Absorption and Malabsorption

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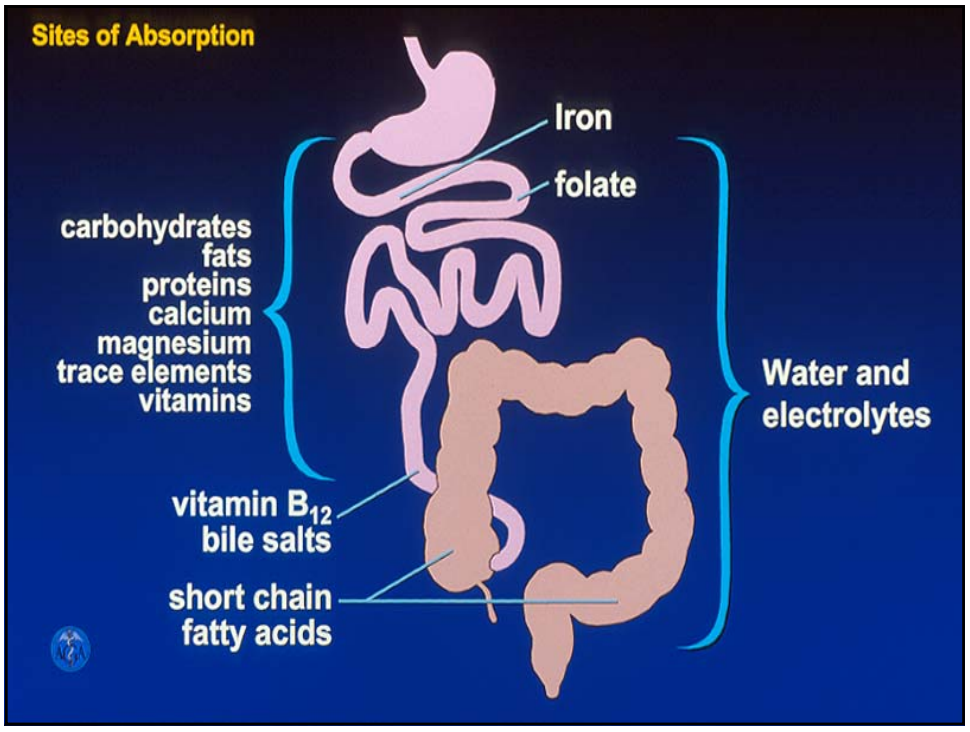
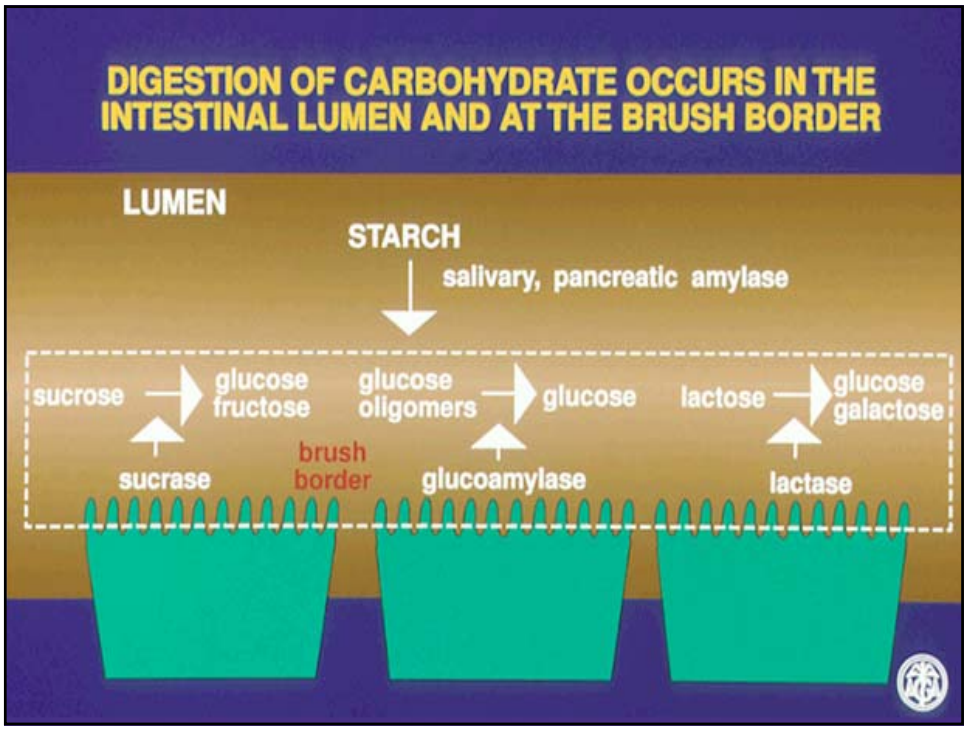


The intestine has a very large surface area for absorption

Type of Surface	Amplification Factor	Surface Area (cm^2)
Mucosal cylinder	1	3,300
Fold of Kerkring	3	10,000
Villi	10	100,000
Microvilli	20	2,000,000

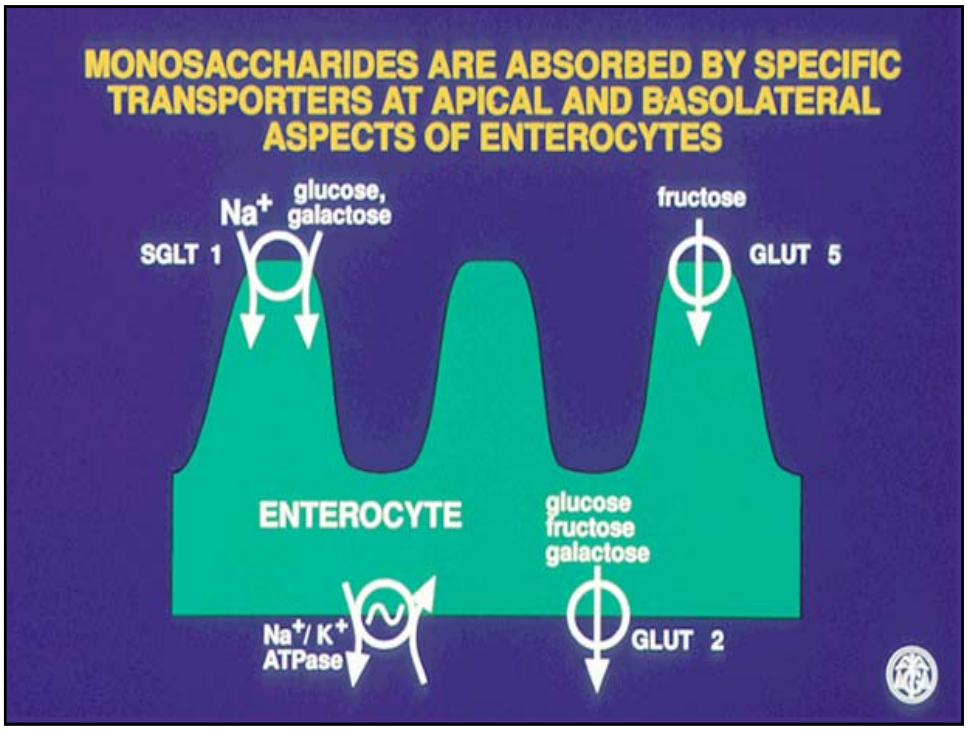
Total surface area = 200 m^2
Double Tennis Court = 175 m^2

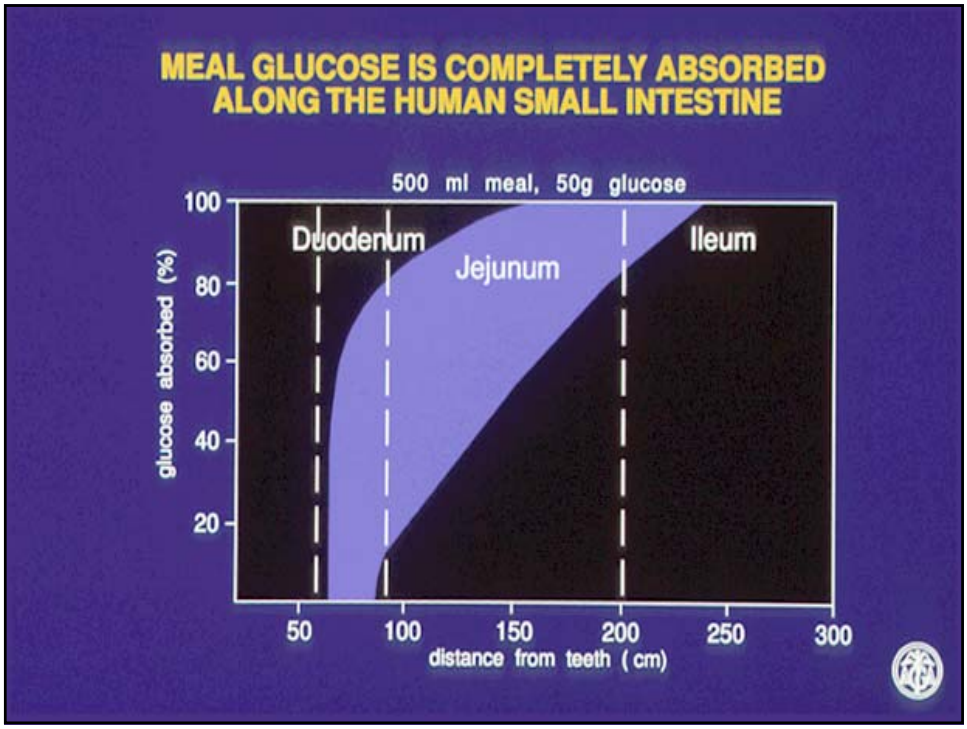


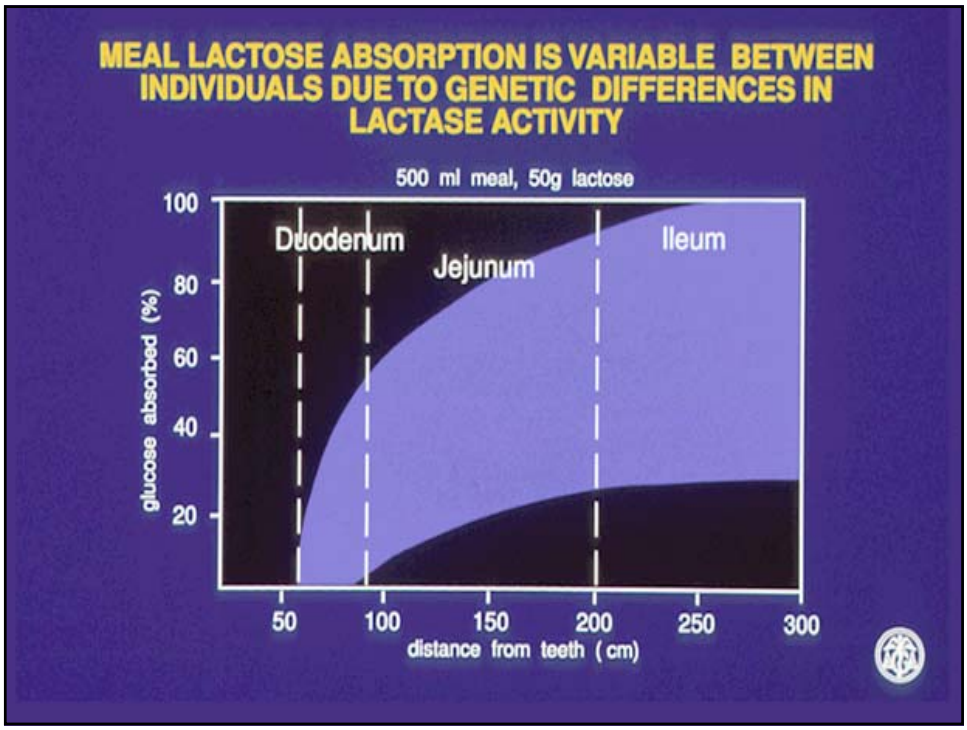
Cell Model

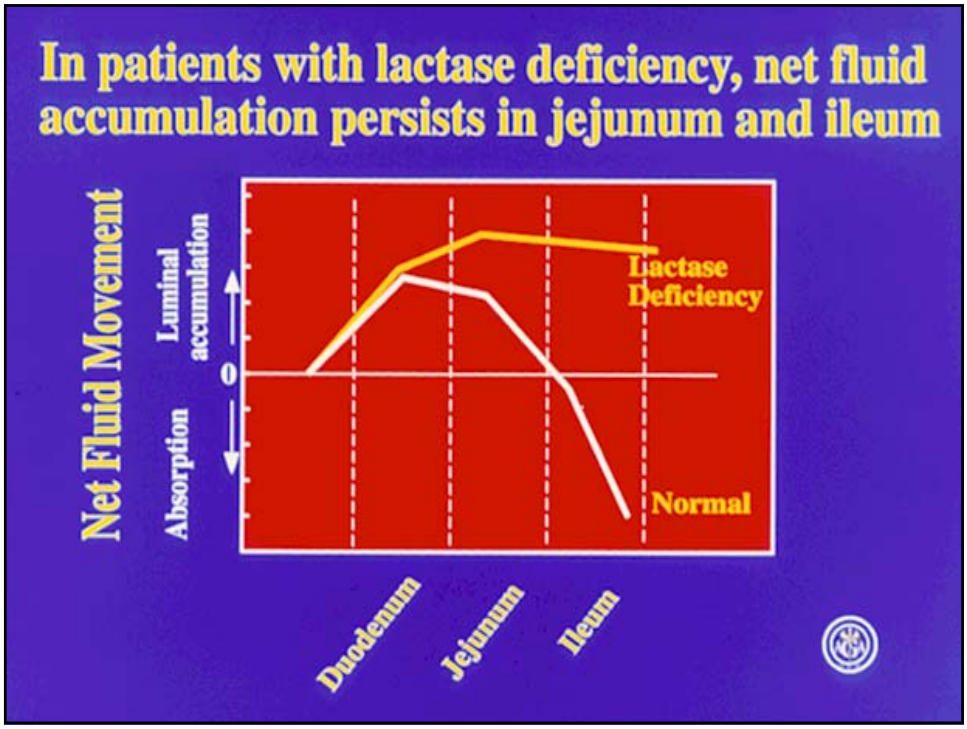
Na+/K+ ATPase on basal-lateral membrane pumps out 3 Na+ and pumps in 2 K+ maintaining an electrochemical Na+ gradient

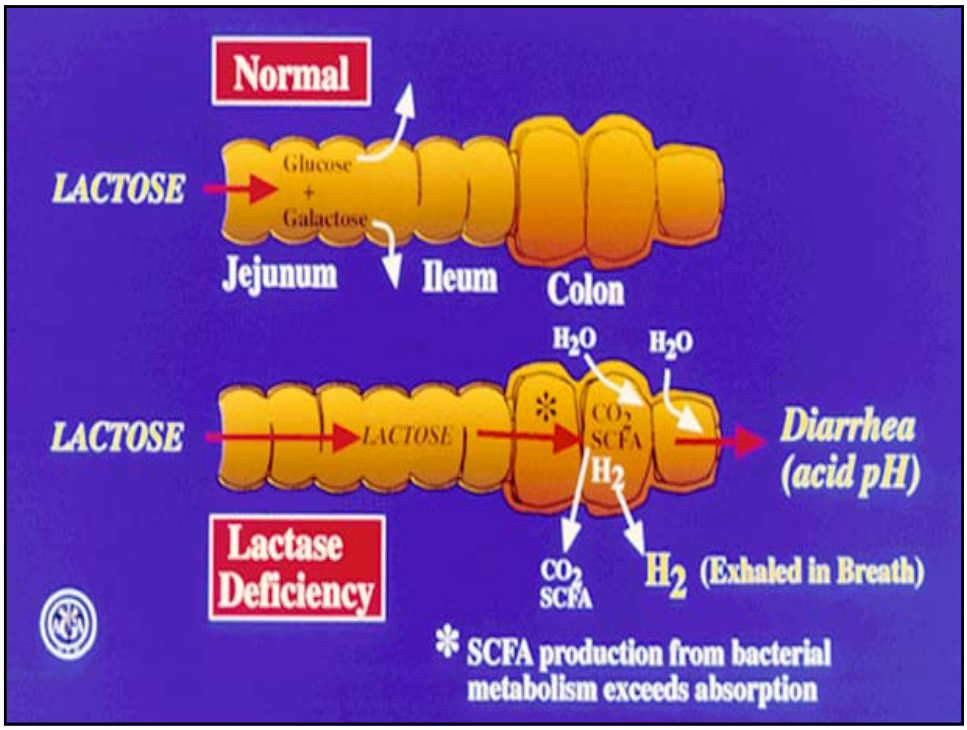
SGLT1 – Sodium/Glucose co-transporter on apical membrane makes use of this gradient

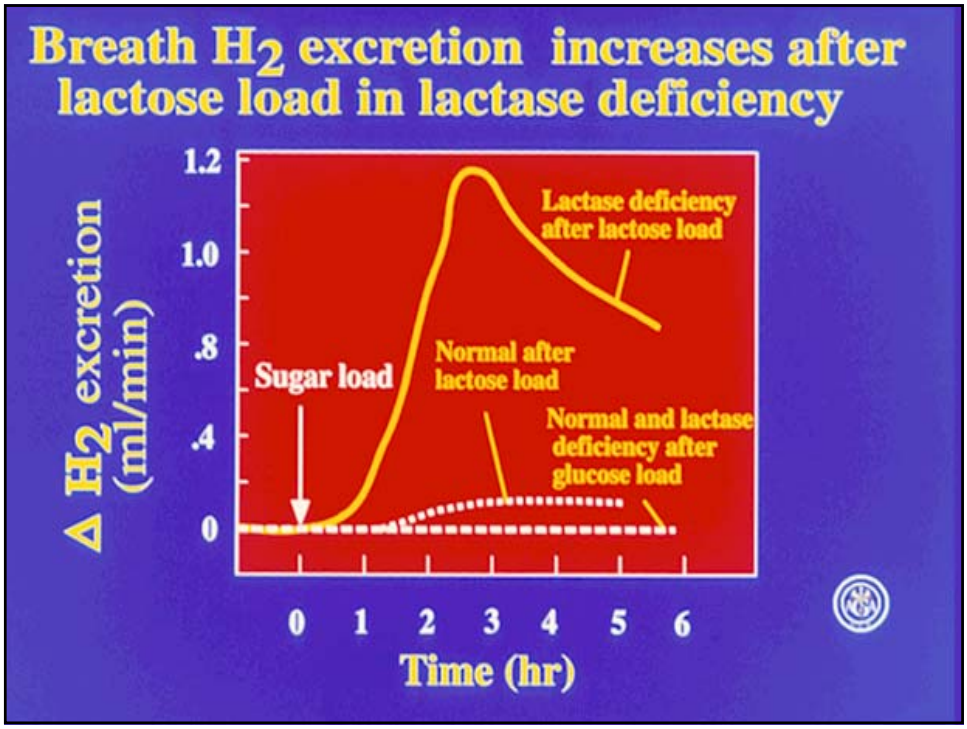


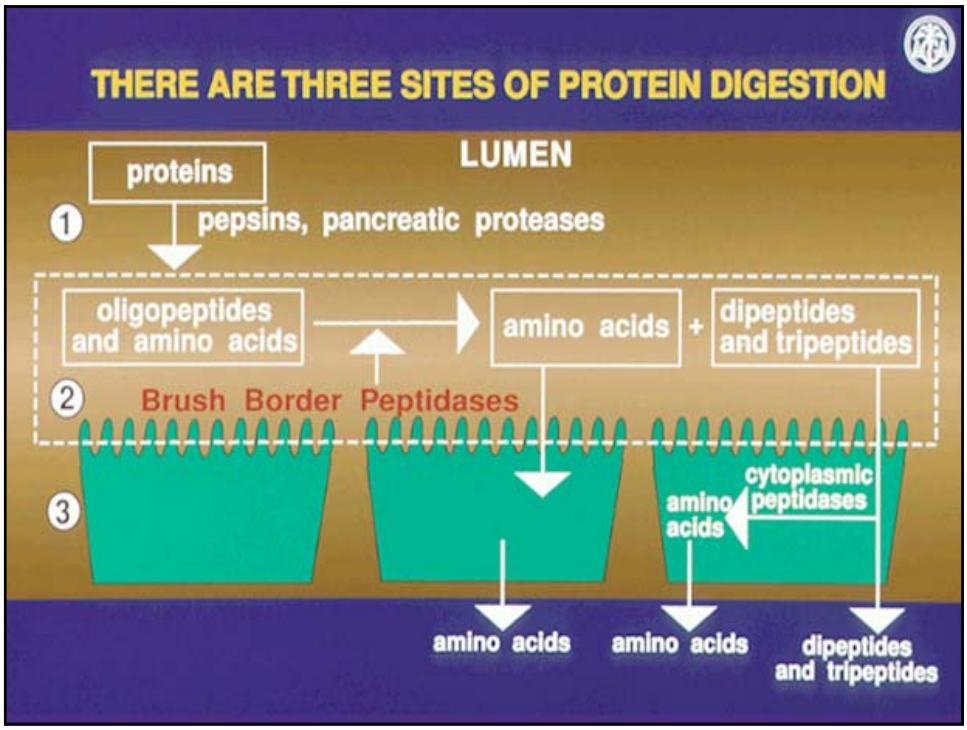

MEAL GLUCOSE IS COMPLETELY ABSORBED ALONG THE HUMAN SMALL INTESTINE
500 ml meal, 50g glucose
Duodenum
Jejunum
Ileum
glucose absorbed (%)
100
80
60
40
20
50
100
150
200
250
300
distance from teeth (cm)


MEAL LACTOSE ABSORPTION IS VARIABLE BETWEEN INDIVIDUALS DUE TO GENETIC DIFFERENCES IN LACTASE ACTIVITY
500 ml meal, 50g lactose
Duodenum
Jejunum
Ileum
glucose absorbed (%)
100
80
60
40
20
50
100
150
200
250
300
distance from teeth (cm)

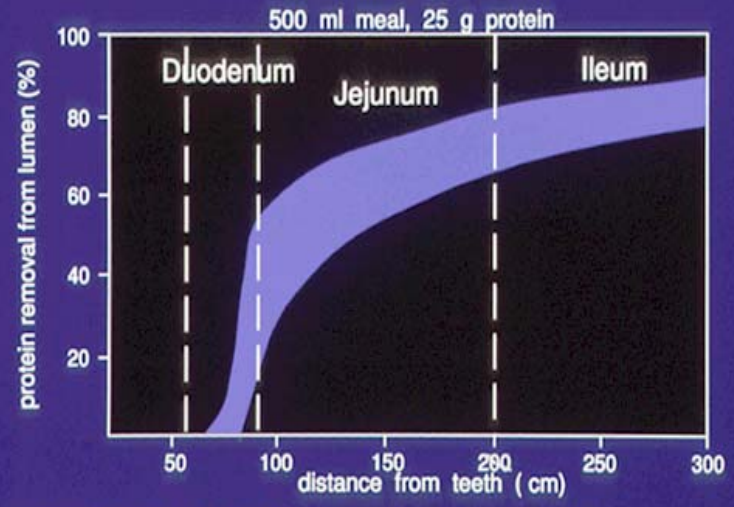

In patients with lactase deficiency, net fluid accumulation persists in jejunum and ileum
Net Fluid Movement
Luminal accumulation
0
Absorption
Lactase Deficiency
Normal
Duodenum
Jejunum
Ileum


Normal
LACTOSE
Glucose
+
Galactose
Jejunum
Ileum
Colon
H_2O
H_2O
LACTOSE
LACTOSE
CO_2
SCFA
H_2
Diarrhea
(acid pH)
Lactase Deficiency
CO_2
SCFA
H_2 (Exhaled in Breath)
* SCFA production from bacterial metabolism exceeds absorption


Breath H_2 excretion increases after lactose load in lactase deficiency
Δ H_2 excretion (ml/min)
1.2
1.0
.8
.4
0
Lactase deficiency after lactose load
Sugar load
Normal after lactose load
Normal and lactase deficiency after glucose load
0 1 2 3 4 5 6
Time (hr)

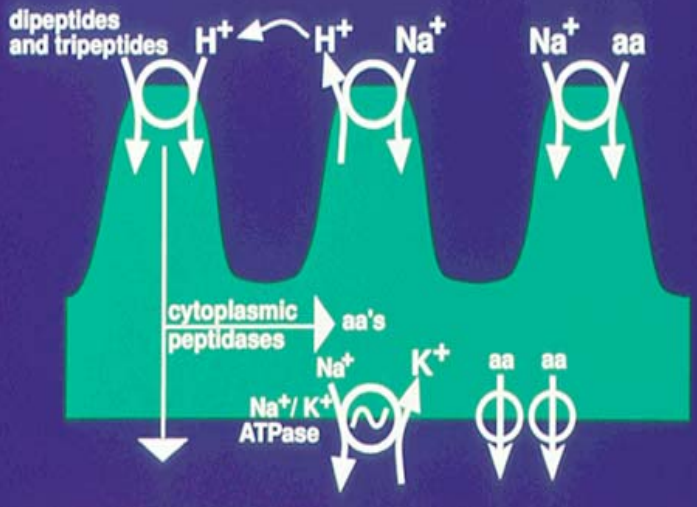

THERE ARE THREE SITES OF PROTEIN DIGESTION
LUMEN
proteins
1
pepsins, pancreatic proteases
oligopeptides and amino acids
amino acids
+
dipeptides and tripeptides
2
Brush Border Peptidases
3
cytoplasmic peptidases
amino acids
amino acids
amino acids
dipeptides and tripeptides

REMOVAL OF DIETARY PROTEIN BY DIGESTION AND ABSORPTION OCCURS THROUGHOUT THE SMALL INTESTINE



- protein digestion is slow in onset and incomplete

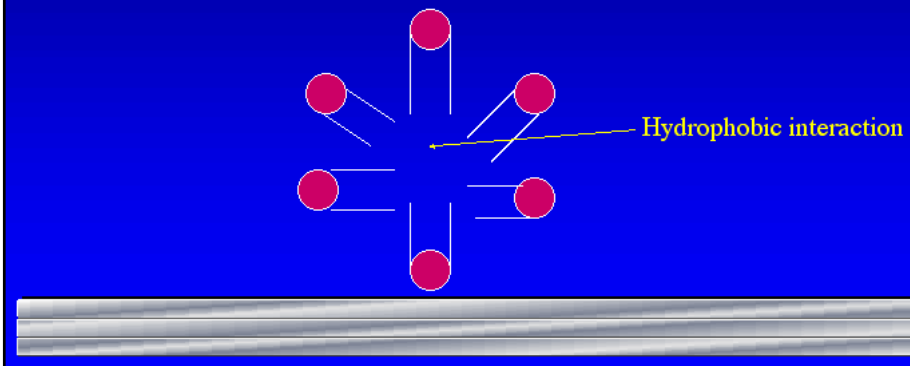
AMINO ACIDS, DIPEPTIDES AND TRIPEPTIDES ARE ABSORBED BY SPECIFIC TRANSPORTERS



- There are at least five apical transporters for aa's - each one transports a specific group of aa.

What is a Micelle?

- An organized aggregate of molecules containing polar (or ionic) heads and non-polar tails
  - Non-polar tails point inwards and polar heads point outwards, interacting with water molecules.



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A MIXED MICELLE IS COMPOSED OF POLAR AND NON-POLAR LIPIDS

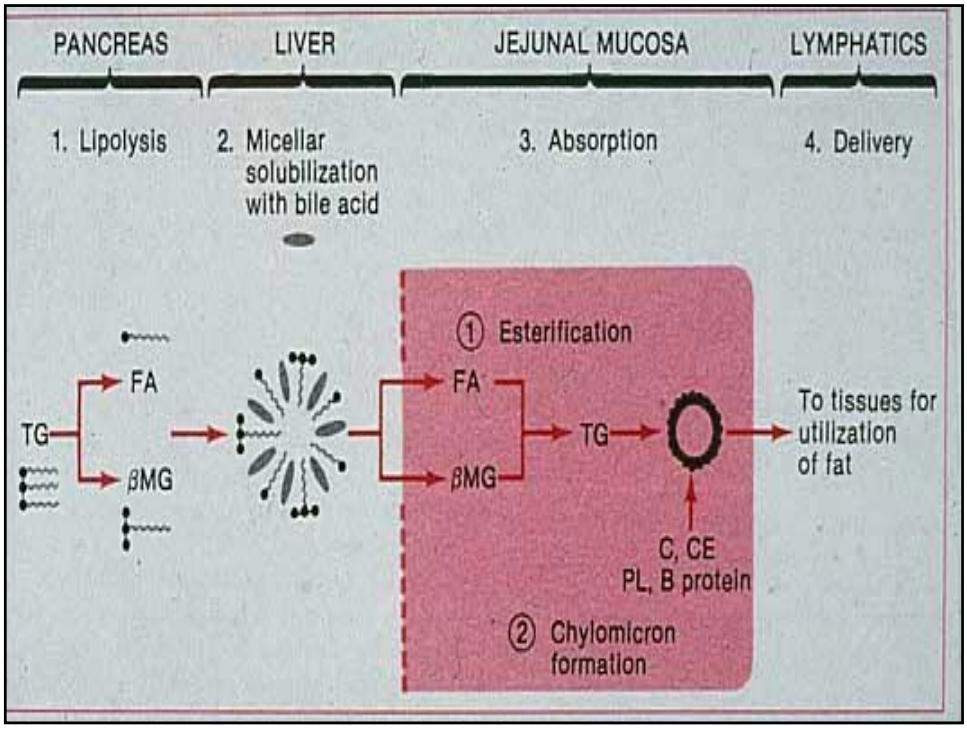
COMPOSITION OF A MIXED MICELLE

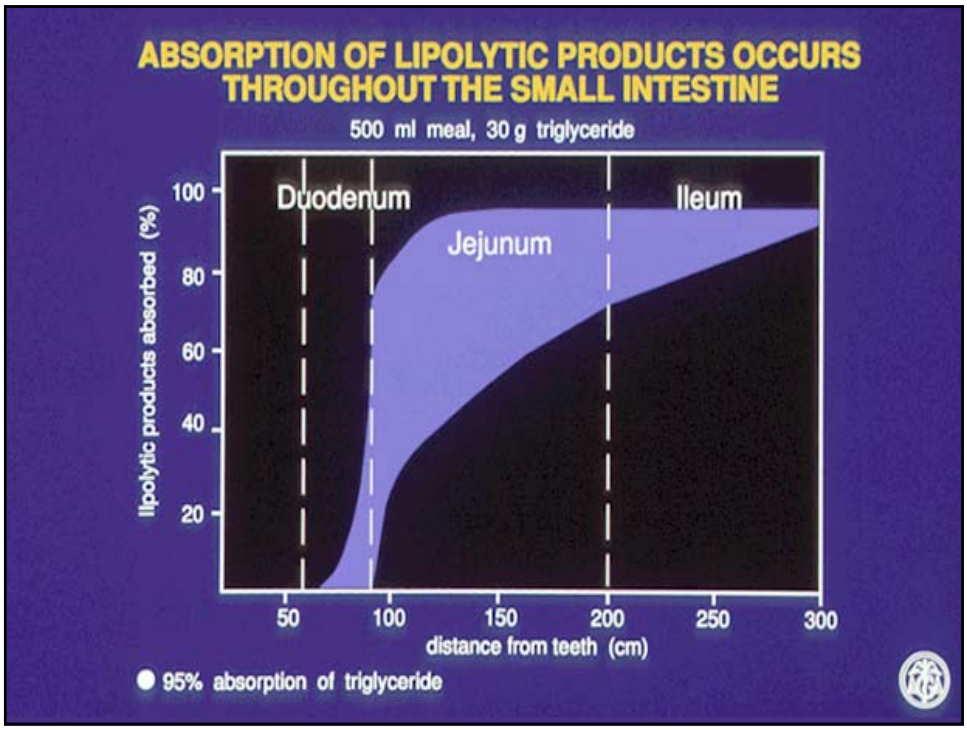
Polar

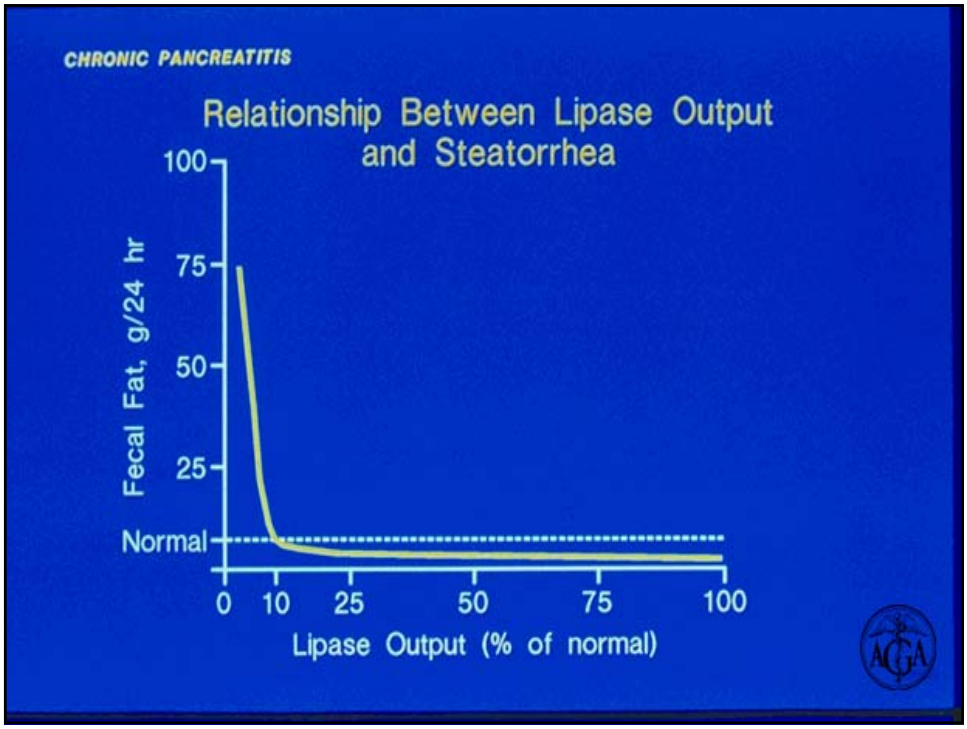
- bile acids
- fatty acids
- monoglyceride
- lecithin
- cholesterol
- fat soluble vitamins

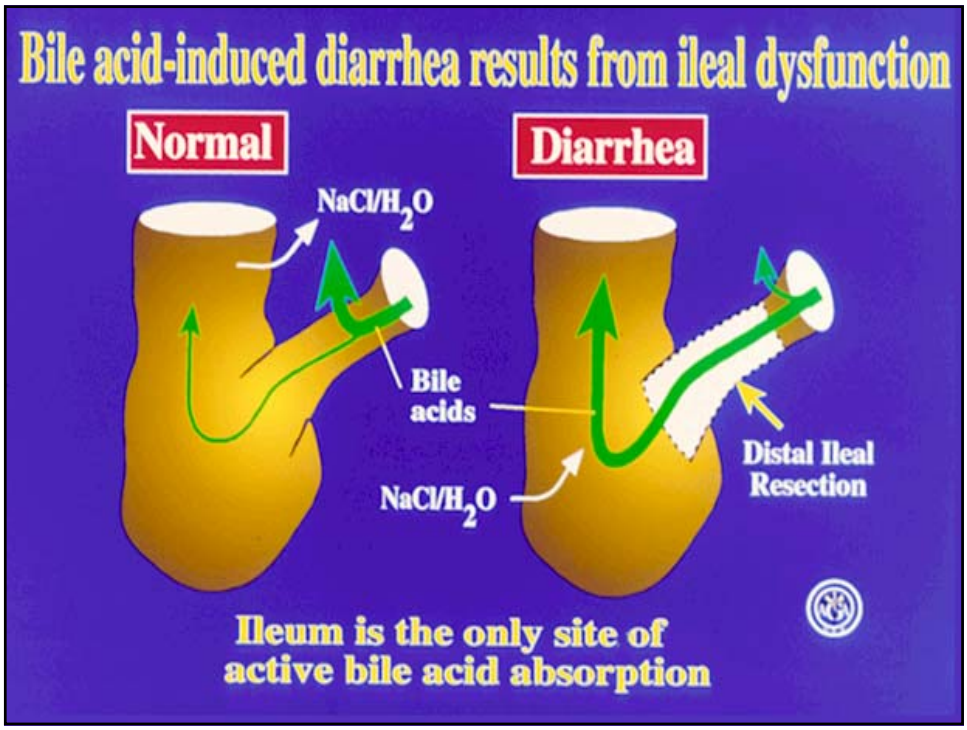
Non-Polar

- Bile acids and polar lipids are located at the outer surface of a micelle while non-polar lipids are located in the center


PANCREAS
LIVER
JEJUNAL MUCOSA
LYMPHATICS
1. Lipolysis
2. Micellar solubilization with bile acid
3. Absorption
4. Delivery
TG
FA
βMG
① Esterification
FA
βMG
TG
To tissues for utilization of fat
C, CE
PL, B protein
② Chylomicron formation

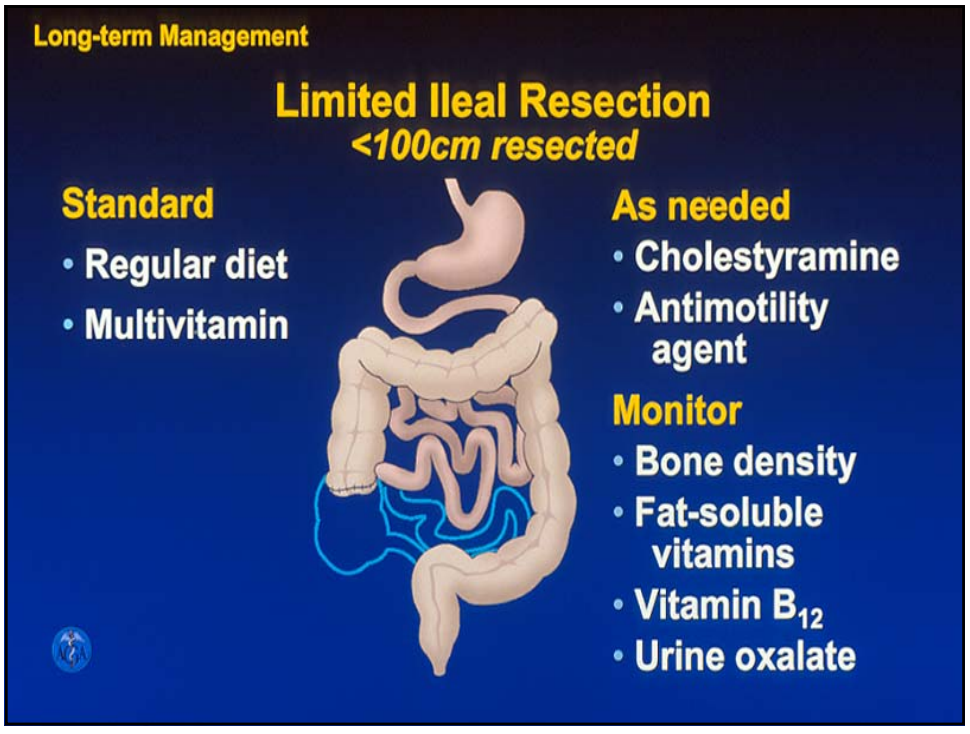

ABSORPTION OF LIPOLYTIC PRODUCTS OCCURS THROUGHOUT THE SMALL INTESTINE
500 ml meal, 30 g triglyceride
Duodenum
Jejunum
Ileum
lipolytic products absorbed (%)
100
80
60
40
20
50
100
150
200
250
300
distance from teeth (cm)
95% absorption of triglyceride


CHRONIC PANCREATITIS
Relationship Between Lipase Output and Steatorrhea
Fecal Fat, g/24 hr
100
75
50
25
Normal
0
10
25
50
75
100
Lipase Output (% of normal)


Bile acid-induced diarrhea results from ileal dysfunction
Normal
Diarrhea
NaCl/H2O
Bile acids
NaCl/H2O
Distal Ileal Resection
Ileum is the only site of active bile acid absorption

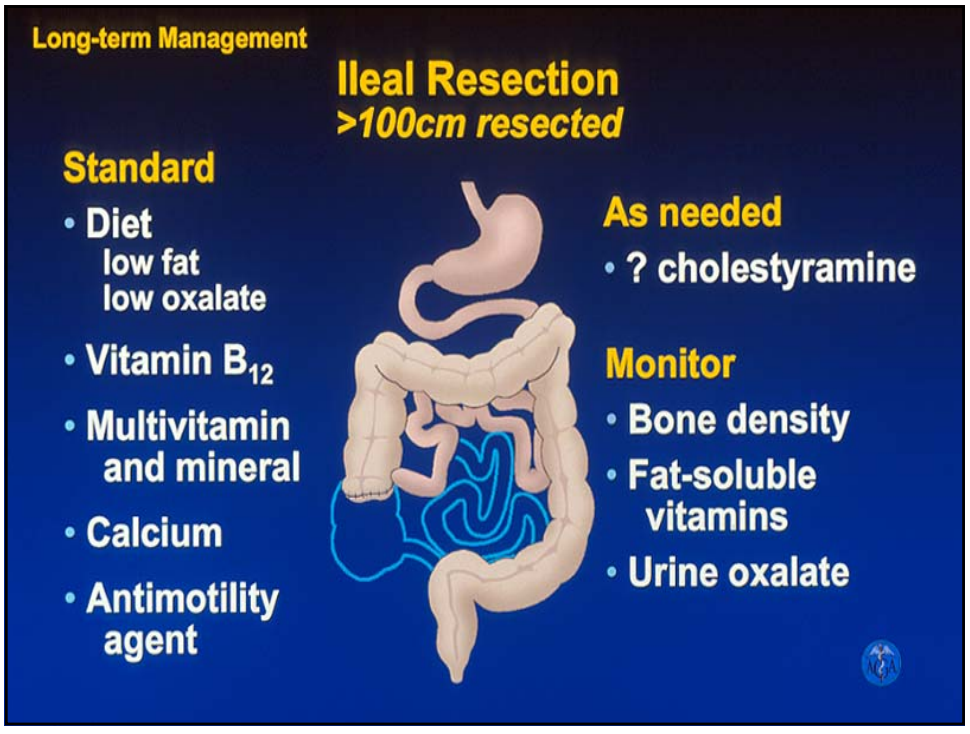
Limited Ileal Resection (<100cm)

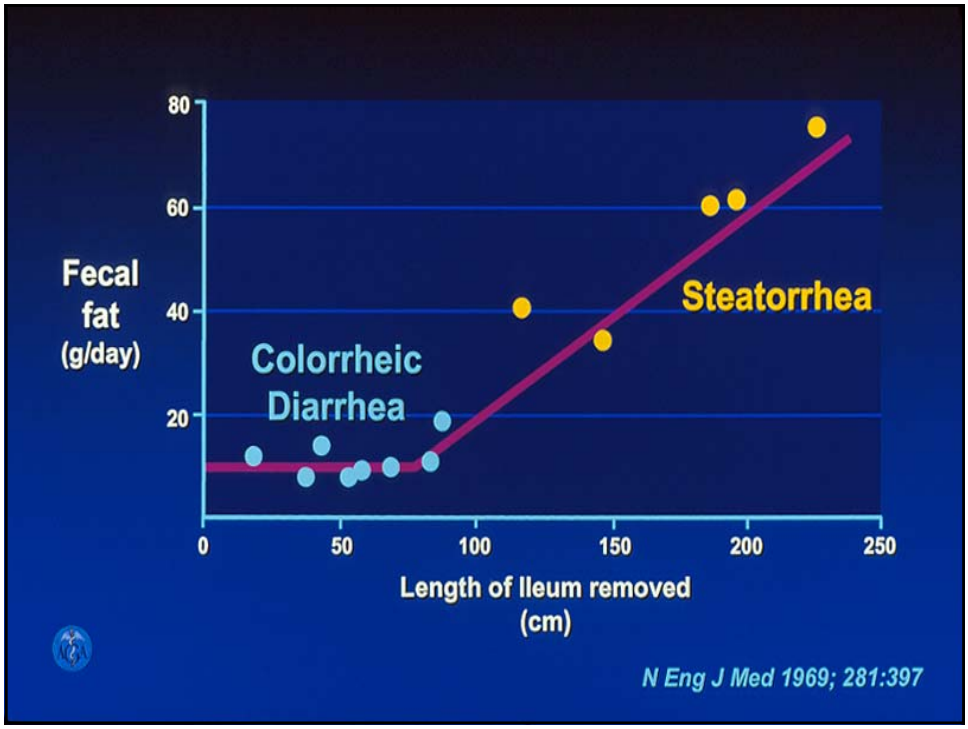
- Increased Bile Salt production by liver able to compensate for losses
- Fat absorption not compromised
- Increased bile salt delivery to colon produces secretory diarrhea, responds to cholestyramine
- Antimotility drugs may counter rapid transit
- B12 absorption may be compromised

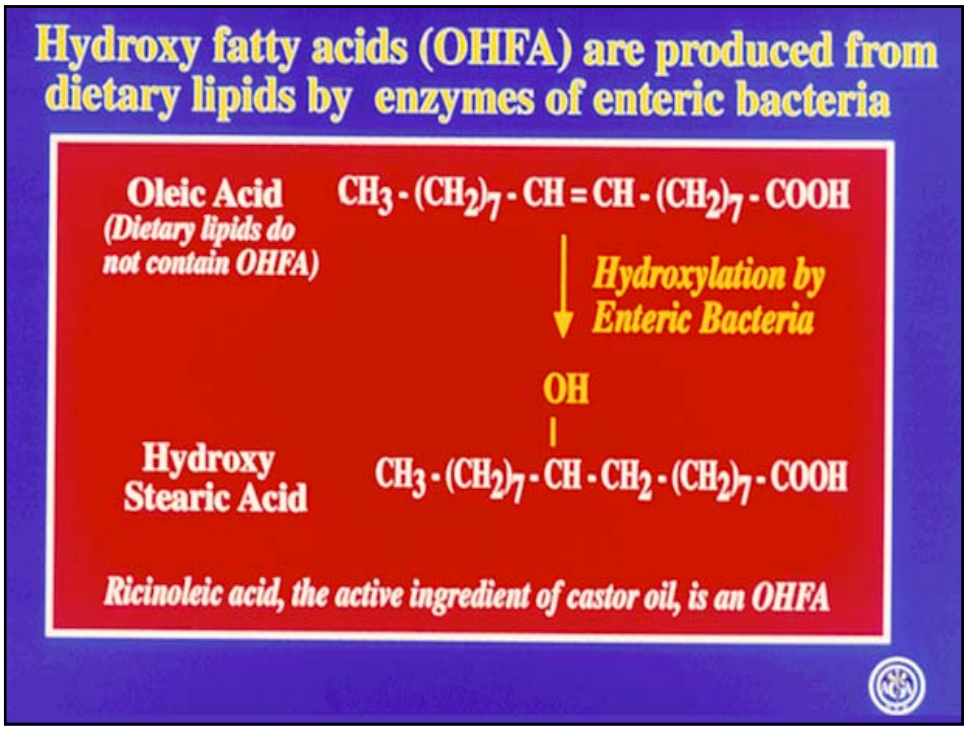


Extensive ileal resection (>100cm)

- Liver can't compensate → Bile Acid pool reduced → Impaired micelle formation → Fatty Acids reach colon → Hydroxylation of FA by colonic bacteria → secretory diarrhea and steatorrhea.
- FA bind Ca^{++} resulting in free oxylate, absorbed by colon → hyperoxyalurea → oxylate renal stones
- B12 supplement always necessary
- High Ca^{++}, low fat, low oxylate diet helpful
- Cholestyramine may worsen diarrhea

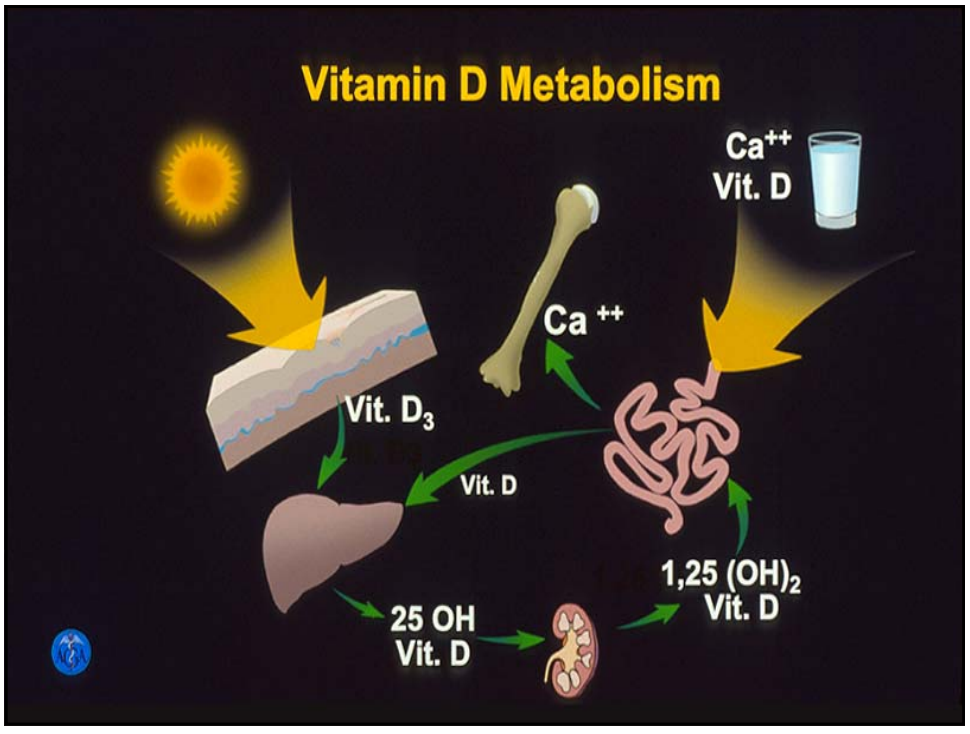


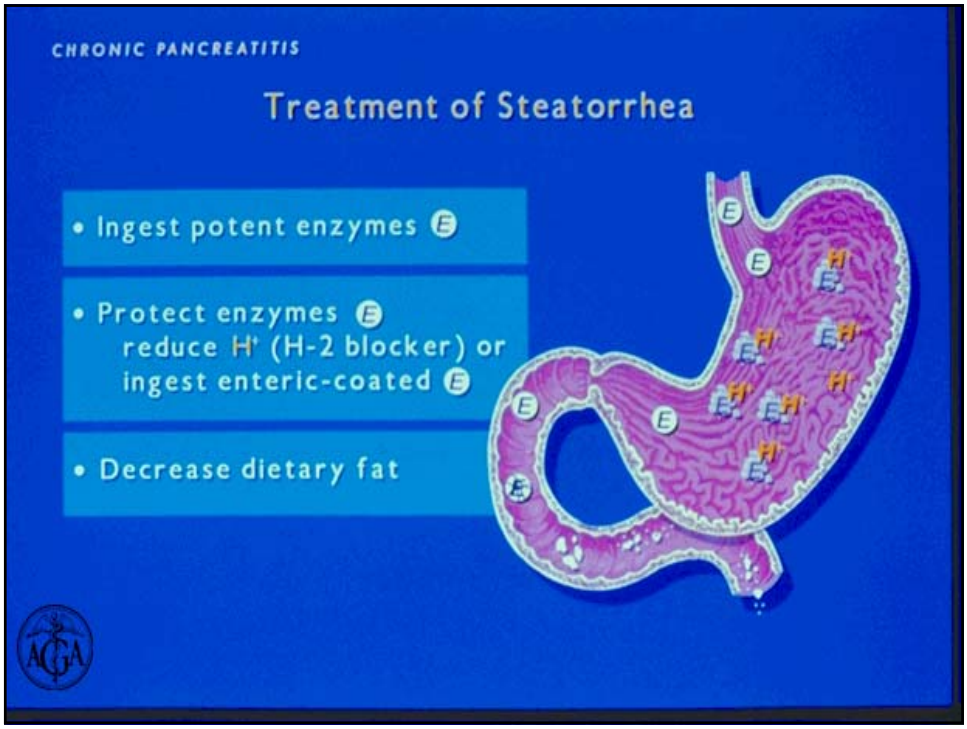

80
60
40
20
Fecal fat (g/day)
Colorrheic Diarrhea
Steatorrhea
0
50
100
150
200
250
Length of Ileum removed (cm)
N Eng J Med 1969; 281:397

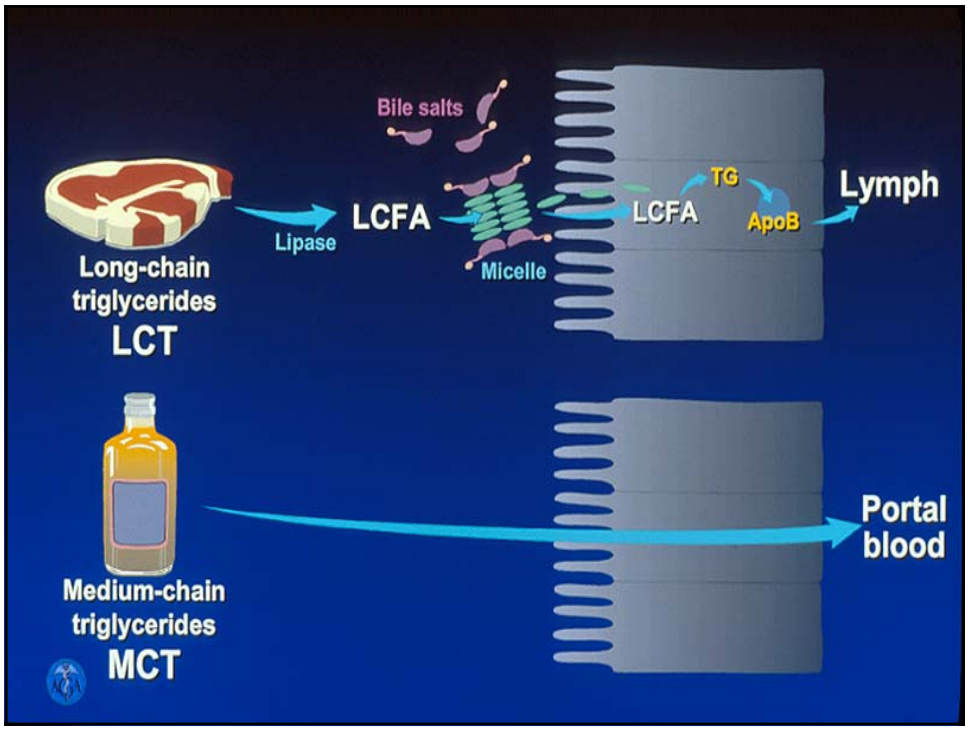

Hydroxy fatty acids (OHFA) are produced from dietary lipids by enzymes of enteric bacteria
Oleic Acid
(Dietary lipids do not contain OHFA)
CH3 - (CH2)7 - CH = CH - (CH2)7 - COOH
Hydroxylation by Enteric Bacteria
OH
Hydroxy Stearic Acid
CH3 - (CH2)7 - CH - CH2 - (CH2)7 - COOH
Ricinoleic acid, the active ingredient of castor oil, is an OHFA

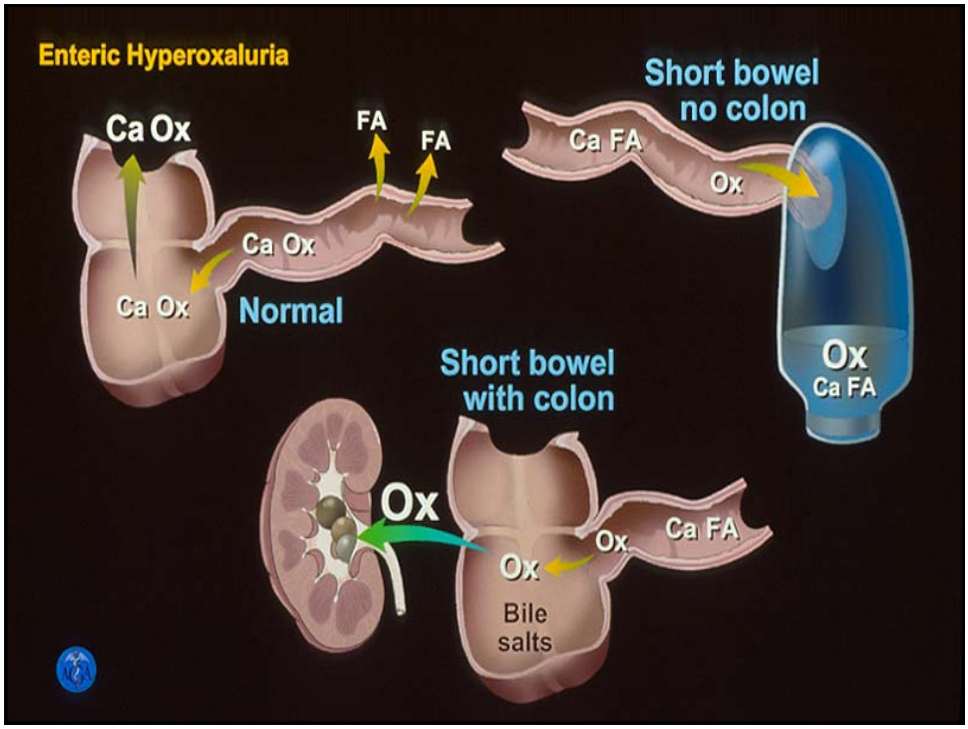
Several features help distinguish bile acid- from fatty acid-induced diarrhea

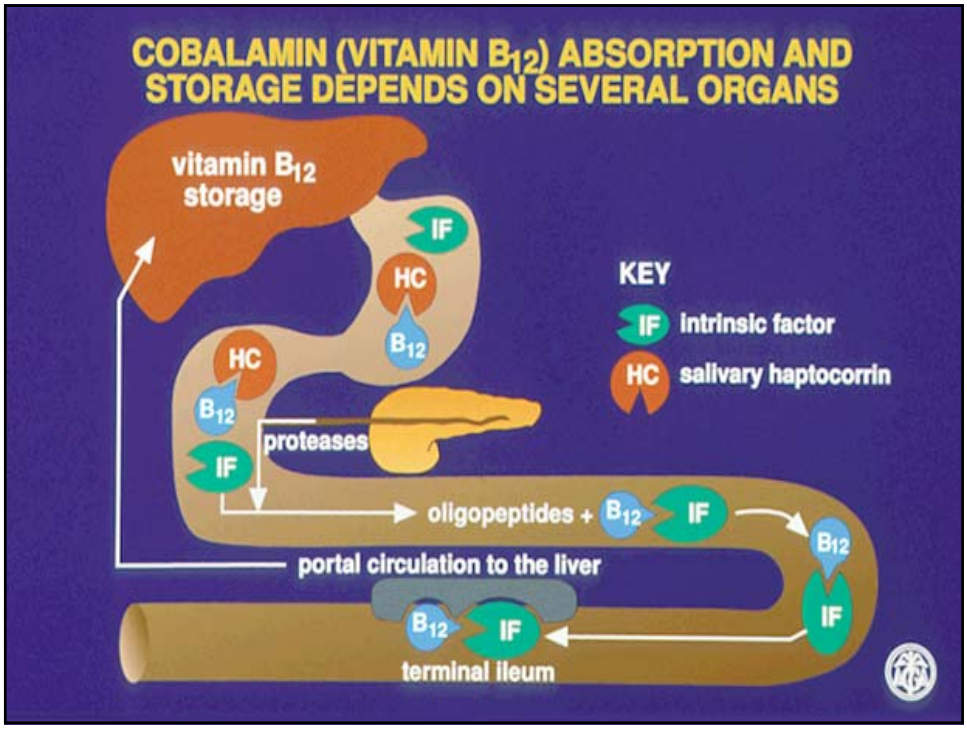
Characteristic	Bile Acid	Fatty Acid
1. Length of resection	small	large
2. Fecal BA output	↑	↑↑
3. Fecal BA loss compensated by hepatic BA synthesis	yes	no
4. BA pool size	normal	↓
5. Duodenal [BA]	normal	↓
6. Steatorrhea	normal or mild	>20 g/24 hrs
7. Responds to low fat diet	no	yes
8. Responds to cholestyramine	yes	no




CHRONIC PANCREATITIS
Treatment of Steatorrhea
• Ingest potent enzymes E
• Protect enzymes E reduce H+ (H-2 blocker) or ingest enteric-coated E
• Decrease dietary fat


Bile salts
Long-chain triglycerides
LCT
Lipase
LCFA
Micelle
LCFA
TG
ApoB
Lymph
Medium-chain triglycerides
MCT
Portal blood


Enteric Hyperoxaluria
Ca Ox
FA
FA
Ca Ox
Ca Ox
Normal
Short bowel
no colon
Ca FA
Ox
Ox
Ca FA
Short bowel
with colon
Ox
Ox
Ca FA
Ox
Bile
salts



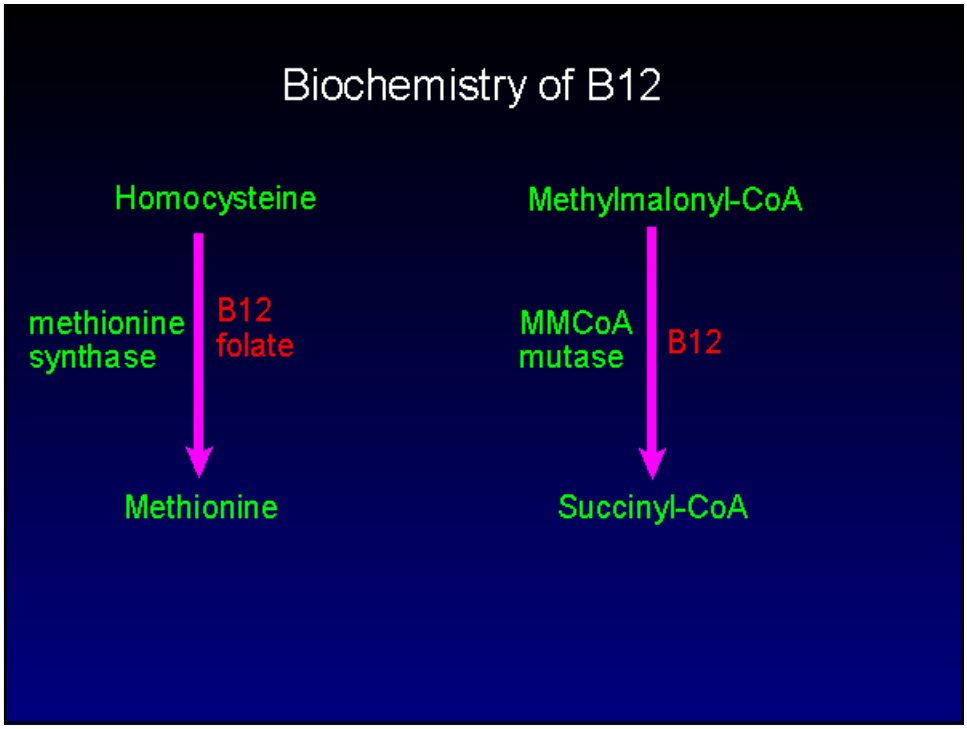
Dietary Cobalamin

"Everything that walks, swims, or flies contains Vitamin B12. Nothing that grows from the ground contains Vitamin B12."

Decreased absorption in elderly.

Daily requirement from diet only 1mcg/d

Deficiency can be seen in strict vegans



Causes of B12 Deficiency

- Inadequate Intake
  - Vegans
- Inadequate liberation from food
  - Food Cobalamin Malabsorption
- Lack of Intrinsic Factor
  - Pernicious Anemia, Gastrectomy
- Impaired proteolytic degredation of R-B12 complex
  - Pancreatic Insufficiency, ZE Syndrome

Causes of B12 Deficiency

- Infection (competition for luminal B12)
  - Bacterial overgrowth
    - strictures
    - blind loop
    - motility disorders
  - Diphyllobothrium latum

Causes of B12 Deficiency

- Absent or non-functioning Ileal mucosa
  - Crohn's Disease, Tropical Sprue, Lymphoma, TB, Ileal Resection
- Abnormal translocation across enterocyte
  - Juvinile PA, Transcobalamin II Deficiency, Imerslund-Grasbeck syndrome
- Drugs
  - Colchicine, Biguanide, Nitrous Oxide, PAS

SCHILLING TEST AS A MEASUREMENT OF VIT B12 ABSORPTION

Stage	Food-Cobalamin Malabsorption	Pernicious Anemia or Gastrectomy	Pancreatic Insufficiency	Bacterial Overgrowth	Ileal Resection or Disease
1) Vit B12	**Normal**	Decreased	Decreased	Decreased	Decreased
2) Vit B12 + Intrinsic Factor		**Normal**	Decreased	Decreased	Decreased
3) Vit B12 + Pancreatic Enzymes			**Normal**	Decreased	Decreased
4) Abx followed by Vit B12				**Normal**	Decreased

Vitamin and Mineral Deficiencies

Manifestations

Vitamin B_{12} / Folate Iron	anemia, glossitis, cheilitis, angular stomatitis, diarrhea*, paresthesias*, ataxia* *Vitamin B_{12} only
Vitamin D Calcium / magnesium	osteoporesis, osteomalacia, paresthesias, tetany
Zinc	anorexia, diarrhea, rash, alopecia
Vitamin A	night blindness, dry eyes, hyperkeratosis, diarrhea
Vitamin K	ecchymoses, bleeding
Vitamin E	paresthesias, ataxia, retinopathy

It’s 9:55. I’m so outta here!

Good Luck on Final, Boards, and Wards.