

Malabsorption Mysteries: Decoding the Puzzle for Better Patient Outcome



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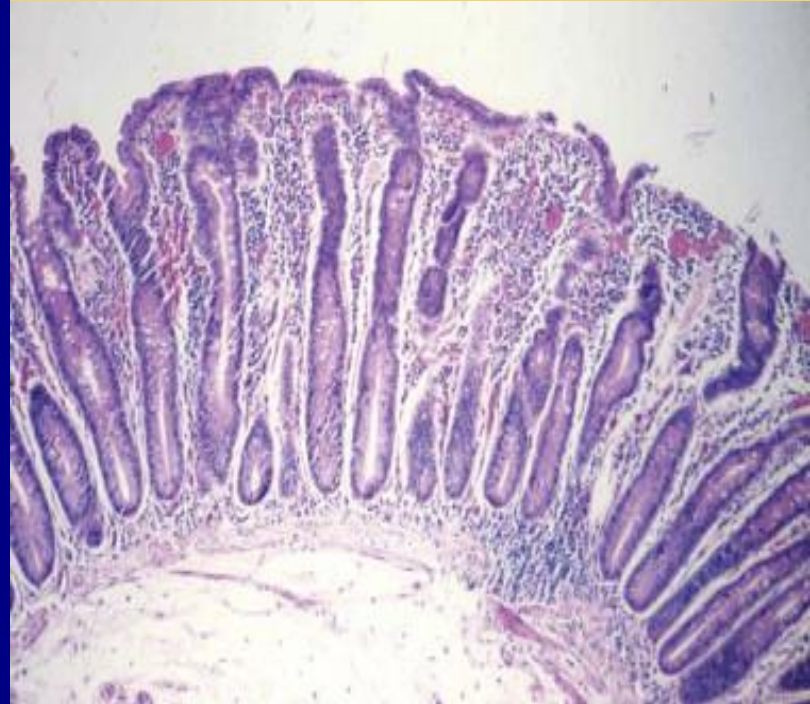
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Case 1



- 36 yo man presents for evaluation of iron deficiency anemia. No GI symptoms. No aspirin/NSAIDs.
- IgA tTG antibody positive
- Small bowel biopsy done
- What result would you expect on the D-xylose test?



Case 2



- 47 yo man h/o alcoholism c/o constant vague abdominal pain, one “constipated” stool/day and 20 pound weight loss
- CT scan shows pancreatic atrophy
- Lab tests
 - Serum carotene 50 mcg/dl (normal > 80)
 - 72 hr fecal fat 28 g/day (normal < 7)
 - 5 hr urinary D-xylose 7.5 g (normal > 4)
- What's the next step?
 - Further testing? What test(s)?
 - Treatment? With what?

Case 3

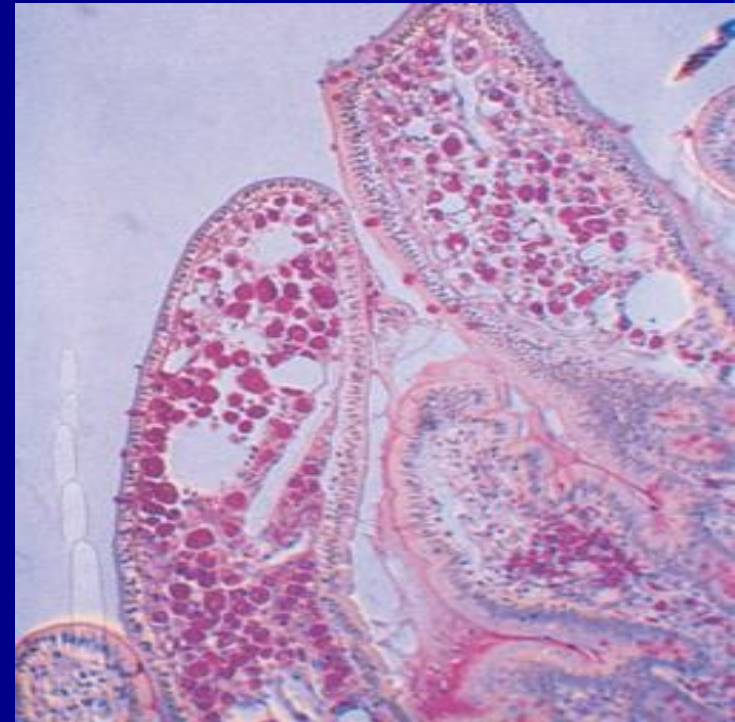


- 62 yo woman with h/o prior **gastric surgery** (Roux-en-Y **GJ**) for PUD c/o early satiety, diarrhea, foul-smelling breath and weight loss
- What's the most likely **diagnosis**?
- **What test(s) can confirm the diagnosis?**

Case 4

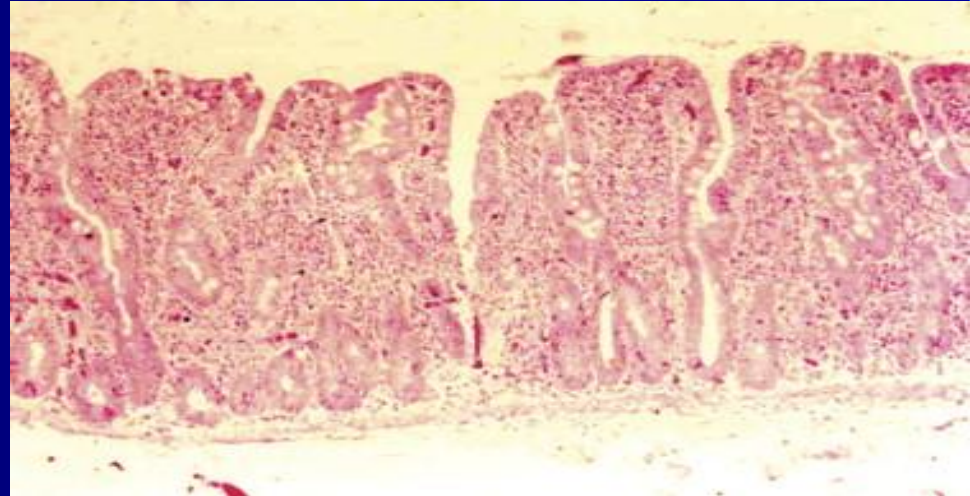


- 75 yo man presents with **FUO**, **arthritis** and **diarrhea**
- Labs show hypoproteinemia
- Sprue antibodies negative
- Negative SIBO breath test
- **Small bowel biopsy done** →
- What is the **diagnosis**?



Case 5

- 22 yo man returns from a prolonged stay in the **Bangladesh** c/o diarrhea, fatigue and 5 pound weight loss
- Hgb 10.5 MCV 104
- Folate low
- D-xylose test decreased
- Celiac antibodies negative
- Small bowel biopsy done
- What's the **diagnosis?** **treatment?**



Outline

- Normal digestion and absorption
- Classification of malabsorption
- Tests of malabsorption
- Clinical approach to diagnosis

Malabsorption vs. Maldigestion

Decreased intestinal absorption of macronutrients and/or micronutrients

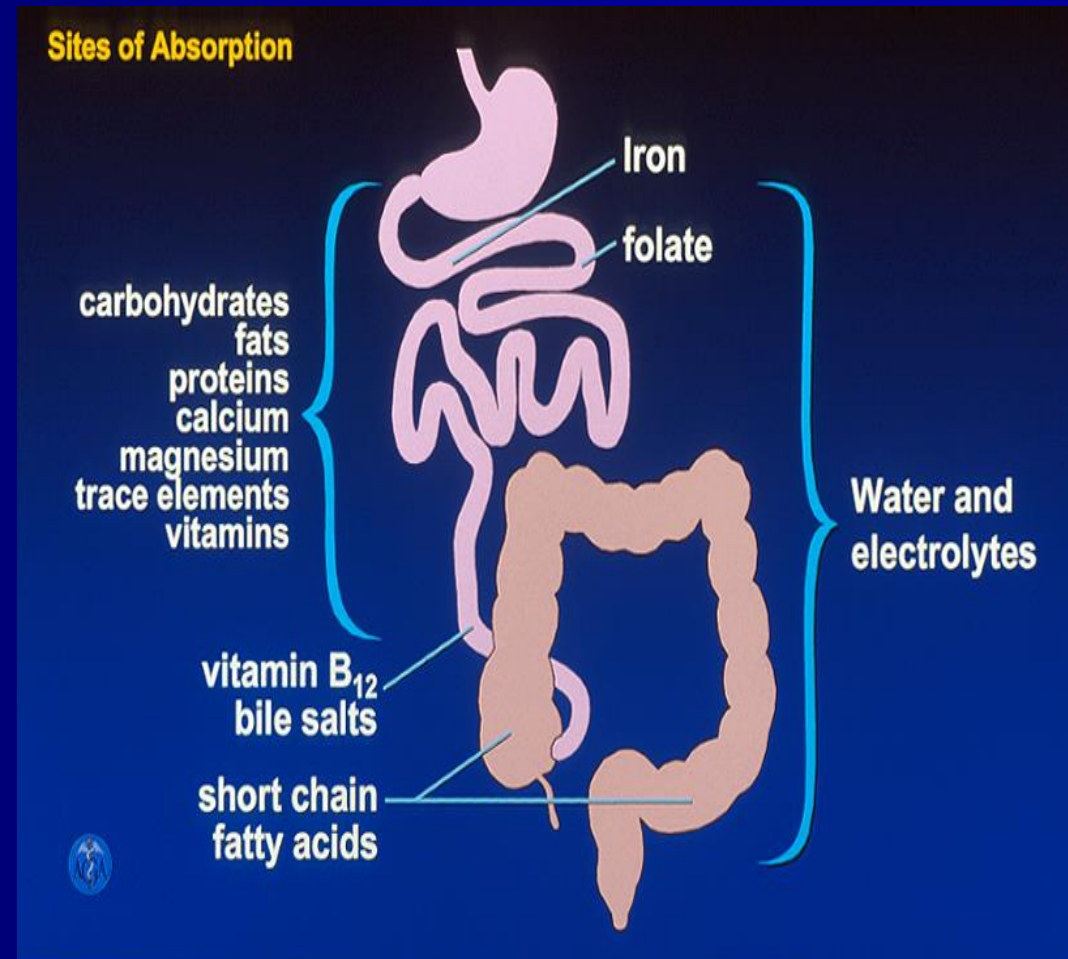
- “malabsorption” – defect in mucosal phase
- “maldigestion” – defect in intraluminal phase

