
   - Hypergastrinemia.
   - Gastrin secreting carcinoid tumor : mc seen malignancy.
   - Body is generally involved.



   - Patchy atrophy and patchy metaplasia.
   - Risk of Ca stomach is very less.

2. Type B gastritis (EMAG) :
   - m/c type.
   - Hpylori related.
   - Environmental metaplastic atrophic gastritis.
   - Antral predominant gastritis ⟶ Pangastritis.
   - Diffuse atrophy and significant metaplasia ⟶ High chance of adenocarcinoma of stomach.

Eosinophilic gastritis presents with intestinal obstruction.
Russel's body gastritis has pseudotumor endoscopy appearance.
Crohns disease : commonest cause of granulomatous gastritis.
Lymphocytic gastritis is associated with coeliac disease.

Menetrier's disease :

- Hypertrophic gastritis.
- Foveolar hyperplasia with large tortuous mucosal folds which leaks proteins (protein losing gastropathy).
- Mediated by TGF alpha, linked with CMV infection in children.
- Body and fundus involvement.
- Hypoalbuminemia + edema + UGI symptoms.
- Premalignant condition.
- Endoscopy with full thickness biopsy is mandatory.
- Treatment : monoclonal antibody against EGFR (cetuximab).

DIARRHEA AND MALABSORPTION

Malabsorption 00:08:43

malabsorption :

Diminished digestion and diminished absorption of major nutrients.

maldigestion + malabsorption = malassimilation .

macronutrients :

- Carbohydrate.
- Protein.
- Fat :
  - most sensitive macro nutrient to changes in intestine to malabsorption.
  - most calorie dense macronutrient.

most common finding /clinical signs/ symptom : Diarrhea .

Hallmark of malabsorption : Steatorrhea.

Steatorrhea :

- Passage of pale voluminous greasy bulky malodorous stool.
- Steatorrhea tends to manifest as diarrhea :

Unabsorbed fat moves to colon
↓
Osmotic load increases /osmolality of colon increases.
↓
Draws water from colon epithelial cells.
↓
Diarrhea.

- Diarrhea produced due to steatorrhea called as osmotic diarrhea.

Bristol stool chart 00:16:45

Constipation corresponds to :

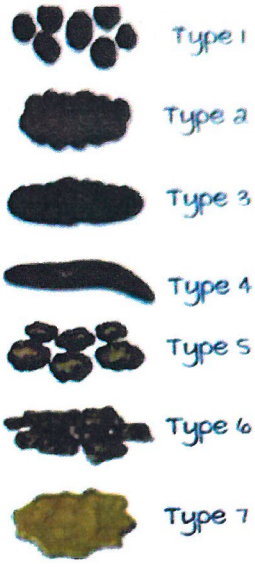
- Type 1 : Severe.
- Type 2: mild.

Diarrhoea corresponds to :

- Type 6 : mild.

Type 7 : Severe.

Type 3 and 4 : Normal.



Classification :

1. Osmotic diarrhea.
2. Secretory diarrhea.
3. Factitious diarrhea.

Osmotic diarrhoea :

Manifestation and result of steatorrhea

Diarrhea : 24 hour stool with water content > 200 - 225ml.

Diagnosis :

Approach -

Based on index of suspicion

Prove /define steatorrhea

Assess for carbohydrate and protein malabsorption

Establishes malabsorption

Locate the exact site of malabsorption.

To define steatorrhea :

- 72 hour fecal fat estimation test (quantitative test)
- Qualitative test :

  Easier.

  Stains used :

  1. Sudan III.
  2. Sudan black.
  3. Oil Red O.

  used to check for fat estimation.

72 hour fecal fat estimation

00:22:46

Patient given diet containing minimum 100 g (100g-130 g) of fat for 5 consecutive days.

On day 3rd, 4th and 5th look for 24 hour fecal fat.

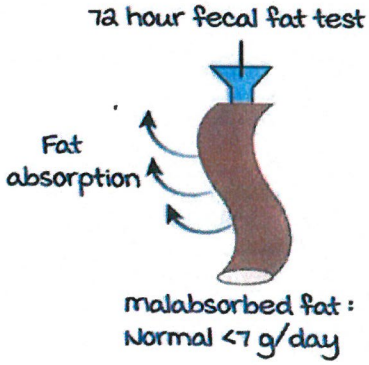
In case of steatorrhea alone,

If > 7 g/day or ≥ 7% of stool is fat for 3 consecutive days implies positive test.

In case of steatorrhea + diarrhoea:

If fat is > 14 g/day implies positive test.

Also known as:
1. Qualitative or Quantitative stool fat
2. Stool lipid
3. 72 hours fecal fat
4. Fat stain oil red O
5. Fecal Qualitative or Quantitative



Secretory diarrhea

00:26:49

Causes:

- Toxin → ETEC (Community acquired / travellers diarrhea).
- Toxin → Vibrio cholera.

