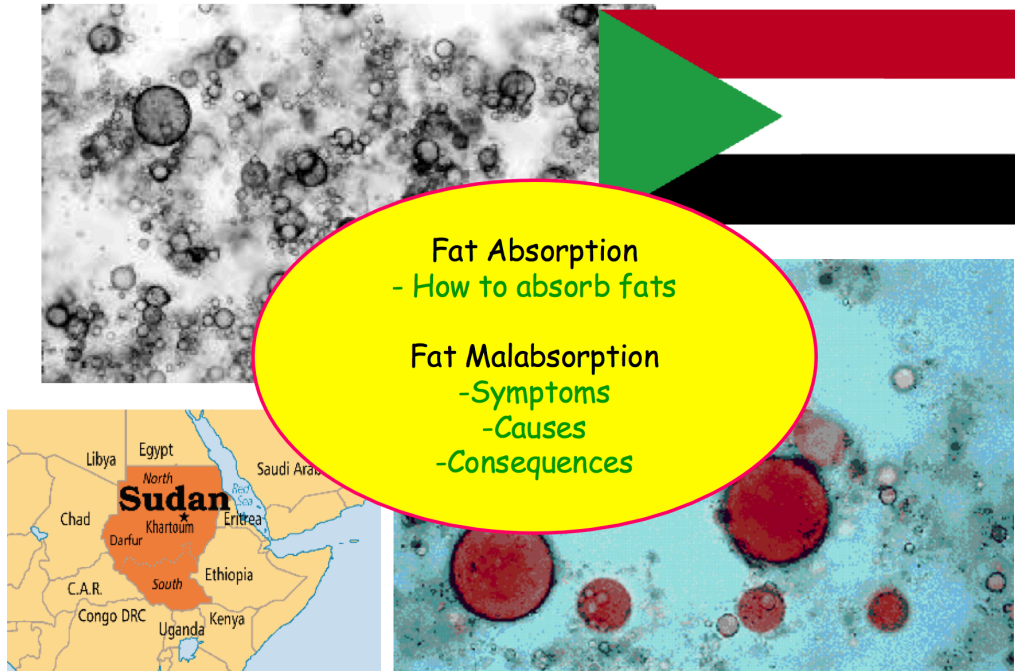
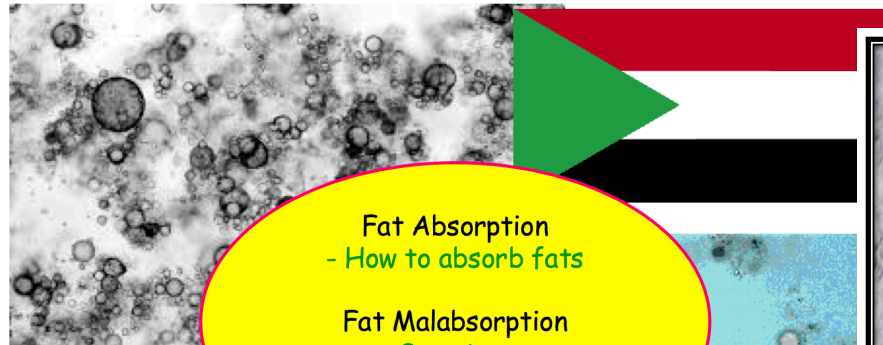


Podcast (Video Recorded Lecture Series):
Malabsorptive Diarrhea for the USMLE Step One Exam



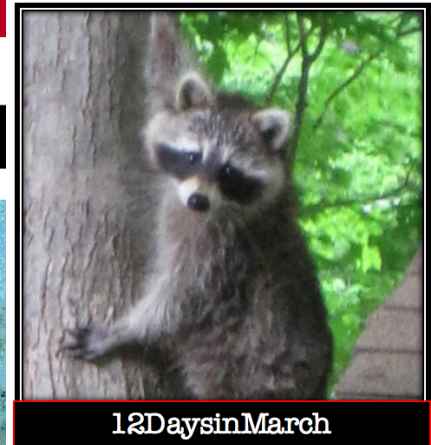
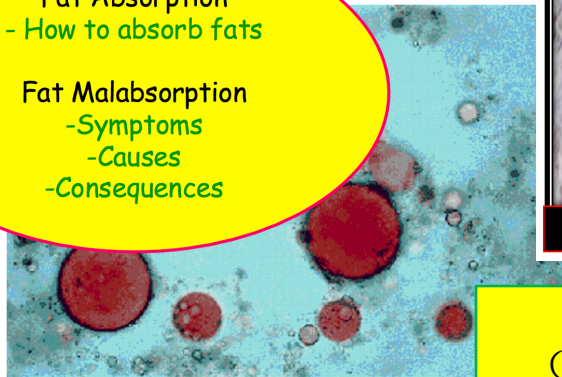
Howard J. Sachs, MD
www.12DaysinMarch.com
Email: Howard@12daysinmarch.com

Podcast (Video Recorded Lecture Series):
Malabsorptive Diarrhea for the USMLE Step One Exam



Fat Absorption
- How to absorb fats

Fat Malabsorption
- Symptoms
- Causes
- Consequences



12DaysinMarch

Tutorial Services
(check website for details)

Howard J. Sachs, MD
www.12DaysinMarch.com
Email: Howard@12daysinmarch.com

GI Conditions for the Boards

Patients don't present with:

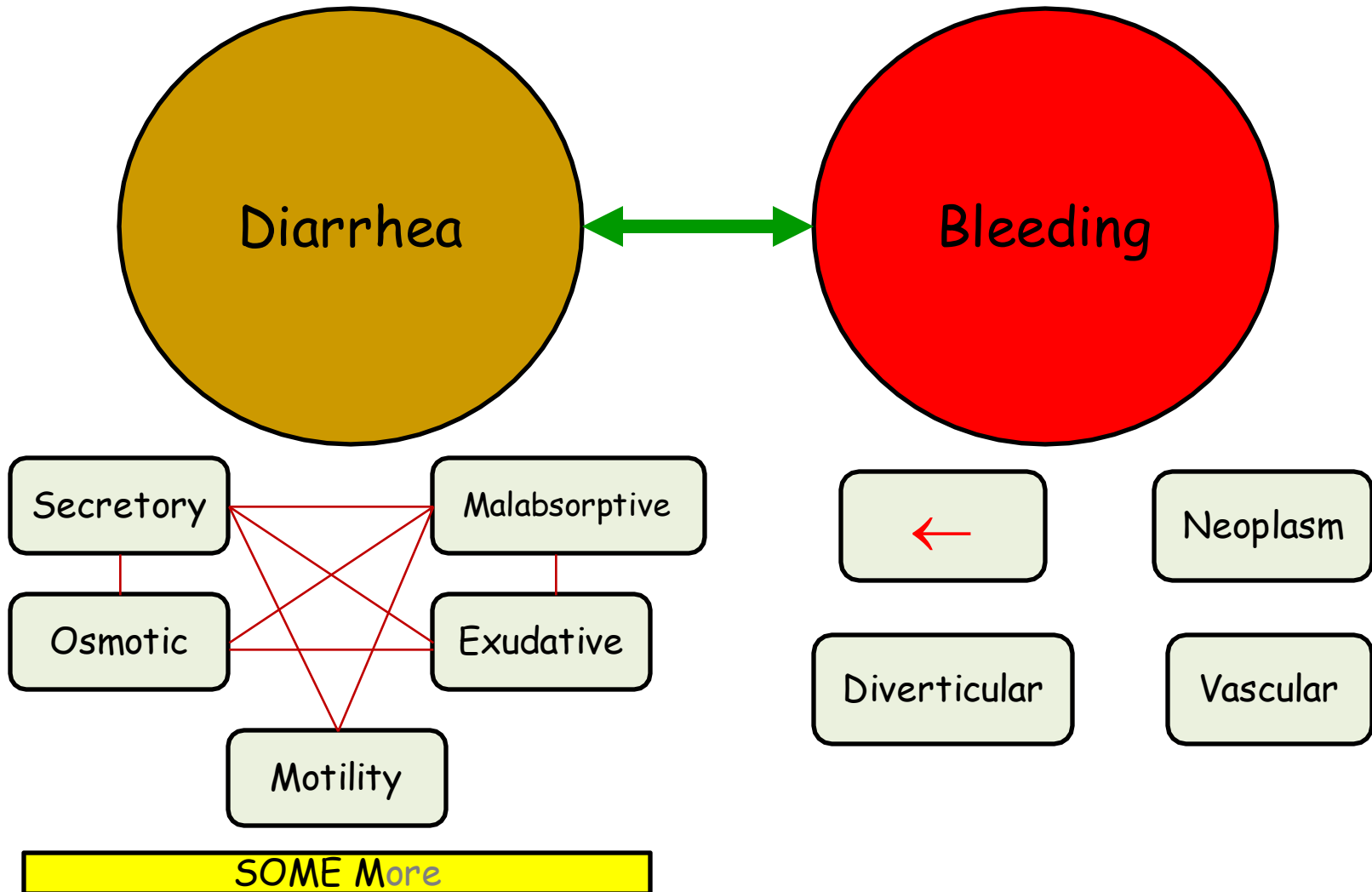
Sprue, Whipple's Giardia

Gastrinoma, VIPoma, Carcinoid

Crohn's, UC

Neoplasm, Angiodysplasia, Diverticulosis

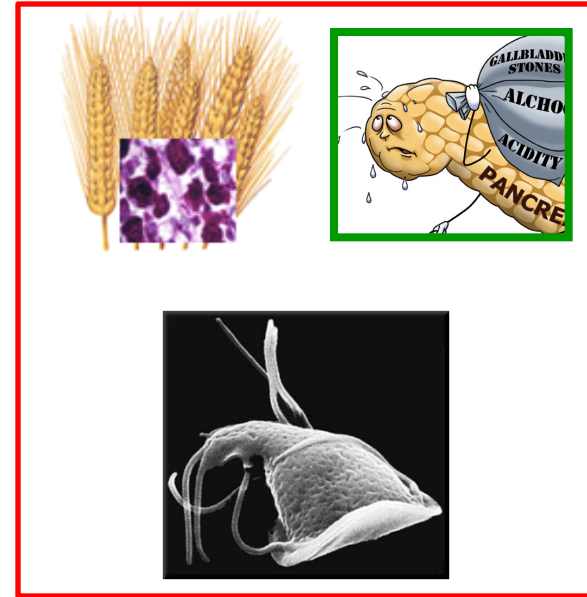
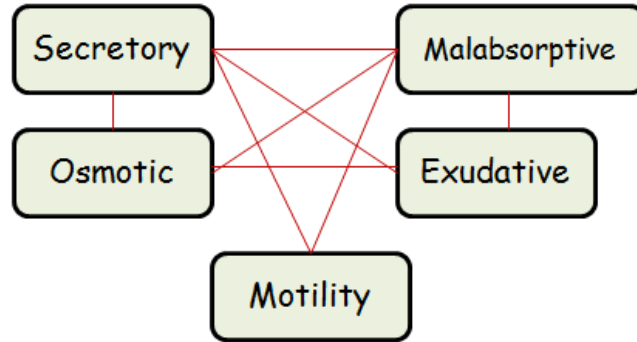
Travels Through The Small & Large Bowel (hopefully not too fast)



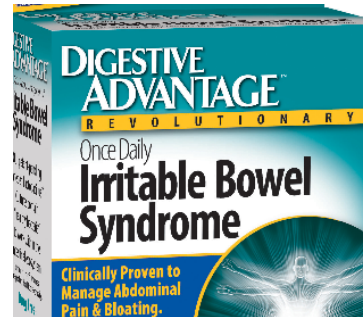
Diarrhea

Infectious
Endocrine

Lactose



'Colitis'
(all causes)





Presentation of the Conditions and the
Metabolic Consequences (Derivatives)



Vitamin Deficiencies
Fat Malabsorption



Presentation of the Conditions and the
Metabolic Consequences (Derivatives)



Vitamin A (vision/skin/cornea/ductal epi)
Almost exclusively in liver disease questions
(PBC - failure of bile salts)

Vitamin E
Steatorrhea w/ hemolysis
and/or neuropathy

Vitamin D (bone)
Kidney failure
Pancreatic failure

Vitamin K (bruising)
Liver failure
Warfarin

Patient with **poorly controlled** Crohn's and has bruising.
What's up with that?



Presentation of the Conditions and the **Metabolic Consequences** (Derivatives)



Vitamin A (vision/skin/cornea/ductal epi)
Almost exclusively in liver disease questions
(PBC - failure of bile salts)

Vitamin E
Steatorrhea w/ hemolysis
and/or neuropathy

Vitamin D (bone)
Kidney failure
Pancreatic failure

Vitamin K (bruising)
Liver failure
Warfarin

Patient with **poorly controlled** Crohn's and has bruising.
What's up with that?

- Platelet number: should be normal
- Platelet dysfunction: from NSAIDs for sacroiliitis?
- Trick question: it's erythema nodosum?
- Coagulopathy: Enterohepatic failure of **Bile Salts** → **Vit K deficiency?**



Presentation of the Conditions and the **Metabolic Consequences** (Derivatives)



Vitamin Deficiencies

Fat Malabsorption

A (how abundant are the stores and where are they?)

D (bone changes: check 25-OH Vit D)

K (coagulopathy: PT)

E (rarely seen in clinical setting?)

Water Soluble Vitamins/Minerals

B-12 (anemia, neuro s/s, CBC, MCV, level/including methylmalonic acid)

Folate (anemia: CBC, ↑ MCV)

Iron (anemia: CBC, ↓ MCV)

Nutritional Indices

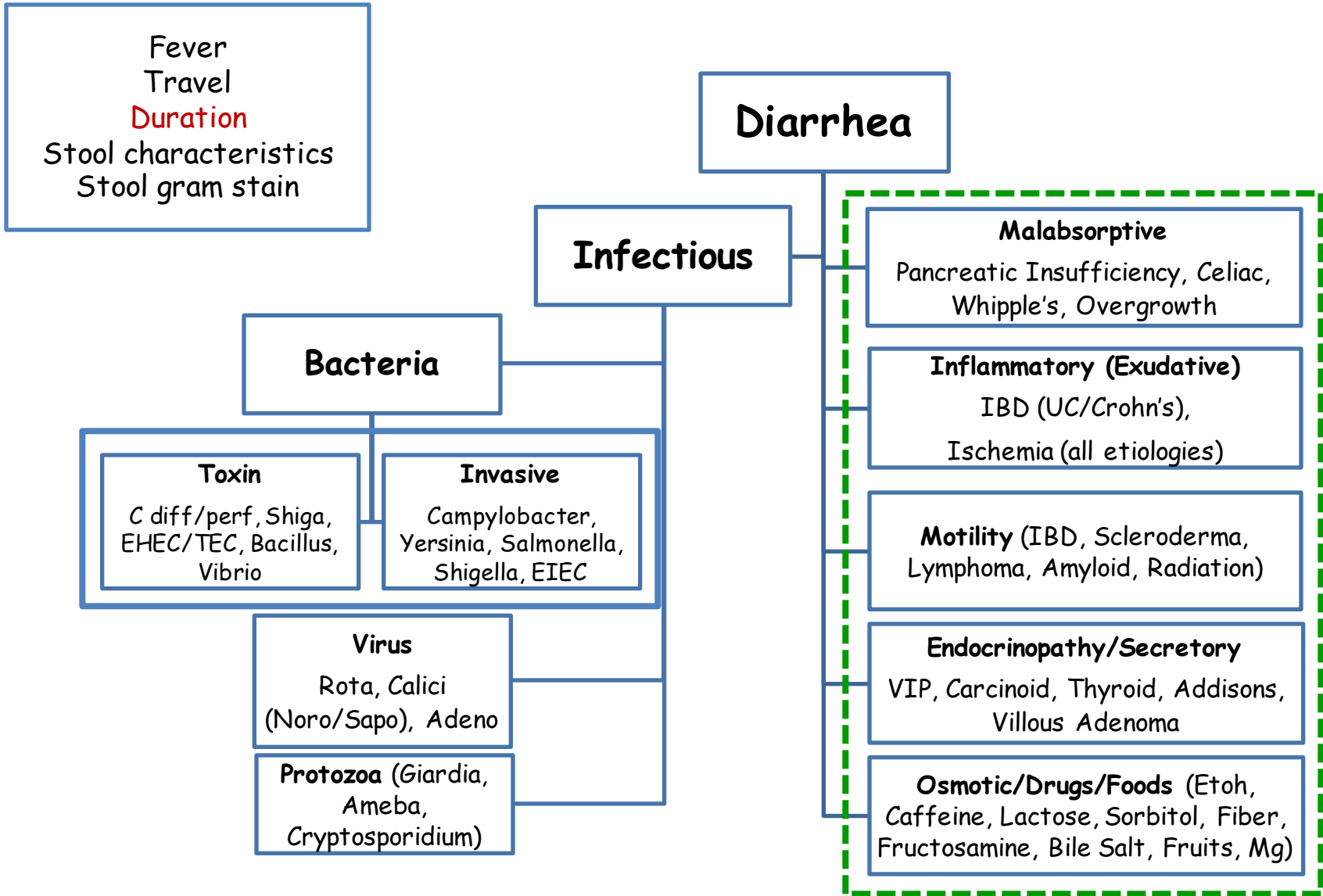
Total Protein

Albumin (edema)

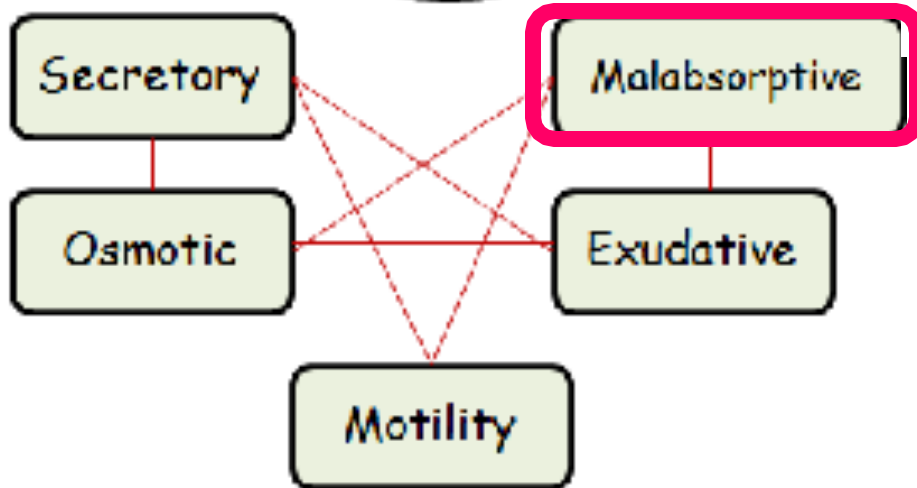
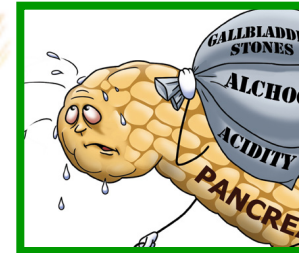
Anemia: SOB, fatigue, LH

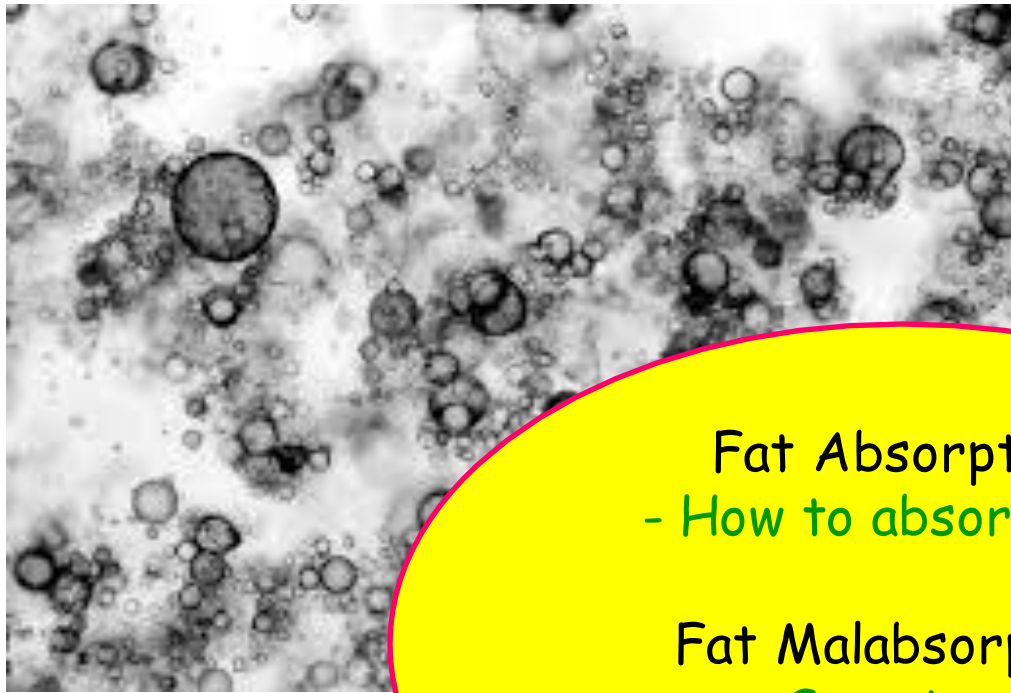


Oscar



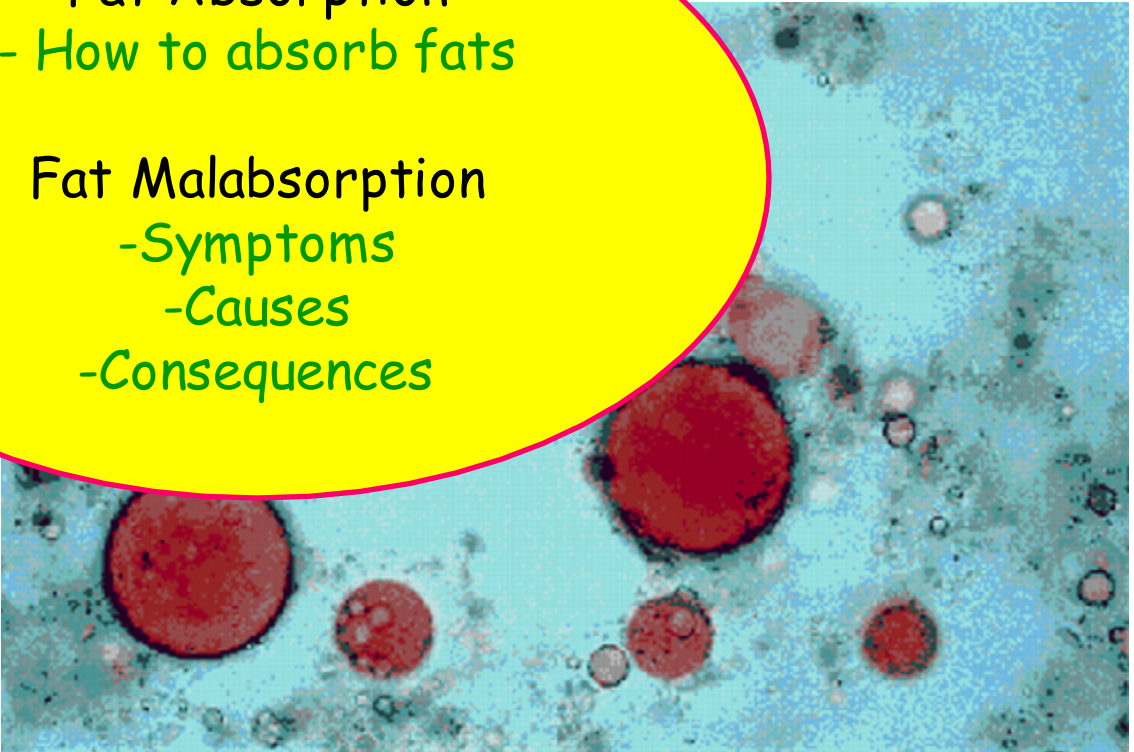
Misc: HIV associated infections, portal HTN, Food allergy, Rare disorders (Behcet's)





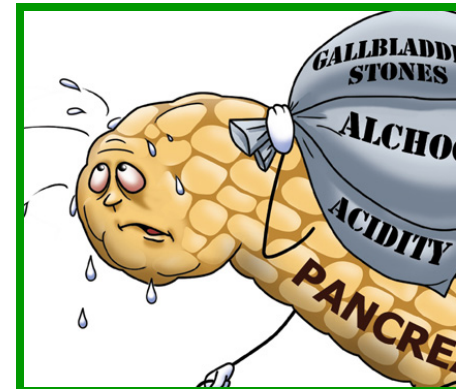
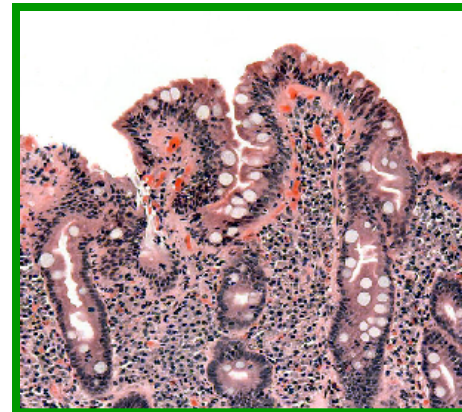
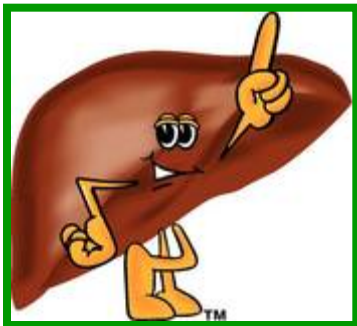
Fat Absorption
- How to absorb fats

Fat Malabsorption
- Symptoms
- Causes
- Consequences





Sine qua non of Fat Malabsorption?
Foul Smelling, Greasy, Floats

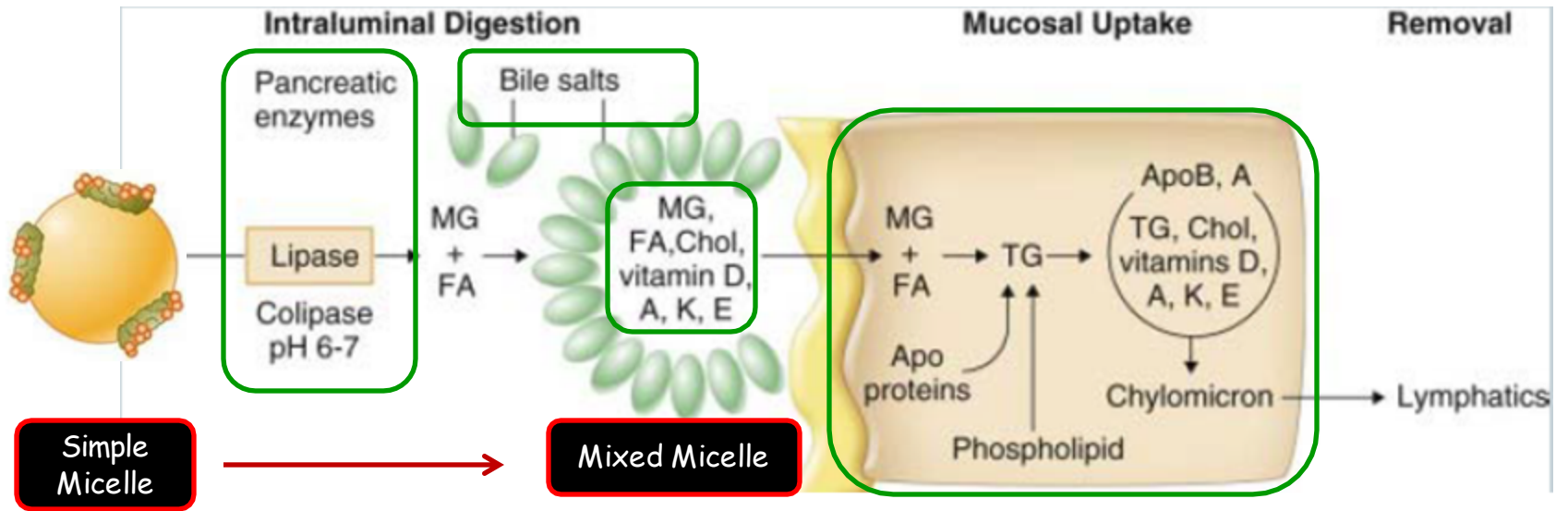


Deficiencies (language): Vit A, Vit D, Vit K

Bile

Lipase

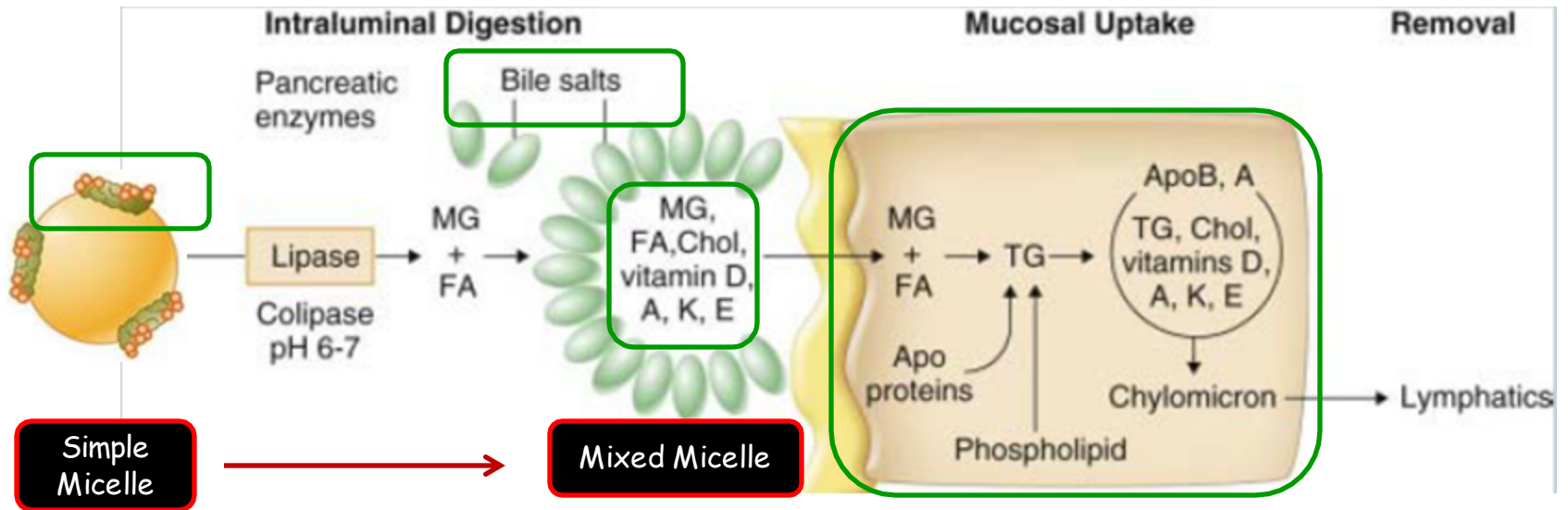
Enterocyte



Bile

Lipase

Enterocyte

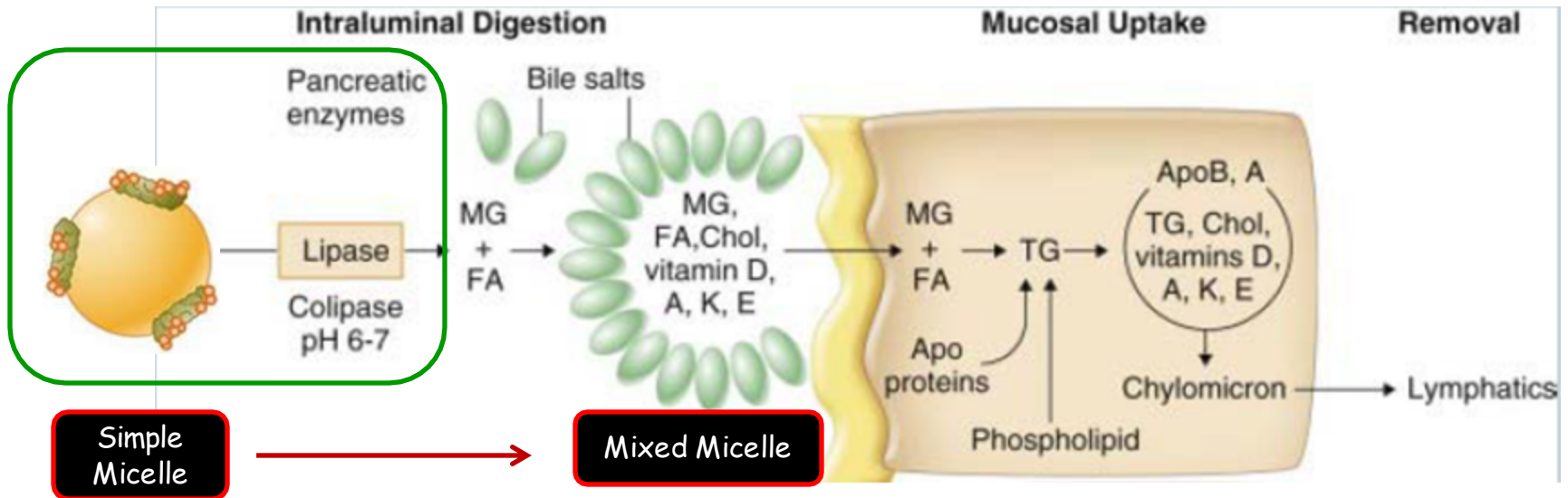


Bile Salts
Deficiency
Liver Disease (CF/PBC)
Obstruction
Failure of Enterohepatic
Circ (TI)

Bile

Lipase

Enterocyte



Simple Micelle

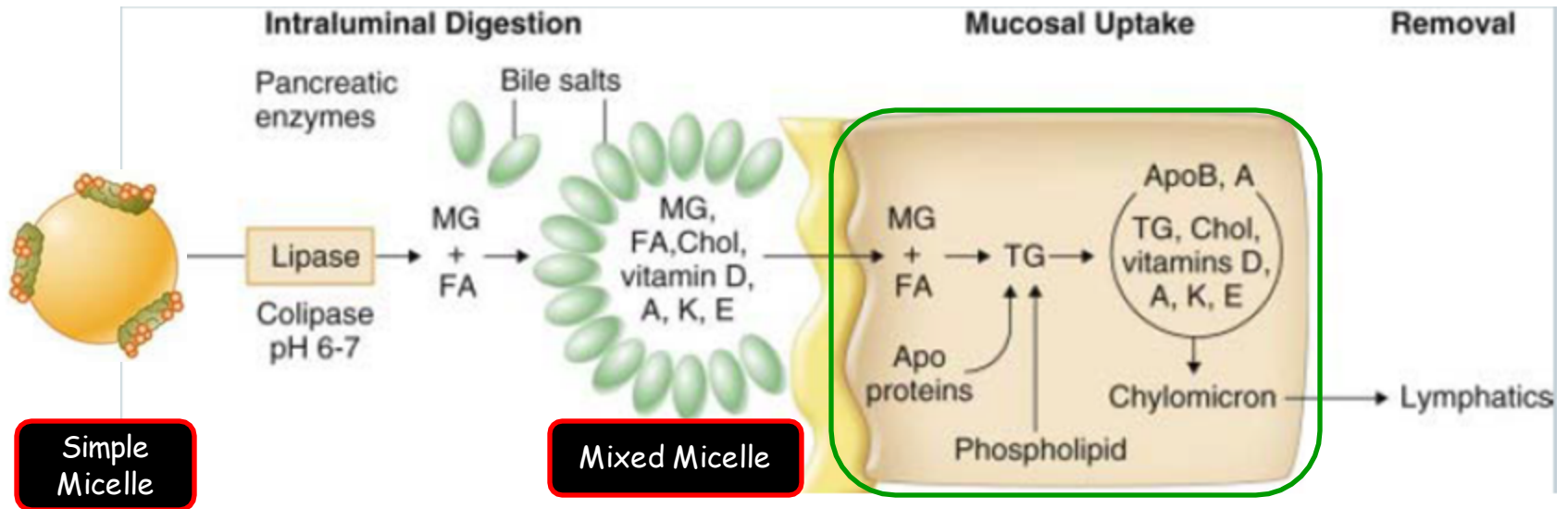
Mixed Micelle

Pancreas
Releases (co)lipase
Deficiency
Alcohol → Chr Panc
CF
(Inactivated by
Gastrinoma)

Bile

Lipase

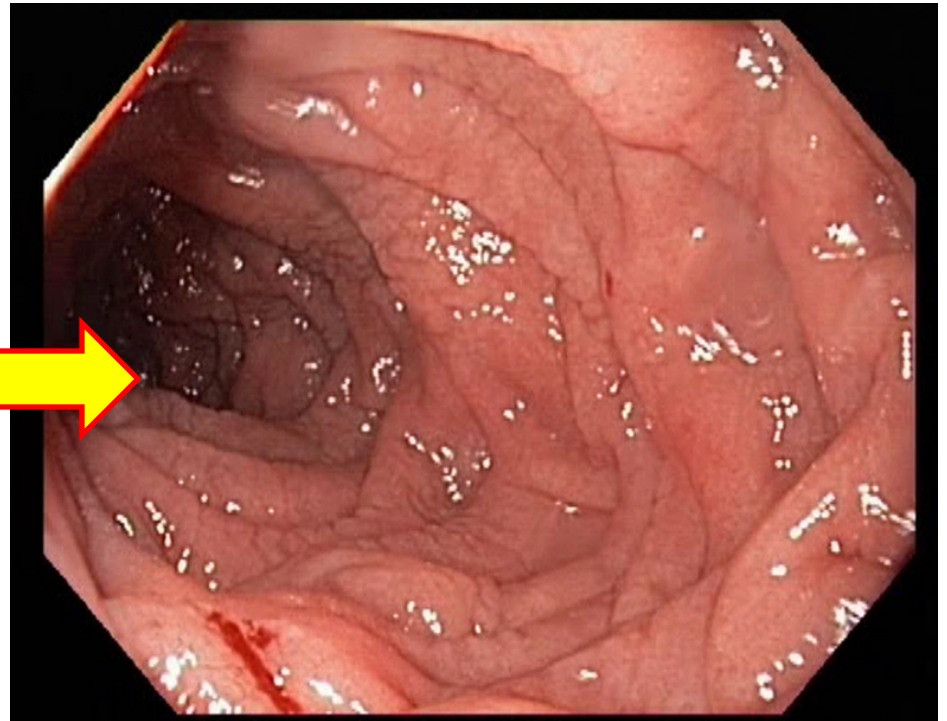
Enterocyte



Enterocyte
Deficiency
Loss of Villi
Loss of Function
Loss of Number



When you lose villi & microvilli, what is the likely consequence???



Malabsorption (enterocyte failure)

When you lose villi & microvilli, what is the likely consequence???

Normal duodenal

Duodenal mucosa

WYNTK about Celiac Disease:

- