MEDICINE VOL.01

ED.08

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DIARRHEA

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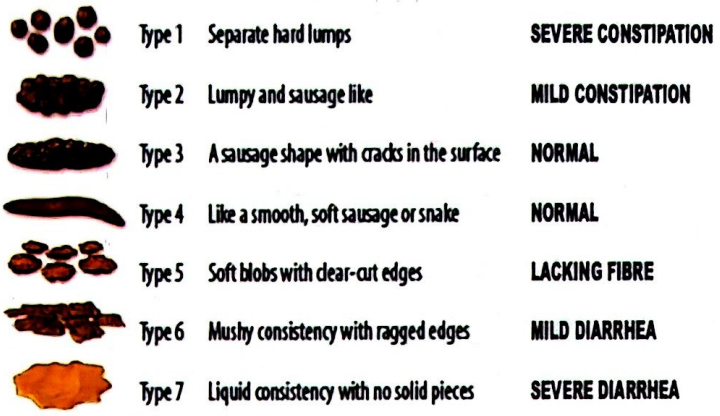
Definition :

- Stool water content >200 mL/24 hours.
- According to Bristol stool chart :
  - Type 1 & 2 : Constipation.
  - Type 6 & 7 : Diarrhea.



Bristol stool chart

Physiology of absorption :

1. Luminal.
2. Mucosal :
   - Small intestine (majority).
   - Maximum absorption.
3. Post mucosal.

Macronutrients for absorption :

- Fat :
  - Most calorie dense nutrient.
  - Most specific nutrient affected in malabsorption.
- Carbohydrates.
- Proteins.

Frequency Classification

00:03:00

	Acute	Persistent	Chronic
Duration	<2 weeks (Nuisance symptom)	>2 weeks	>4 weeks

ETIOLOGY

Acute diarrhea :

Infectious : Viral infection (m/c).

- m/c in adults : Norovirus.
- m/c in children : Rotavirus.
- Self-limiting.

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Chronic diarrhea :

D/d	Etiology
Osmotic	malabsorption
Secretory	• Tumor • Toxin
Inflammatory	Inflammatory bowel disease

Note :

Malassimilation :

- Maldigestion + malabsorption.
- Diminished intestinal digestion/absorption of one or more nutrients.

Pathological Classification

00:10:13

I. OSMOTIC DIARRHEA

Most consistent clinical symptom of malabsorption.

Steatorrhea :

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Hallmark of malabsorption.

Definition : Passing of pale, bulky, fatty, malodorous, greasy stools.

Clinical presentation : Diarrhea (most consistent clinical finding).

Pathology :

↓ fat absorption in small intestine

↓ In colon

Unabsorbed Macronutrients ↑ stool osmolality (osmotically active)

↓

Stool draws water from large intestinal epithelial cells

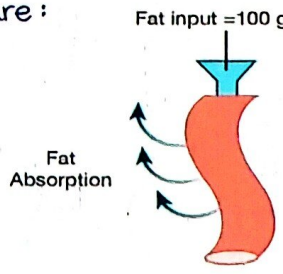
↓

Osmotic diarrhea

Investigations :

1. 72 hour fecal fat test : Gold standard.

Procedure :



Normal : <7 g/day

- >7 g/day for 3 days (D3, D4, D5)
- Stool fat excretion ≥7 %

} Steatorrhea

2. Qualitative stool fat :
   - Sudan III.
   - Sudan IV.
   - Oilred O.

Feedback

2. SECRETORY DIARRHEA

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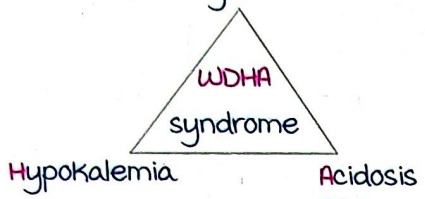
Etiology :

a. Toxins
- ETEC, V. cholera (heat labile toxin)
- Enteropathogenic virus (rotavirus)

b. Tumours : VIPoma → Watery Diarrhoea



Note : No structural damage seen.

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	Osmotic diarrhoea	Secretory diarrhoea
Stool osmotic gap	Increased (>100 mOsm/kg)	Normal/decreased (< 50 mOsm/kg). ↑ stool $Na^+ + K^+$ (By toxins).
Response to fasting	Improvement	No change
Stool pH	<5.5 (Fermentation of unabsorbed carbohydrates → Acids)	>6.0

Note : Stool osmotic gap

- Measured osmolality (osmometer) – calculated osmolality

  290 – 2 (Stool $Na^+ + K^+$)

- Normal : 50–100 mOsm/kg.

3. FACTITIOUS DIARRHEA

Clinical presentation :

- Adolescent female.
- Chronic diarrhea.
- Fatigue.
- Weight loss.