Tumour: VIPoma (Vasoactive intestine peptide - oma).

mechanism:

Toxin/Tumor is responsible for increase in secondary messengers like cAMP leading to drawing of water.

VIPoma:

Hypokalaemia.

metabolic Acidosis.

Also called as Watery Diarrhoea Hypokalemic Acidosis/ Watery Diarrhoea Hypochloride Hydriacidosis (WDHA).

Example of normal anion gap metabolic acidosis (8 to 12 Anion gap).

Gaps :

- Serum anion gap.
- Urine anion gap.
- Stool osmotic /osmolality gap.

Serum anion gap

00:29:32

Serum anion gap : $Na^+ - (Cl^- + HCO3^-) = 8\text{-}12$ meq/L.

$Na^+ + \text{Unmeasured Cation} = Cl^- + HCO_3^- + \text{unmeasured anion}$

$Na^+ - (Cl^- + HCO_3^-) = \text{unmeasured anion} - \text{unmeasured anion}$

Anion Gap = Unmeasured anion – unmeasured cation.

Example :

Keto acid is an unmeasured anion and it increases in :

Diabetic Ketoacidosis.

Alcoholic Ketoacidosis.

Starvation Ketoacidosis.

Lactic anion is an unmeasured anion and in lactic acidosis anion gap increases.

Normal anion gap metabolic acidosis

00:30:52

Definition : Loss in bicarbonate is compensated by increase in chloride hence anion gap remains same.

Also called as Hyperchloremic metabolic Acidosis

Causes :

- Renal Tubular Acidosis Type I and Type 2.
- VIPoma.
- Post Ureterosigmoidstomy.

High anion gap is seen in :

Diabetic Ketoacidosis.

Alcoholic Ketoacidosis.

Starvation Ketoacidosis.

Ethylene glycol poisoning.

Uremic Ketoacidosis.

Lactic acidosis.

methanol

Ethanol.

Urine anion gap 00:32:50

To differentiate between renal tubular acidosis type 1 / 2 and VIPoma for normal anion gap metabolic acidosis.

Urine Anion Gap = Urine Na^+ + urine K^+ – urine Cl^-.

Urine Anion Gap = Unmeasured anion – Unmeasured cation.

Urine Anion Gap ⟶ Negative : Normal.

⟶ Positive : Abnormal.

In VIPoma : UAG is negative.

In RTA : UAG is positive.

Stool osmotic gap 00:35:32

Osmolality measured by osmometer.

Stool osmotic gap = measured osmolality – calculated osmolality.

= (290 to 300) – 2 (Stool Na^+ + stool K^+).

In malabsorption (fat) measured osmolarity increased (as it includes fat also) but calculated osmolality remains unchanged (includes K^+ only).

Hence, widened or increased stool osmotic gap.

Osmotic diarrhoea vs secretory diarrhea 00:39:06

Stool osmotic gap :

> 100 mosm/kg. ⟶ Osmotic diarrhoea

50 – 100 mosm/kg ⟶ Normal.

Normal value / 25 – 50 mosm/kg ⟶ Secretory diarrhoea.

Stool output with fasting :

In osmotic diarrhoea : On fasting, stool output drastically reduces.

Osmotic diarrhoea is dependent on food intake volume.

Hence, diarrhoea improves with fasting.

Supervised vs unsupervised stool collection 00:41:36

Unsupervised Stool Collection vs Supervised Stool Collection

Patient No.	Unsupervised Stool Collection			Supervised Stool Collection
	Osmolality	Sodium	Potassium	Osmolality
	mOsm/Kg	mmol/liter		mOsm/Kg
1	16	<10	2.0	279
2	19	<10	1.9	227

Example : 16 year old female with 5-6 months of ongoing diarrhoea but no apparent weight loss .
On suspicion, supervised stool collection was done and the osmolality increased from low to normal range suggesting of factitious diarrhoea .
In factitious diarrhoea there is reduced stool osmolality and after superficial normal stool osmolality.

In diarrhoea diagnosis is done :
1. Anatomically.
2. Pathological.
3. Aetiologically.

Small bowel vs large bowel disease 00:46:00

On confirmation of malabsorption as responsible for diarrhoea

Site : 1. Small Bowel Disease.
2. Large Bowel Disease : Infection.
Inflammatory Bowel Disease (Ulcerative Colitis)

Small bowel diarrhoea :
Causes : 1. Malabsorption.
2. In Ileum (Distal 3/5) : Tuberculosis.
Crohn's Disease.
3. Toxins : ETEC.
Cholera .

Large bowel diarrhoea :
Causes : Invasive Organism -

1. Salmonella.
2. Shigella (Just 100 organisms sufficient for invasion).
3. Campylobacter.
4. Ulcerative Colitis (Rectum).

Small bowel disease	Large bowel disease
Large volume watery non-bloody stools. Normal frequency of defecation or mildly increased. Maybe associated with 1. weight loss. 2. Steatorrhoea. 3. Vomiting.	Small volume stools mixed with pus, blood, mucus. Increased frequency of defecation. No associated symptoms.

Findings used to Differentiate Small Bowel From Large Bowel Diarrhea

Finding	Small Bowel	Large Bowel
Frequency of defecation	Normal to mildly increased	markedly increased
Fecal volume	Normal to increased	Decreased
Fecal mucus	Absent	Often present
Fecal blood	Melena	Hematochezia
Tenesmus	Absent	Often present
Urgency	Absent	Often present
Dyschezia	Absent	Often present
Vomiting	may be present	Infrequently present
Weight loss	Often present	Infrequently present
Steatorrhea	may be present	Often present

Tenesmus

00:52:21

Type of constipation associated with repeated attempts of

strained defecation with no passage of stool.
Sometimes passage of minimal blood occurs.
Seen in large bowel aetiology.

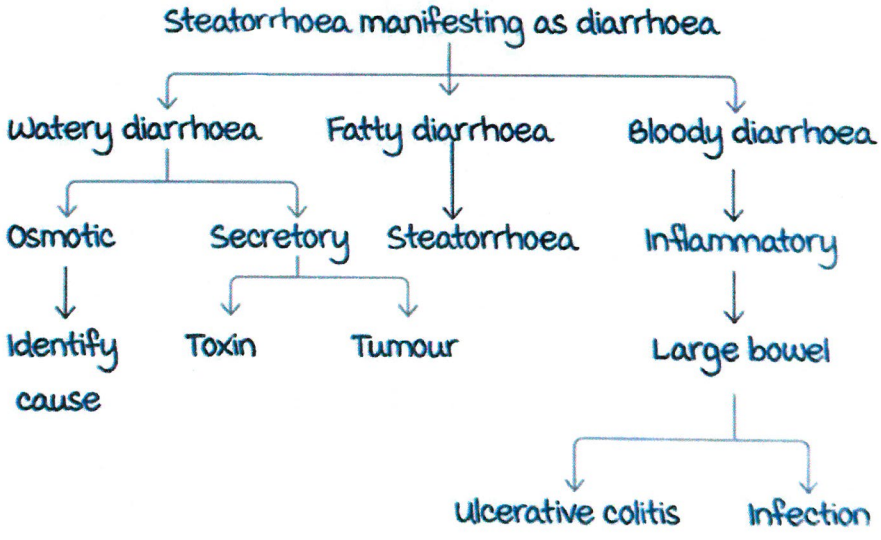
Duration based classification 00:53:06

Acute infectious.
Chronic persistent → On multiple evaluation → Anatomical diagnosis.

Classification of Diarrhea

Frequency Classification	
Acute	≤14 days in duration
Persistent	>14 days in duration
Chronic	>30 days in duration

Diagnosis algorithm 00:53:58



MISCELLANEOUS CAUSES OF MALABSORPTION

Introduction 00:00:30

Defects in lipid digestion and absorption in steatorrhea :

Phase : Process	Pathophysiologic defect	Disease example
Digestive		
Lipolysis formation	Decreased lipase secretion	Chronic pancreatitis
micelle formation	Decreased intraduodenal bile acids	Absorptive
Absorptive		
Mucosal uptake & reesterification	Mucosal dysfunction	Celiac disease
Postabsorptive		
Chylomicron formation	Absent betalipoproteins	Abetalipoproteinemia
Delivery from intestine	Abnormal lymphatics	Intestinal lymphangiectasia

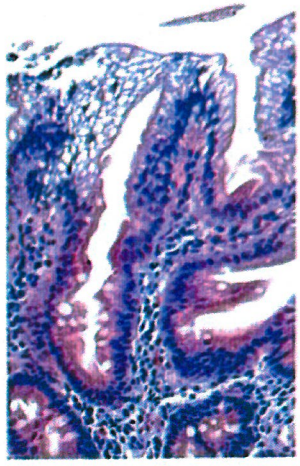
Triglyceride + Apo B48 $\xrightarrow{\text{MTTP}}$ Chylomicron.
MTTP : Microsomal triglyceride transport protein.

Defect in MTTP or in Apo B48 : Abetalipoproteinemia.

Abetalipoproteinemia 00:01:34

- AR inheritance.
- MTTP defect : No chylomicrons formation (hypolipidemia).
- Vit E deficiency : Along with diarrhea, patient presents with neurological symptoms especially, neuropathy and ataxia.

- PS : Acanthocytes are seen.
- Biopsy : Postprandial biopsy (vacuolations seen).



The small bowel mucosa shows the characteristic clear enterocytes (due to lipid accumulation)

Vitamin E absorption :

Affected in 3 steps in the pathway of vitamin E absorption.

st pathway :
First, along with other fat soluble vitamins, the fat malabsorption decreases the absorption of vitamin E.

↓

2nd pathway :
Second, the small amount of vitamin E that may be absorbed cannot be efficiently secreted by the intestine because of the defect in the chylomicron secretion.

↓

3rd pathway :
Third, any vitamin E that is delivered to the liver also cannot be secreted because of the defect in the VLDL secretion.