Diet

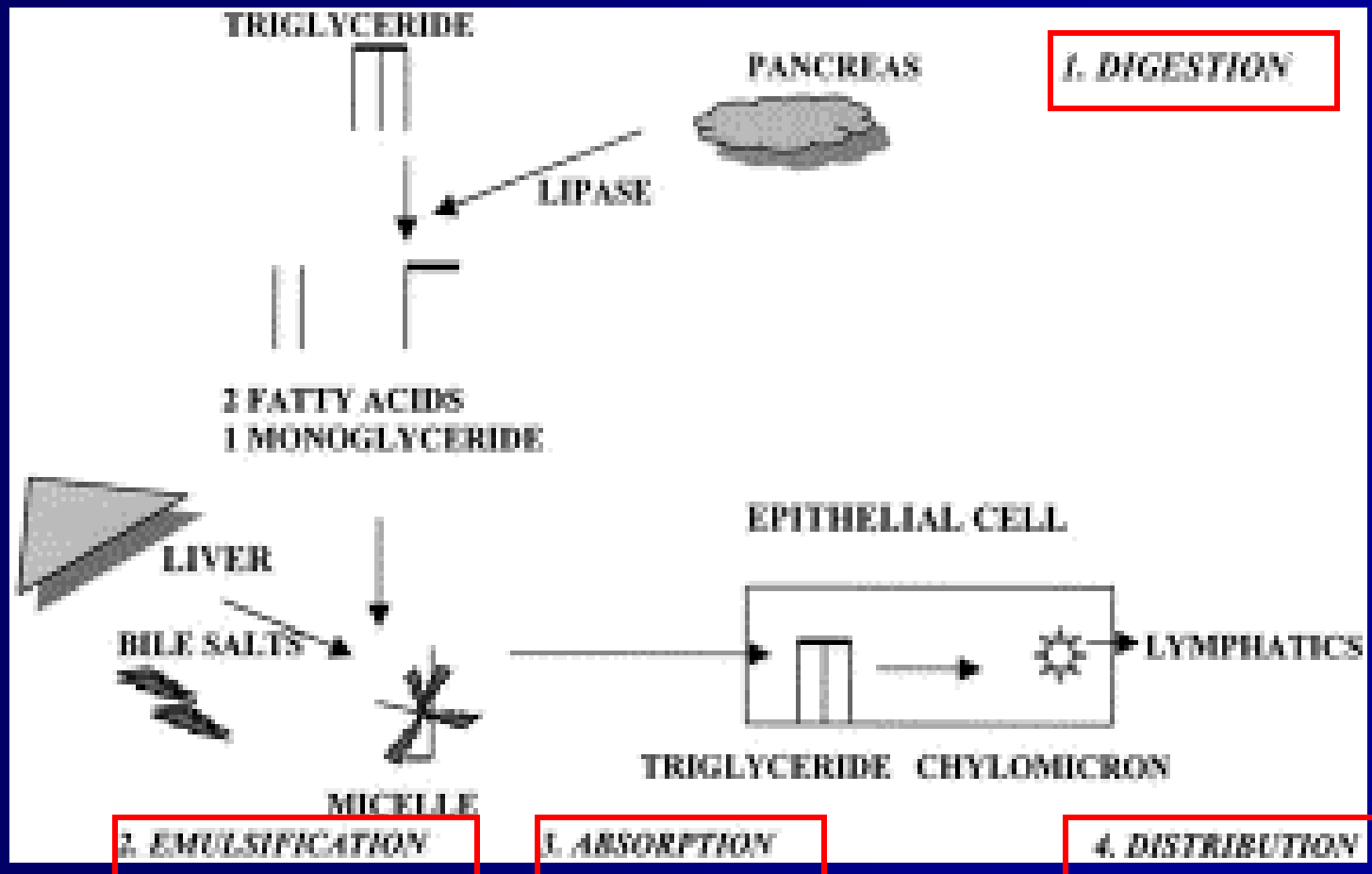


Normal Digestion and Absorption

- Mechanical mixing
- Enzyme and bile salt production
- Mucosal function
- Blood supply
- Intestinal motility
- Commensal gut flora



Fat Digestion and Absorption



Carbohydrate and Protein Digestion and Absorption



Digestion → **Absorption** → **Distribution**



Classification of Malabsorption

- Luminal
- Mucosal
- Postabsorptive
- Overt
- Subclinical
- Asymptomatic
- Global/Total
- Partial
- Selective
- CHO
- Protein
- Fat
- Intestinal vs Pancreatic

Classification of Malabsorption

- **Luminal phase**
 - Substrate hydrolysis
 - Digestive enzyme deficiency/inactivation, inadequate mixing
 - Fat solubilization
 - Diminished bile salt synthesis/secretion, increased loss
 - Luminal availability of nutrients
 - Diminished gastric acid/intrinsic factor, bacterial consumption
- **Mucosal phase**
 - Brush border hydrolysis
 - Epithelial transport
- **Postabsorptive processing**
 - Enterocyte, lymphatic

Mechanisms of Fat Malabsorption

- Pancreatic insufficiency
- Bile acid deficiency
- Small intestinal bacterial overgrowth
- Loss of absorptive surface area
- Defective enterocyte function
- Lymphatic disorders

Mechanisms of Carbohydrate Malabsorption

- Selective disaccharidase deficiency
- Disruption of brush border/enterocyte function
- Loss of mucosal surface area
- Pancreatic insufficiency

Mechanisms of Protein Malabsorption

- Pancreatic insufficiency
- Disorders with impaired enterocyte function
- Disorders with decreased absorptive surface
- Protein-losing enteropathy

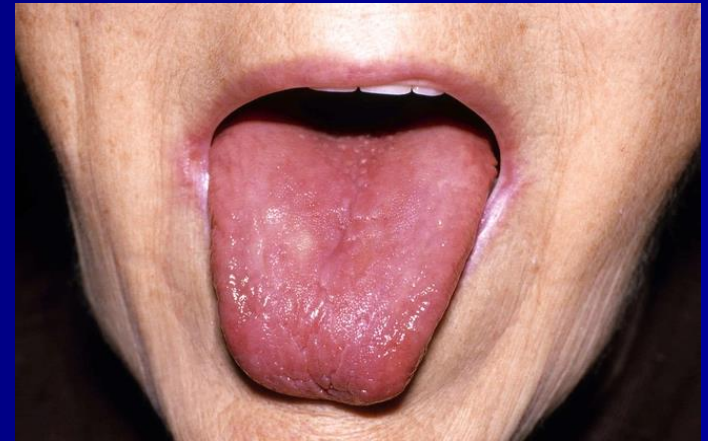
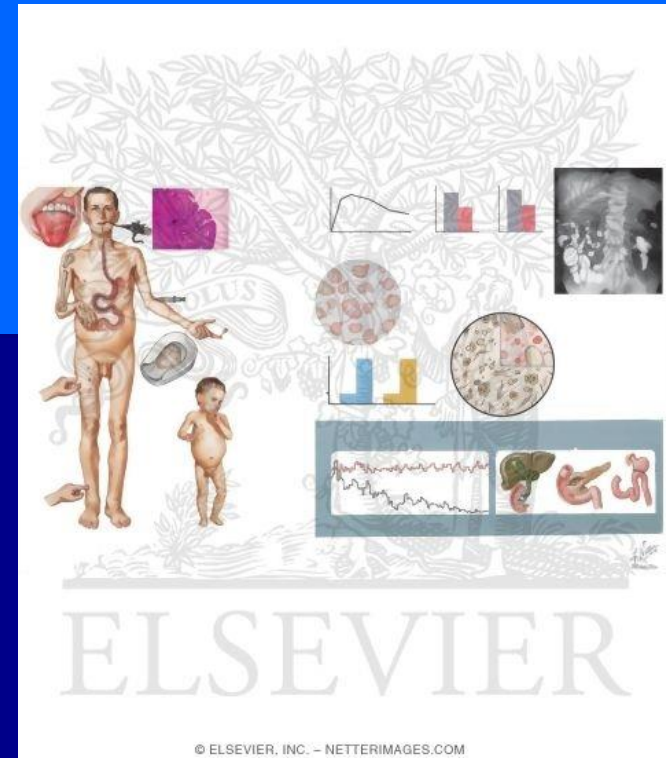
Clinical Presentation

- Diarrhea
- Steatorrhea
- Weight loss
- Bloating, distension, gas, borborygmi
- Anorexia or hyperphagia
- Nausea, vomiting
- Abdominal discomfort
- Muscle atrophy
- Edema
- Signs/symptoms of specific vitamin deficiencies

History and Exam

- Prior GI surgery
- h/o chronic pancreatitis
- h/o liver, GI disorder
- h/o CTD, diabetes
- h/o radiation therapy
- Diet and medications
- Alcohol/drugs
- h/o chronic sinus or respiratory infections
- Recent travel history
- Timing of onset
- Bowel habits/stool characteristics
- Associated GI and systemic complaints
- Evidence of malnutrition or micronutrient deficiencies on exam

Physical signs



Overview of Tests for Malabsorption

- Blood tests
 - Fecal fat determination
 - Imaging studies
 - Endoscopy with biopsy and aspirate
 - Breath tests
-
- D-xylose test, Schilling test, Secretin/CCK test

"Screening" Laboratory Tests

■ Blood tests

- CBC
- Electrolytes, Mg, Phos, Ca
- Albumin, protein
- Vitamin B12, Folate, Iron
- Liver tests
- PT/INR, cholesterol
- Carotene (?)

■ Stool tests

- Inspection
- Hemocult
- O&P
- Qualitative fat

Fecal Fat Determination

Quantitative

- “Gold standard” to diagnose maldigestion
- 72 hour collection optimal
- Normal < 7 g/day
- Limited use in clinical practice due to issues with collection/processing

Fecal Fat Determination

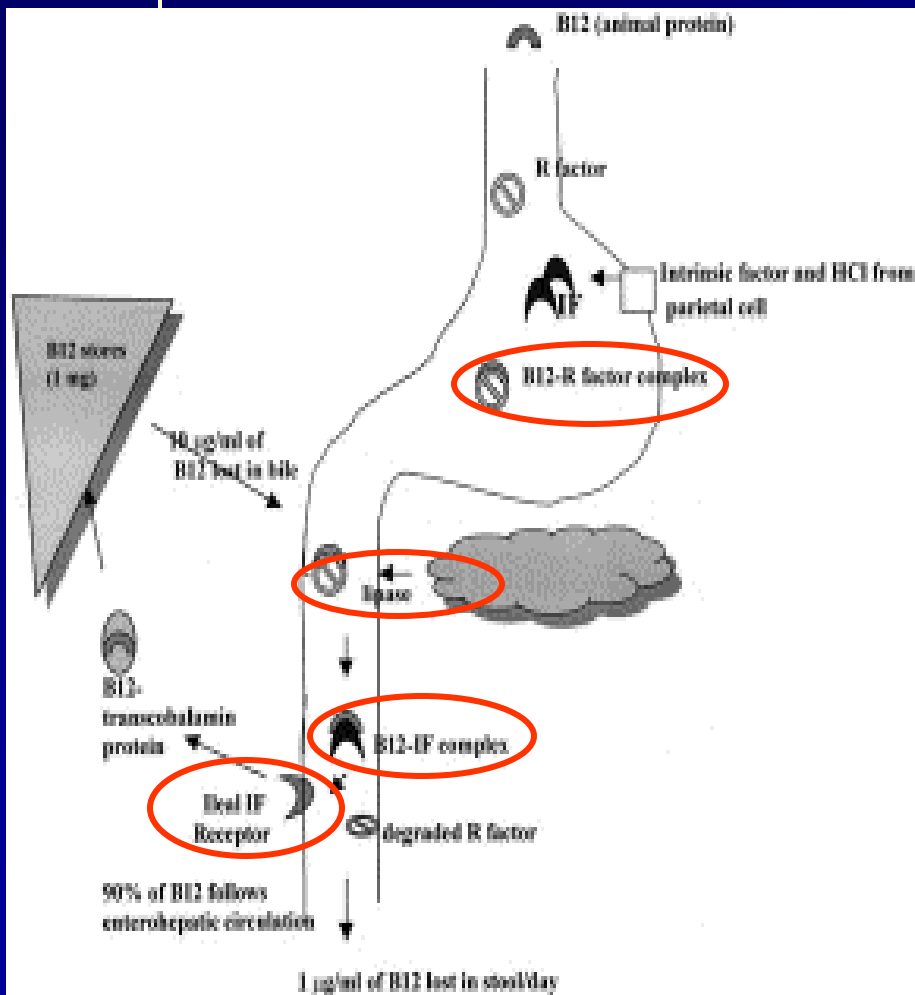
Qualitative

- Random spot sample
 - Qualitative (Sudan stain)
 - Semi-quantitative (#/size of droplets)
 - Acid steatocrit
- Fallacy
 - Helpful only if abnormal
 - Less sensitive for mild-moderate steatorrhea
 - Variable reproducibility

D-xylose Test

- Indicates malabsorption secondary to mucosal dysfunction
- Oral load with 25 g D-xylose
 - 5 hr urine collection (normal > 4 g)
 - 1 hr and 3 hr serum samples (normal > 20 mg/dl at 1 hr, > 18.5 mg/dl at 3 hr)
- Numerous factors affect results
- Role in clinical practice controversial
 - ? Use in special populations

Vitamin B12 Absorption and Schilling Test



- Determine **etiology** of B12 deficiency
- 1 mcg radiolabeled cyanocobalamin ingested and 1 mg non-labeled B12 administered IM
- 24 hr urine collection
- Recovery of < 9% abnormal
- Numerous causes of false positives/negatives

4 Stages of the Schilling Test

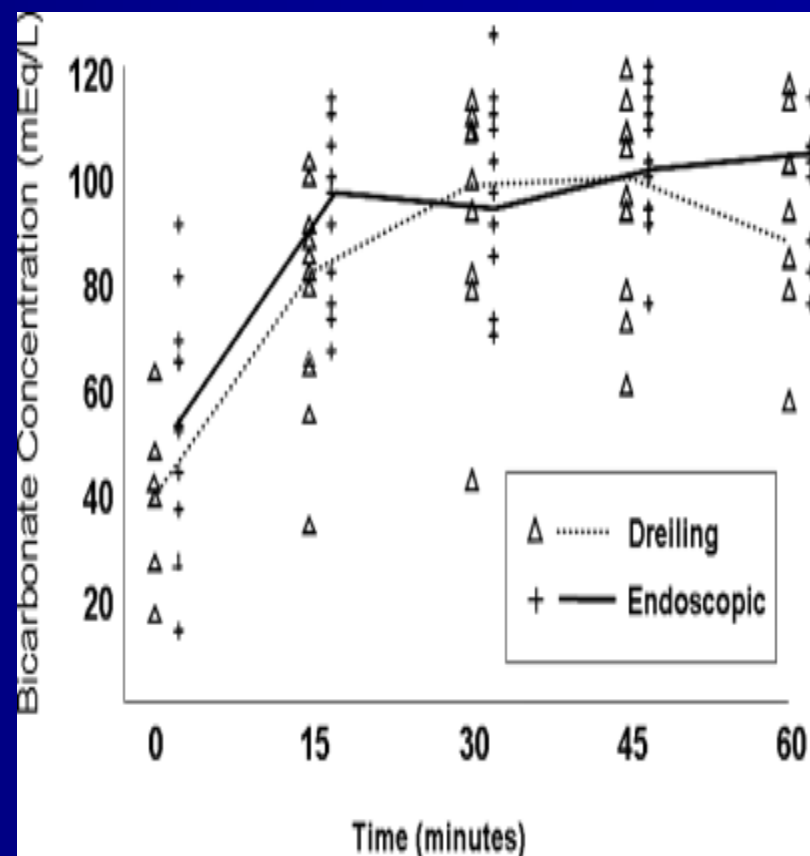
Condition	Stage 1 (B12)	Stage 2 (IF)	Stage 3 (enzymes)	Stage 4 (antibx)
B12 Malabsorption	Decreased			
Pernicious anemia	Decreased	Normal		
Chronic pancreatitis	Decreased	Decreased	Normal	
SIBO	Decreased	Decreased	Decreased	Normal
TI resection	Decreased	Decreased	Decreased	Decreased

Direct Pancreatic Function Tests

- Gold standard
- Quantitative stimulation tests using either secretin or CCK or test (Lundh) meal
- Requires Dreiling tube placed into duodenum with collection of contents for an hour
- Analyzed for bicarbonate (secretin) or amylase/lipase/trypsin (CCK)
- Low concentrations ($< 80\text{-}90 \text{ mEq/L HCO}_3^-$; $< 780 \text{ IU/L lipase}$) consistent with pancr. insuff.
- Limited by availability, invasiveness, expense

Endoscopic Pancreatic Function Tests

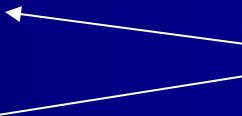
- Uses endoscope instead of Dreiling tube
 - Results not affected by sedation or analgesia
- Correlates well with conventional test (in healthy subjects)
- Number of advantages
 - More widely available, less costly/uncomfortable, no radiation exposure
- ? Practicality of 1 hr endoscopy
 - Timed specimens at 30/45 min sufficient



Stevens T et al. AJG 2006

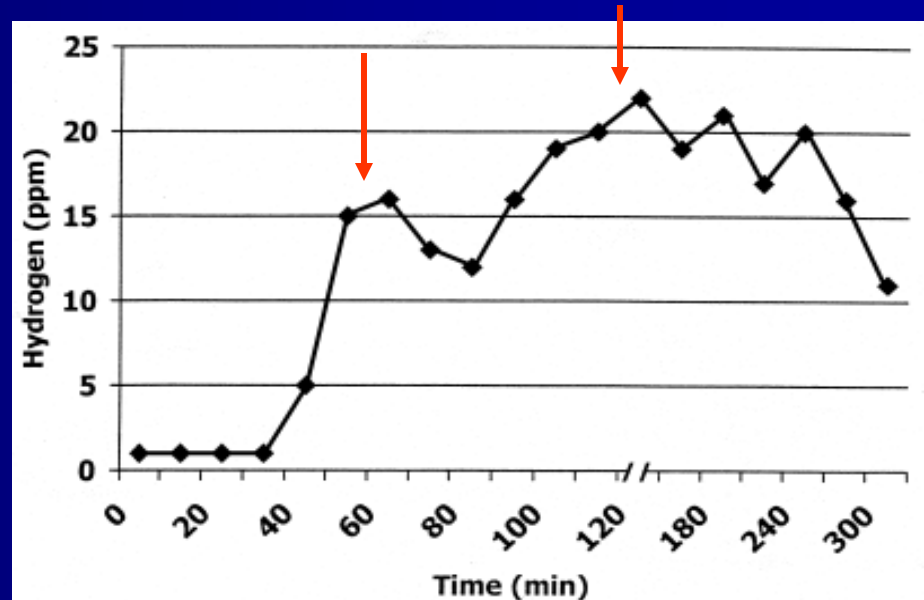
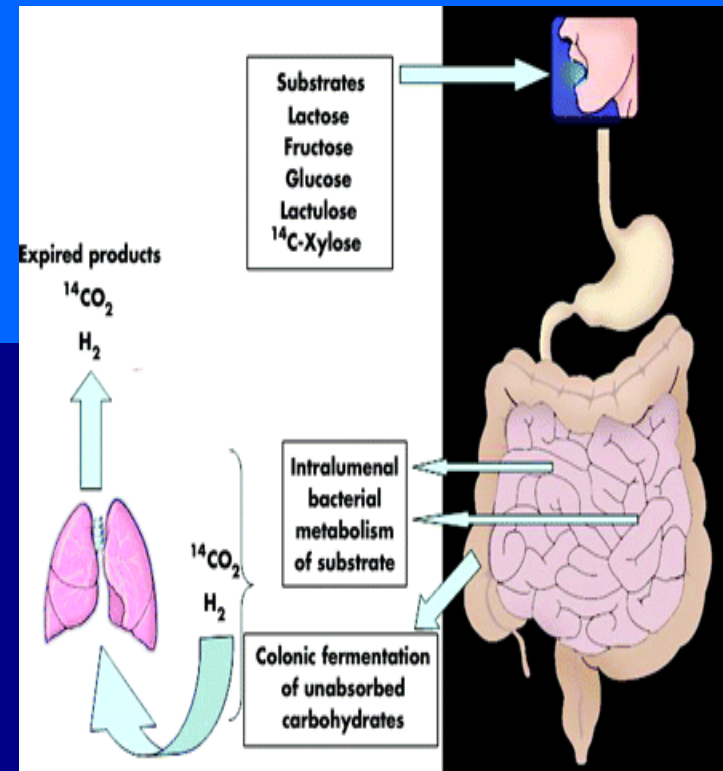
Indirect Pancreatic Function Tests

- Serum trypsinogen/trypsin
 - Fecal chymotrypsin
 - Fecal elastase-1

 - Pancreolauryl test
 - Bentiromide test
 - Trial of pancreatic enzymes
- “Tubeless tests”
- 

Breath Tests

- **Specific carbohydrate malabsorption**
 - Lactose, fructose, sucrose
 - Hydrogen
- **Small intestinal bacterial overgrowth**
 - Glucose, lactulose
 - Hydrogen
 - Xylose, glycocholate
 - ^{14}C
- **Fat malabsorption**
 - ^{14}C -triolein
 - Historical interest mainly

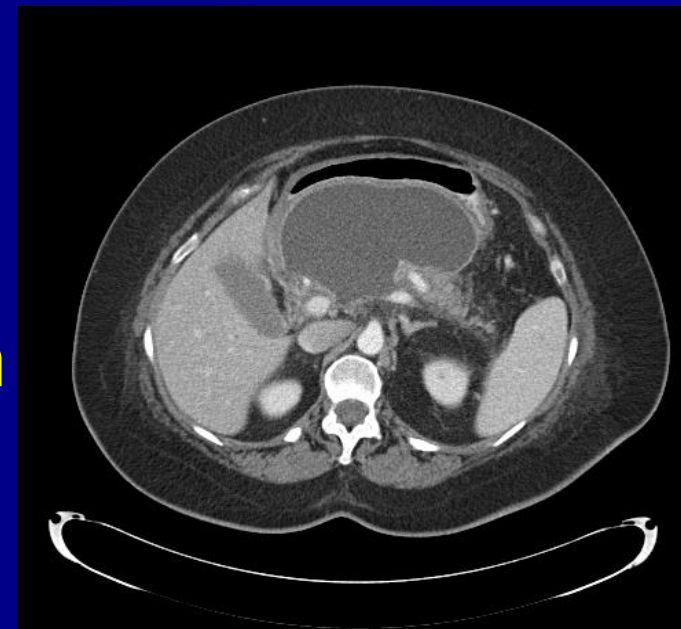
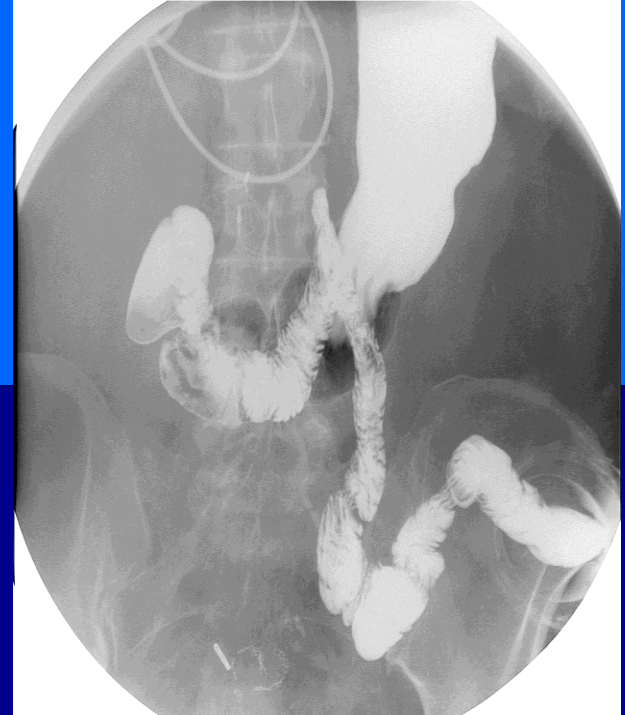


Small Bowel Culture

- “Gold Standard” test for SIBO
 - Abnormal > 10^5 cfu/ml
- Many limitations
 - Invasive
 - Expensive
 - Contamination
 - Many bacterial uncultivable
 - Difficulty culturing anaerobes

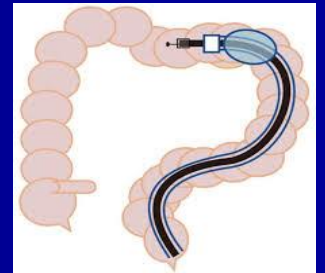
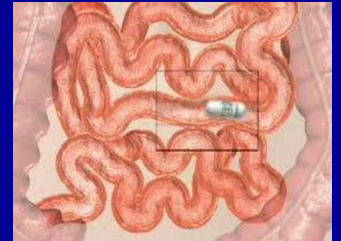
Imaging Studies

- **Barium contrast small bowel series**
 - Anatomical lesions, transit
 - Flocculation, decreased folds, segmentation, dilation
- **CT/MR enterography**
 - Detect bowel and pancreatic lesions
- **Enteroscopy, VCE, high resolution magnification endoscopy, chromoendoscopy**



Instruments for small intestinal examination

- Video Capsule Enteroscope
- Double Balloon Enteroscope
- Single Balloon Enteroscope



Imaging Studies

■ ERCP

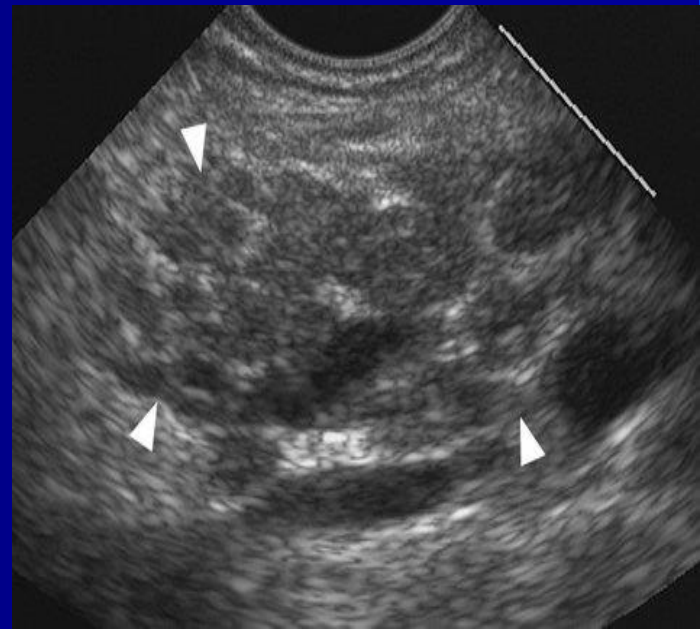
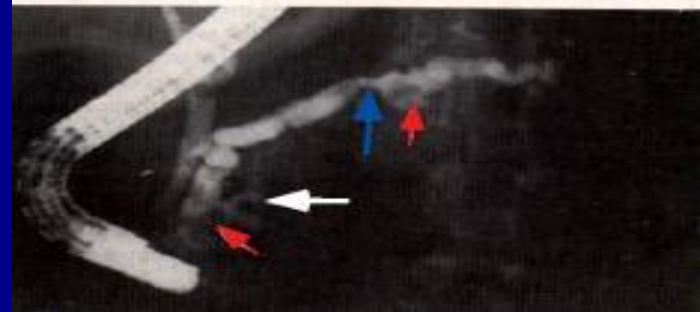
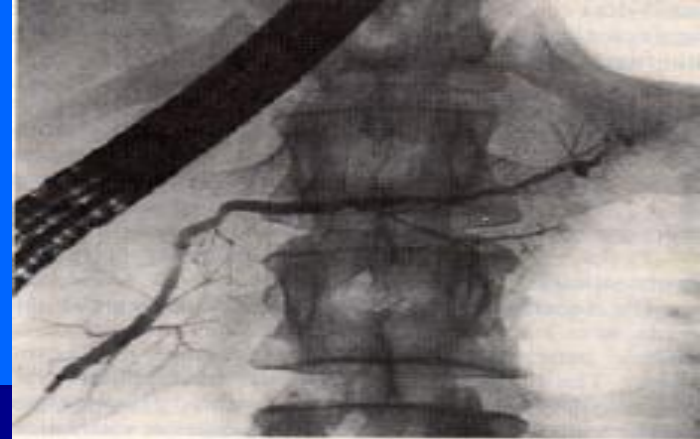
- Detect ductal abnormalities
- Other diagnostic/therapeutic applications

■ MRCP

- Detect ductal and parenchymal abnormalities

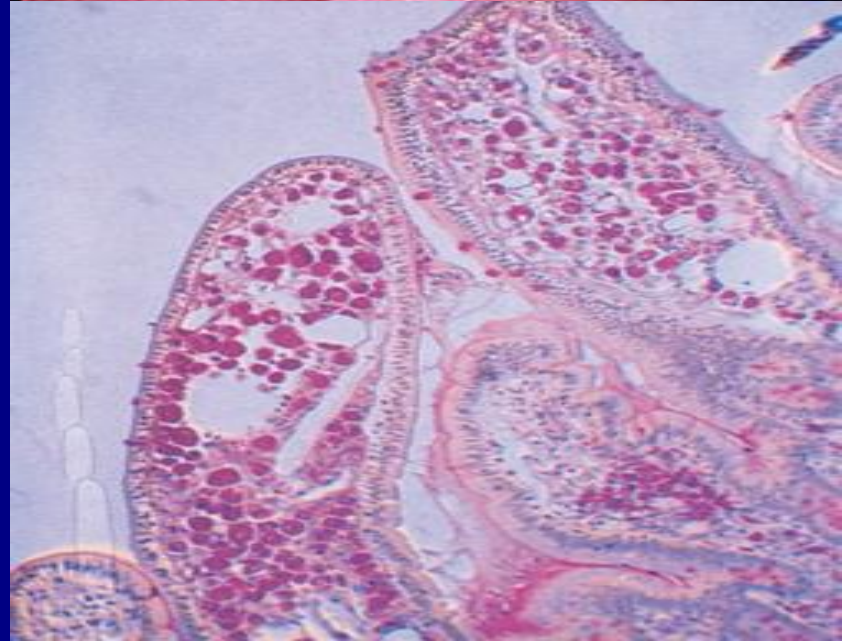
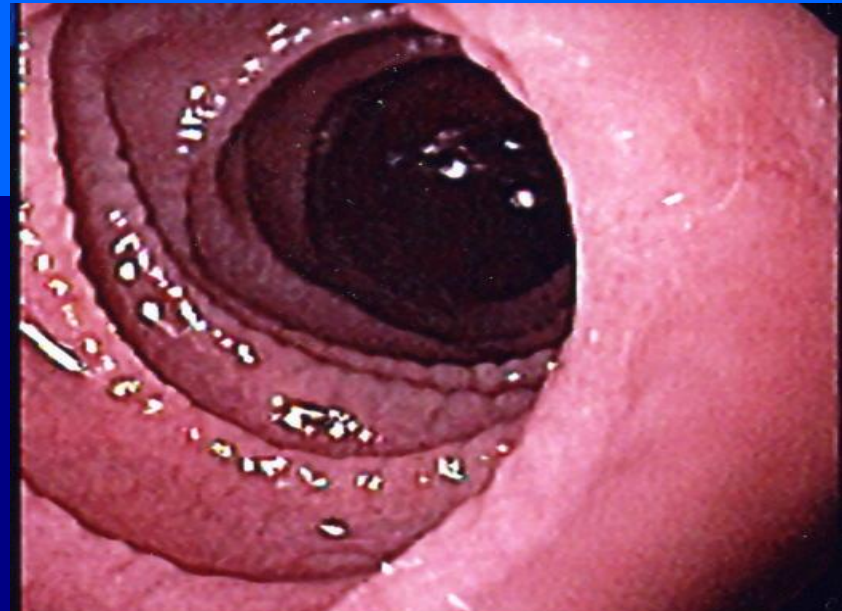
■ EUS

- Detect ductal and parenchymal abnormalities
- Allows tissue sampling
- Interobserver variability problematic



Endoscopy and Small Bowel Biopsy

- Visual assessment
 - Decreased folds, scalloping, mosaic pattern, “frosted” appearance, inflammatory changes
- Histologic assessment
 - Diagnostic
 - Supportive of diagnosis
 - Normal



Tests of Fat Malabsorption

- Fecal fat collection
- Spot fecal fat
- ^{14}C -triolein, ^{13}C -triglyceride breath tests
- Near infrared reflectance analysis (NIRA)
 - Can measure fecal fat, nitrogen and CHO
 - As accurate but less time consuming than 72 hr fecal fat collection
 - Not widely available

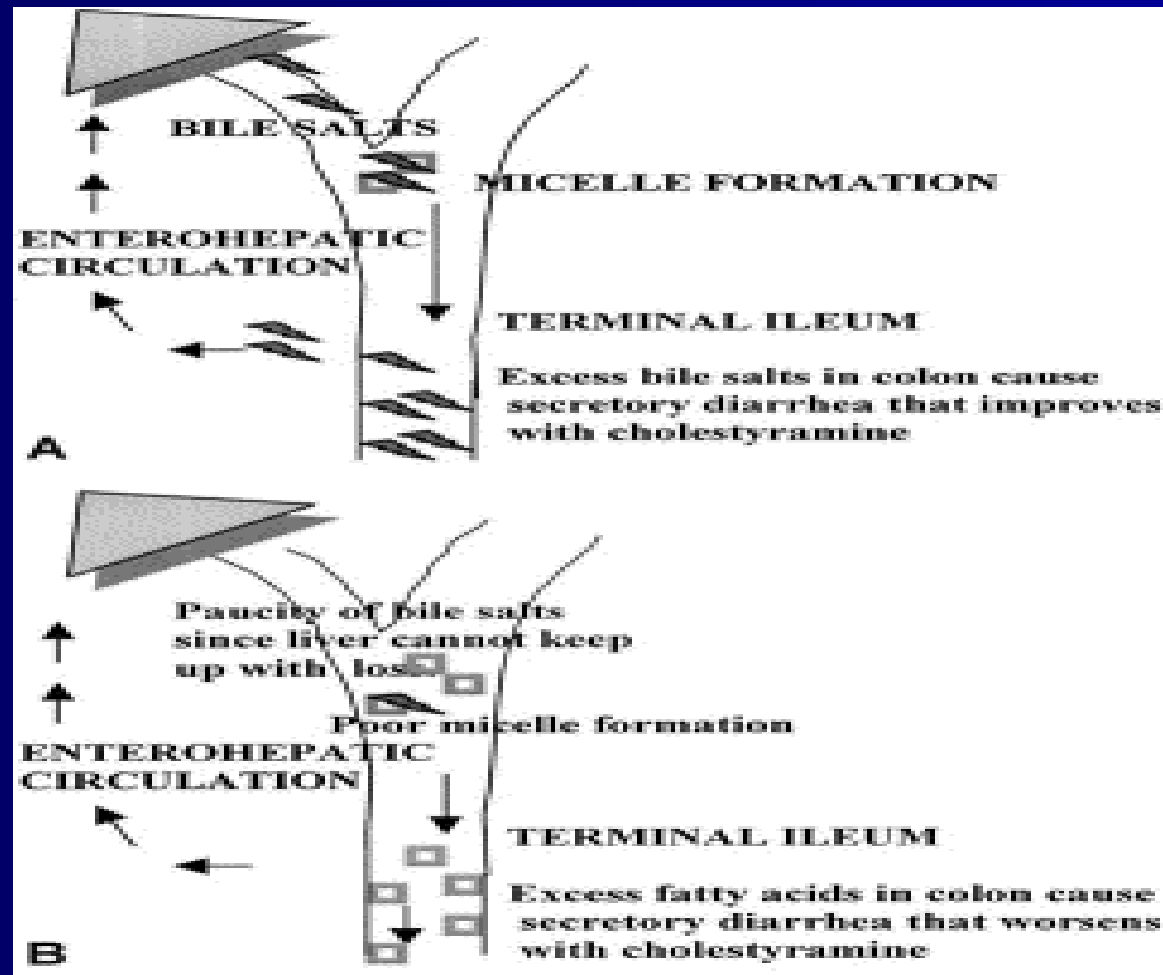
Tests of Carbohydrate Malabsorption

- Oral breath tests
- Quantitative analysis of fecal CHO
- Stool pH
- Oral tolerance tests
- Direct assay of mono- and disaccharidases

Tests of Protein Malabsorption

- Nutrient balance studies with fecal nitrogen measurement
- Radioisotopic methods
 - ^{51}Cr -labeled albumin
 - $^{99\text{m}}\text{Tc}$ -labeled transferrin
 - ^{125}I -labeled albumin
- Indirect methods
 - Fecal α -1 antitrypsin clearance ($> 25 \text{ mg/d}$)

Terminal Ileal Resection and Malabsorption



< 100 cm

Bile Acid

> 100 cm

Fat

Three Major Malabsorptive Areas

- Small bowel mucosal disease
- Small bowel bacterial overgrowth
- Pancreatic insufficiency

Management of Malabsorption syndrome

- **Dietary Modifications:** Gluten-free diet in coeliac disease, Lactose avoidance in lactose intolerance
- **Replacement:** of Nutrients, electrolytes and fluid may be necessary.
- **Pancreatic enzymes:** are supplemented orally in pancreatic insufficiency
- **Antibiotic Therapy:** Tropical sprue, Small Bowel Bacterial Overgrowth.
- **Specific therapy:** Giardiasis, Anti TB Drugs, Crohn's disease.

Take Home Points

Approach to Suspected Malabsorption

- History
 - Physical exam
 - Routine “screening” labs
 - Stool analysis
- ↓
- Selective tests based on above findings
- ↓
- H₂ breath tests, Celiac Abs, Abd imaging, EGD w/bx, Colon w/bx, PFT, ERCP/MRCP/EUS, Angio, Fecal α 1-AT, Fat pad aspirate*
- Treat based on underlying disease or type of malabsorption

Conclusion

- Clinical presentations of malabsorption syndrome are diverse and variable in severity.
- Investigations are to be performed both to confirm the presence of malabsorption and to determine the underlying cause.
- Ultimately, which direct the management of the cases.

Thank you