Feedback

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Findings :

Stool collection	Stool osmolality
Unsupervised (mixed with water)	Very low (~ 16 mOsm/kg)
Supervised	Normal (~ 279)

Anatomical Classification

00:32:48

SMALL INTESTINAL V/S LARGE INTESTINAL DIARRHEA

		Small intestinal diarrhea	Large intestinal diarrhea
Etiology		• Osmotic. • Secretory : – ETEC. – Vibrio cholera.	• Infections : Invasive organisms (Shigella). • Inflammation : Ulcerative colitis.
Clinical presentation		Large (↓ nutrient absorption)	Small
Diarrhoea	Volume		
	Consistency	Watery	Watery
	Frequency/ urgency	↓	↑
	Pus/blood/ mucus	Absent	Present
	Tenesmus	Absent	Present
	Dyschezia	Absent	Present
Abdominal pain		Absent	Present
Fever		Absent	Present
Abdominal cramps		Present	Present
Bloating		Present	Present
Weight loss		Present (If persistent)	Rare
Vomiting		Maybe present	Rare
Steatorrhoea		Present	Absent

APPROACH TO DIARRHEA

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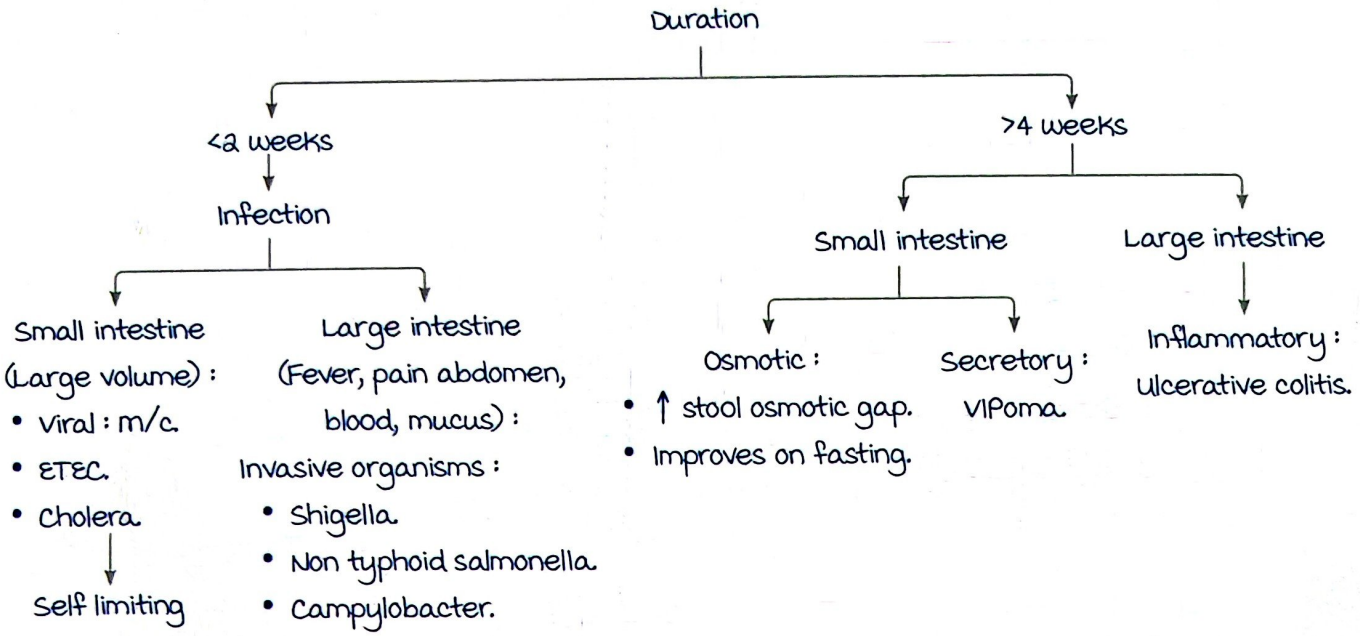

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PHYSIOLOGY OF GIT ABSORPTION AND SELECTIVE MALABSORPTION

Basics of Absorption

00:01:30

STAGES OF ABSORPTION

1. Luminal : Enzymes mediated.
2. Small intestinal mucosal : Enterocyte.
   Villi → Brush borders contains enzymes.
3. Post mucosal : Mucosal epithelial cell → Into blood.

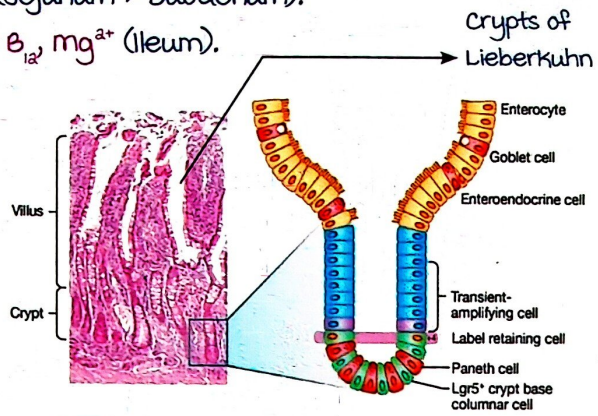
ANATOMY

Small intestine :

Proximal (2/5) : Maximum absorption (Jejunum > Duodenum).

Distal (3/5) : Absorption of Bile acid, Vit B_{12}, Mg^{2+} (Ileum).

Histology :



Small intestine mucosa with villi and crypts

1. Mucosa :

a. Enterocyte :

- Villi (specific feature) :
  - Surrounded by crypts of Lieberkuhn.
  - Contains brush-border.
- Crypts :
  - Paneth cells (at base) : Produce immunological substances (alpha defensins, lysozymes, phospholipase A2).
  - Enteroendocrine cells.
  - Goblet cells.
- Continuous renewal : every 48–72hrs.

b. Lamina propria : Glands, blood vessels.

c. Muscularis mucosa : Tight attachment.

Note :

Plica circularis : Visible mucosal folds on luminal surface of small intestine.

Interstitial cells of Cajal : Pacemaker cells of small intestine → Basal Electrical Rhythm.

2. Submucosa :

- Brunner's glands (In duodenum) → Secretes bicarbonate (Alkaline).
- Peyer's patches (In ileum).
  - Macroscopic lymphoid aggregates.
  - In typhoid : Hypertrophy.

3. Muscularis Propria.

4. Serosa.

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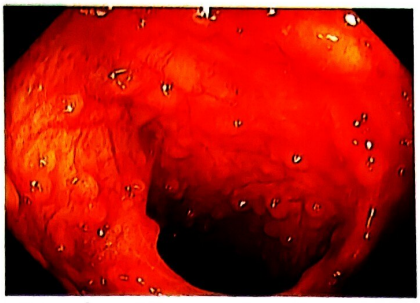

Peyer's patches on ileocolonoscopy

Fat Absorption

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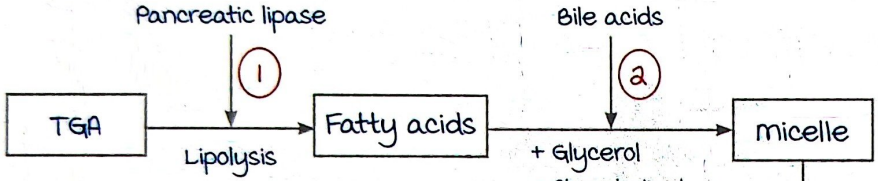
LUMINAL PHASE OF ABSORPTION

Mechanism :

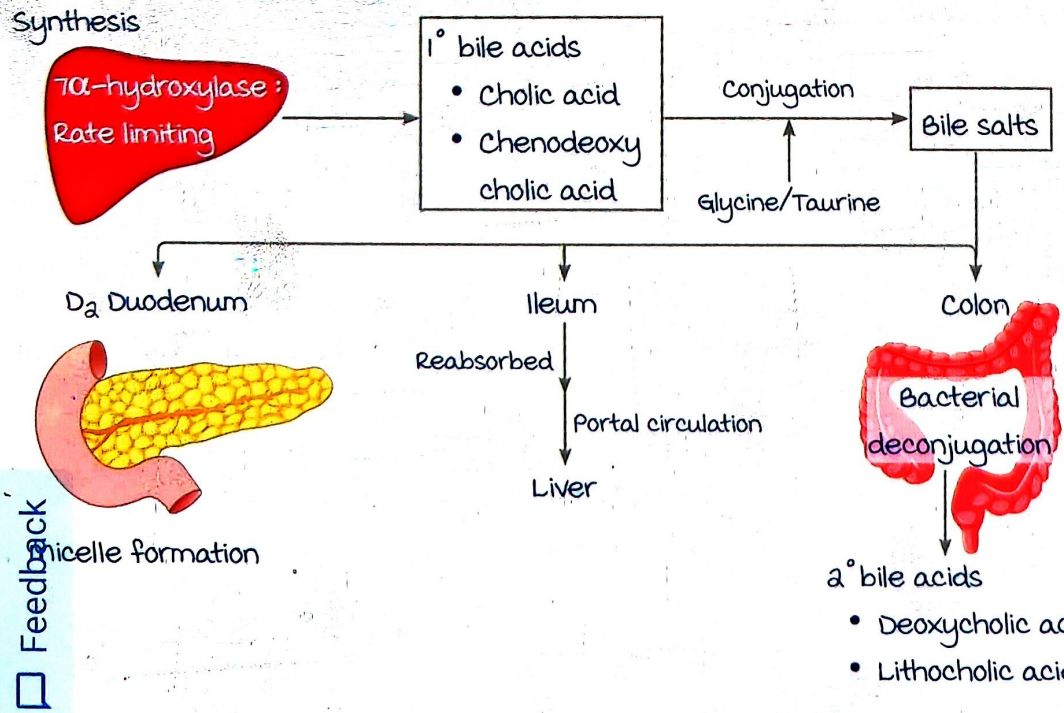


1. Chronic pancreatitis
2. Bile acid defect

Bile Acid Physiology :

- Formation & excretion : 500g.
- Body pool : 4g (maintained by enterohepatic circulation).

Enterohepatic circulation :



Feedback

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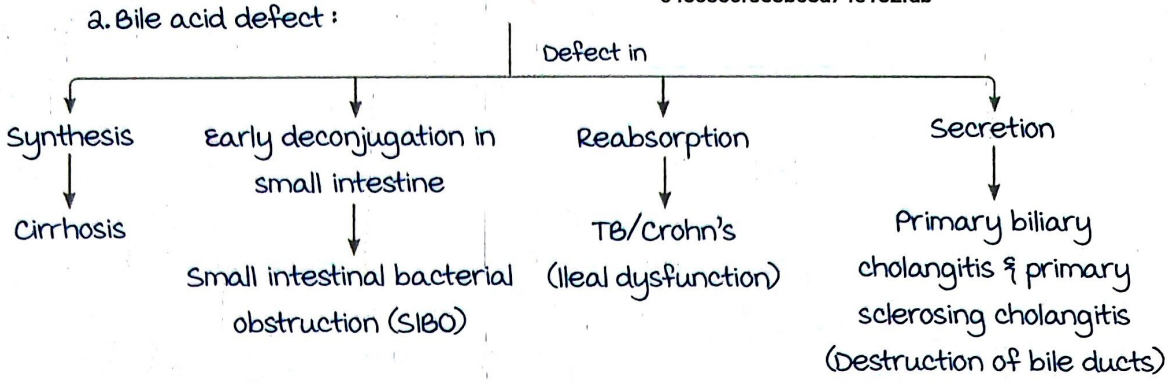
Defects in luminal absorption :

1. Chronic pancreatitis → Affects pancreatic lipase → Lipolysis affected.

2. Bile acid defect :



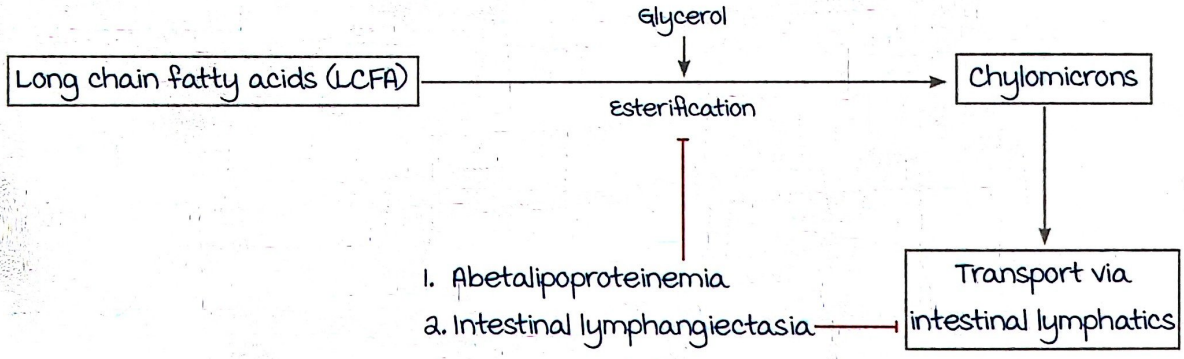
MUCOSAL PHASE OF ABSORPTION

Pathology : Defect in small intestinal mucosal integrity.

Etiology :

- Celiac disease.
- Whipple disease.
- Tropical sprue.

POST-MUCOSAL PHASE OF ABSORPTION



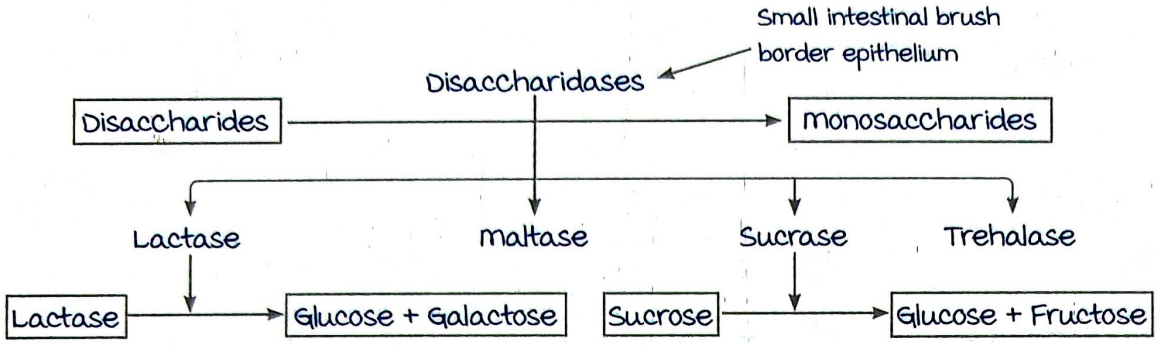
TYPES OF FATTY ACIDS

	Long chain	medium chain	Short chain
Carbon chain length	>12	8-12	<8
Origin	Large quantity in diet as triglycerides	Small quantity in diet (Coconut oil)	Bacterial degradation of unabsorbed carbohydrates in colon.
Primary absorption site	Small intestine	Small intestine	Colon
Require pancreatic lipolysis	Yes	No	No
Require micelle formation	Yes	No	No
Present in stool	Minimal	No	Substantial

Carbohydrate Absorption

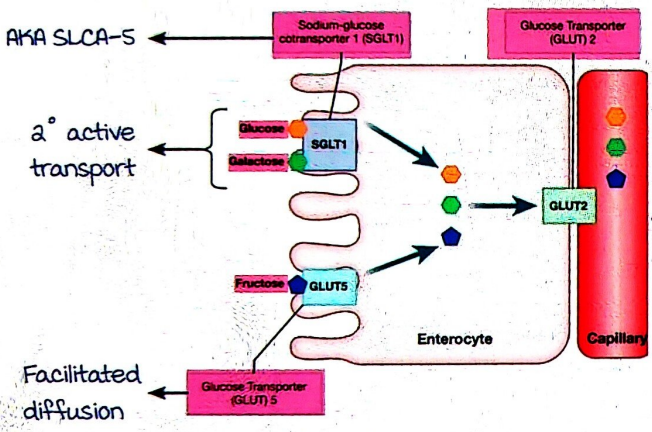
00:28:15 ----- Active space -----

MECHANISM OF CARBOHYDRATE ABSORPTION

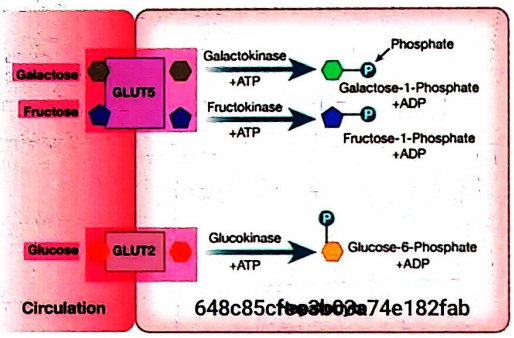


Receptors for absorption :

In the gut :



In the liver :



Note :

SGLT-1 defect → Familial glucose-galactose malabsorption syndrome.

DEFECTS IN CARBOHYDRATE ABSORPTION

Pathology	Etiology	Malabsorption
Lactase deficiency	• Congenital : Autosomal recessive. • Acquired : – Primary. – Secondary.	Selective.
Small intestinal mucosal defect	• Celiac disease. • Whipple's disease. • Tropical sprue.	Global.

Feedback

----- Active space -----

Proteins

00:34:00

Mechanism of absorption :

Endopeptidase : Enterokinase (Produced by enterocyte brush border).

Trypsinogen → Trypsin

Trypsin → Activate chymotrypsin, elastase.

Exopeptidase : Carboxypeptidase and aminopeptidase (Activated by trypsin).

Transport in small intestinal mucosa : Sodium-amino acid co-transporters.

Defects in protein absorption :

Global malabsorption : Celiac disease, Whipple disease, Tropical sprue.

Selective malabsorption :

- Enterokinase deficiency.
- Neutral amino acid transport defect :
  - Hartnup's disease.
  - Presents as pellagra : Diarrhoea, dermatitis, dementia.
- Dibasic amino acid transport defect → Cystinuria → Excretion of COLA (Cystine, ornithine, lysine, arginine).

Carbohydrate Malabsorption

00:39:45

LACTOSE INTOLERANCE (LACTASE DEFICIENCY)

Physiology :

Lactose (Dietary : Milk, cheese)

Lactase | Brush border

Glucose + Galactose

Etiology :

Congenital : Autosomal recessive (Absent enzyme from birth).

Acquired : ↓enzyme activity.

- Primary (m/c) : Genetic defect (allele persistence).
- Secondary :
  - Infections.
  - Irritable Bowel Syndrome (IBS).

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Pathogenesis :

Undigested carbohydrate

↓

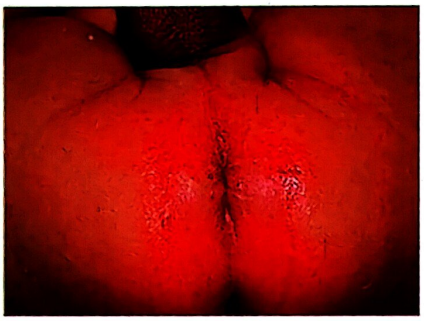
↑ Unabsorbed carbohydrates in colon

↓ Fermented by colonic bacteria :
- Bacteroides fragilis
- Bifdo bacteria
- Lactobacillus

↑ Acid and gases (H_2, methane, CO_2)

Clinical presentation :

- 90 min post prandial : Abdominal distension, bloating, cramps.
- Diaper dermatitis :
  - In children d/t acidic pH.
  - Severe watery diarrhea.
  - Failure to thrive.
  - Irritability.



Diaper dermatitis

Investigations :

1. Stool pH : Acidic.
2. Lactose hydrogen breath test :
   - Principle : Excess lactose in colon $\xrightarrow[\text{by bacteria}]{\text{Fermented}}$ methane + H_2 ⟶ Absorbed ⟶ Tested on breath.
   - Positive test : H_2 > 20 ppm.
3. Lactose-Glucose blood test : Obsolete.

Management :

- Dietary management.
- Ca^{2+} supplementation.

Note :

Protein malabsorption :
- Hartnups disease : Similar to pellagra.
- Cystinuria : Excretion of COLA (Cystine, ornithine, lysine, arginine).

Fat Malabsorption

00:44:23

Post mucosal absorption disorders :

1. Abetalipoproteinemia.
2. Intestinal lymphangiectasia.

Feedback

----- Active space -----

ABETALIPOPROTIENEMIA

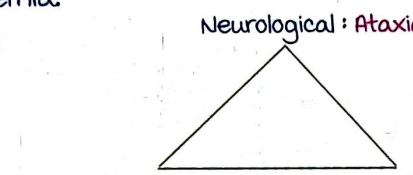
AKA Neuroacanthocytosis.

Etiopathogenesis :

- Autosomal recessive.
- Defect in MTTP (microsomal Triglyceride Transport Protein) → Defect in apoB48 → Defective esterification → No chylomicron formation.

Clinical presentation :

- Hypolipidemia.
- Triad of :



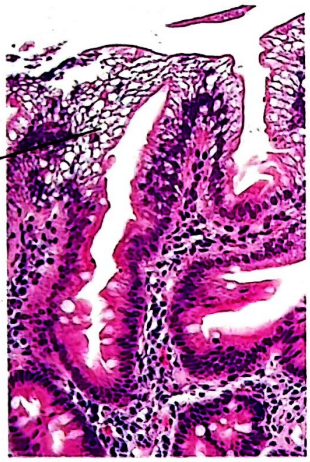
Investigations :

1. Peripheral Smear : Acanthocytes.
2. Post prandial endoscopic biopsy :
   - 100% diagnostic.
   - Vacuolation in enterocytes.

Note :

GI disorders which are 100% diagnostic on biopsy :

- Whipple's disease.
- Abetalipoproteinemia.
- Agammaglobulinemia.

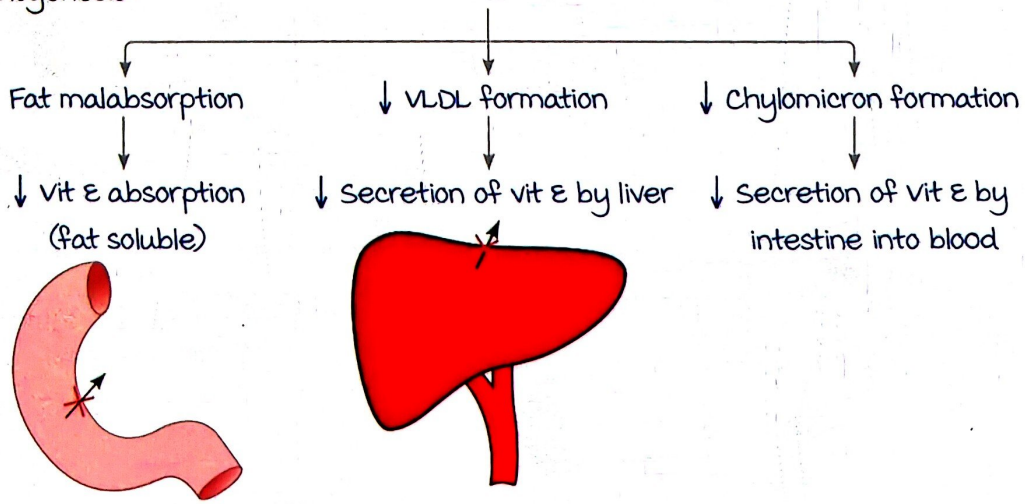


Duodenal biopsy of Abetalipoproteinemia

Vit E deficiency in Abetalipoproteinemia :

Clinical features : Ataxia (Pronounced).

Pathogenesis :



INTESTINAL LYMPHANGIECTASIA

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Physiology :

Chylomicrons —Across intestinal lymphatics→ Blood.

Etiopathogenesis :

Secondary : Lymph node obstruction → ↑ Lymphatic pressure → Exudation.

- Lymphoma.
- Crohn's disease.

Primary : Abnormally dilated lymphatic channel

↓ ↑pressure

Exudation into intestinal lumen

Clinical presentation :

1. Protein losing enteropathy :
   - Most important : Primary intestinal lymphangiectasis.
   - Hypoalbuminemia with hypoglobulinemia.
   - Edema.
   - Ascites.

D/d :

- Nephrotic syndrome : Loss of albumin in urine.
- Liver disease : ↓albumin production.

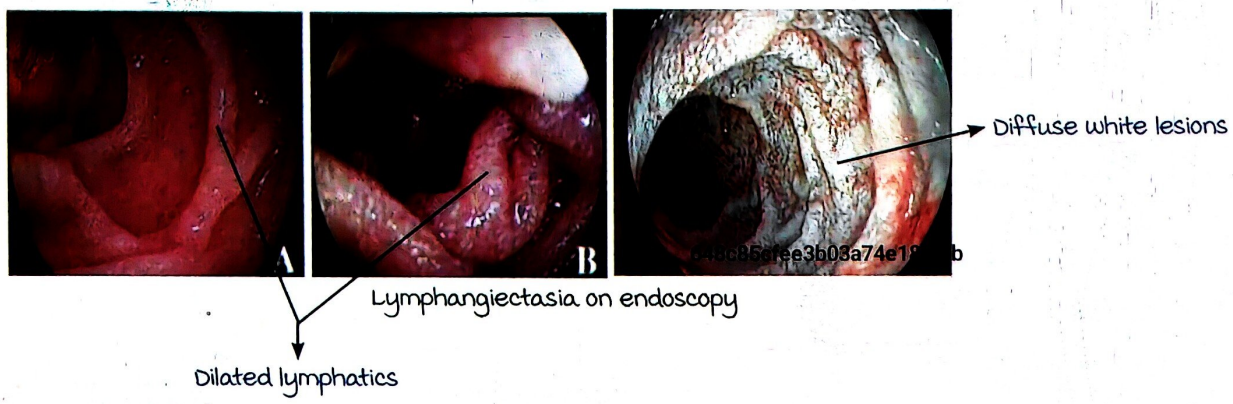
2. Diarrhea :

Investigation :

- Fecal α-1 antitrypsin : Elevated (specific test).
- CT scan : Wall thickening of small intestine.
- Video capsule endoscopy.

Management :

Medium chain triglyceride diet.



Feedback

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CLINICAL FEATURES AND TESTS FOR MALABSORPTION

Steps for evaluating malabsorption :

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1. Confirm the diagnosis → Clinically / By Investigations
2. Confirm global vs selective malabsorption.
3. Confirm the etiology.

Clinical features

00:00:55

System	Scenarios	Features
Gastrointestinal	Osmotic diarrhoea	Site : Small intestine. Duration : >4 weeks. Stool osmotic gap : ↑ Improves on fasting. Most consistent symptom.
	Fat malabsorption	Steatorrhea
	Carbohydrate malabsorption	Abdominal bloating and dyspeptic symptoms
	Protein malabsorption	Foul smelling stools, ascites, edema
	Unexplained weight loss	-
Musculoskeletal	Fat malabsorption (D/t impaired vitamin D and Ca^{2+} absorption)	Tetany, fracture, bone pain
Cutaneous manifestations	Vitamin B_{12}, Niacin deficiency	Hyperpigmentation
	Vitamin C deficiency	Perifollicular hemorrhage, curly hair, spiral hair
	Vitamin K deficiency	Bruisability, ecchymoses
	Zn & Essential fatty acid deficiency	Acrodermatitis
	Vitamin A deficiency	Follicular hyperkeratosis
Miscellaneous	Coeliac disease	Growth retardation
	Anaemia (D/t intestinal malabsorption) : Distal pathology → Vitamin B_{12} deficiency. Proximal pathology → Folate/Iron deficiency.	-
	Vitamin B12/E deficiency. Vitamin B12 deficiency.. Vitamin A deficiency	Peripheral neuropathy, ataxia. Glossitis, cheliosis, stomatitis. Night blindness, xerophthalmia.

----- Active space -----

System	Scenarios	Features	
Miscellaneous	Kidney stones	Normal physiology : Oxalate + Ca^{2+} → Excreted	Malabsorption : Fatty acid + Ca^{2+} → Free oxalate in gut → Oxalate absorbed in colon → Oxaluria → Ca^{2+} oxalate stones

Note :

- Symptoms not seen in malabsorption : Abdominal pain, constipation, fever.
- Differentials of malabsorption (Similar symptoms) :
  - TB : Weight loss, long standing diarrhoea, edema/ascites.
  - Nephrotic syndrome : Protein loss.

Investigations 00:10:05

FAT MALABSORPTION

- Qualitative test : Sudan III.
- Quantitative test (Gold standard) : Fecal fat excretion ≥7 g/day.

Note : Fecal fat excretion test is the gold standard investigation for malabsorption.

CARBOHYDRATE MALABSORPTION

1. D-Xylose test :

- Best and most specific test.
- Composition of D-xylose : Pentose monosaccharide.
- Used to assess intact small intestinal mucosa (D-xylose absorbed here).
- Procedure :

25g of D-xylose given orally after fasting (Early morning)

↓

Collect urine sample (Entire volume passed) after 4-6 hours & check D-xylose levels

- >4.5 g → Interpretation : Normal
- <4.5 g (Positive) → Interpretation : Small intestinal mucosal pathology

----- Active space -----

- False positives seen in (Etiology is not in small intestine) :

Clinical scenario	Reason for false positive
Renal failure	Defective excretion
Rapid intestinal transit (Hyperthyroidism, Vomiting)	Reduced time for absorption in small intestine
SIBO (Small Intestinal Bacterial Overgrowth)	Organisms utilise D-xylose → Reduced absorption
Ascites	Sequestration of D-xylose into the third space → Reduced absorption

2. Lactose tolerance test : Obsolete.

3. Lactose H_a breath test :

- Done for lactase deficiency.
- Deficiency of lactase → Accumulation of lactose in large intestine → Bacterial action on lactose → H_a production.
- Diagnosis : ↑ in breath H_a >20 ppm.

4. Lactulose H_a breath test :

- Metabolised in large intestine to produce H_a.
- H_a produced :
  - Within 90 minutes (Early peaking) : SIBO.
  - >90 minutes : Normal physiology.

OBSOLETE TESTS FOR MALABSORPTION

Test	Etiology
Acid steatocrit test	Fat malabsorption
C-14 Triolein breath test	
C-13 Egg white breath test (Phenol and p-cresol in urine)	Protein malabsorption

Note :

- Stool elastase, chymotrypsin : Pancreatic insufficiency.
- Fecal α-1 antitrypsin : Primary intestinal lymphangiectasia.
- NIRA (Near infrared reflectance analysis) : Newer test for malabsorption.
- Diseases diagnosed on biopsy :
  1. Whipple's disease.
  2. Agammaglobinemia.
  3. Abetalipoproteinemia.

Schilling test :

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Steps :

Phase I : 1000 µg of unlabelled Vitamin B_{12} I.M to saturate stores

↓

Give 1 µg of oral radiolabelled Vitamin B_{12}

↓

Check Vitamin B_{12} level in urine

- <7% → Positive test (malabsorption etiology)
- 7–10% → Normal

Phase II :

Administer

- Intrinsic factor → If >10% urine B_{12} → Perinicious anemia (IF)
- Antibiotics → If >10% → SIBO
- Pancreatic enzymes → If >10% → Chronic pancreatitis

After phase I & 2, if urine B_{12} <7% = Ileal disease.

----- Active space -----

GLOBAL MALABSORPTION

- Defective absorption of :
  a. Carbohydrate.
  b. Fat : most sensitive & specific, most energy dense nutrient.
  c. Protein.
- Small intestinal mucosal dysfunction.
- Causes :
  a. Celiac disease.
  b. Whipple's disease.
  c. Tropical sprue.

Celiac disease

00:01:01

Features :

- AKA celiac sprue/gluten sensitive enteropathy/non tropical sprue.
- Iceberg phenomenon :
  a. Only 50% presents with classical features. } missed diagnosis } Celiac 2023
  b. D/t physician unawareness.
- HLA DQ2/DQ8 : most important predisposition.
- Proximal small intestinal disease (Duodenum, ileum).

TYPES

Classical celiac disease :
50% cases presents with symptoms of malabsorption.

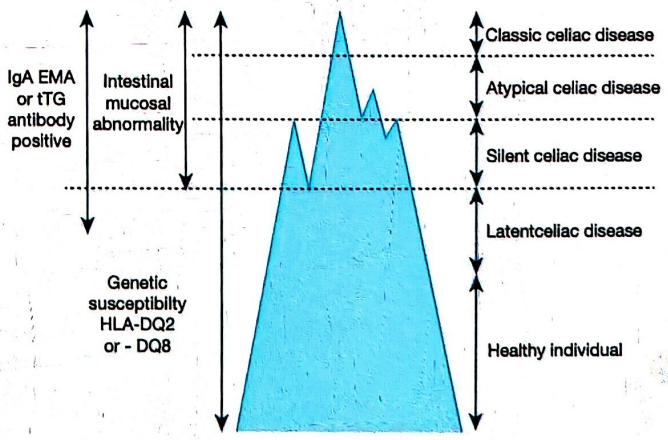
Atypical celiac disease :
Presents with symptoms other than malabsorption.

Silent celiac disease :

- Asymptomatic.
- Serology positive.

Latent celiac disease :

- Asymptomatic.
- Antibodies negative.
- Presence of HLA susceptibility.



EMA, endomysial antibody; Ig, immunoglobulin; tTG, tissue transglutaminase

Celiac iceberg and spectrum of celiac disease

Feedback

PATHOPHYSIOLOGY

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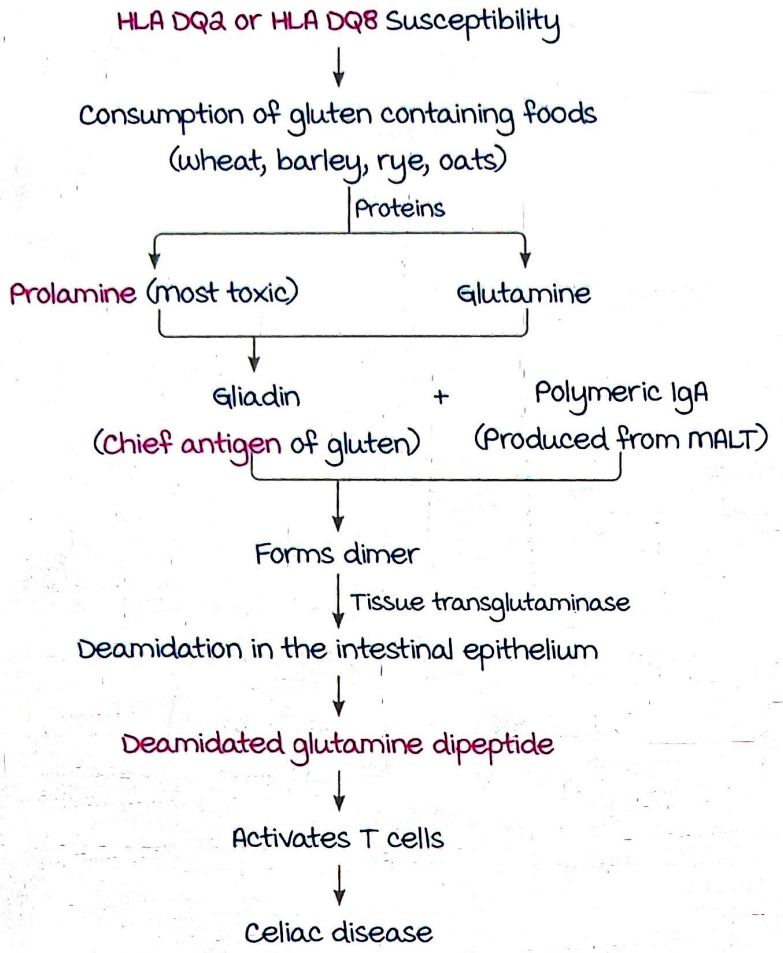

Note :

- Monomeric IgA is produced in bone marrow.
- Vit B_{12}, Mg, bile acid are reabsorbed from distal small intestine → Features not seen in celiac disease

DISEASE PROGRESSION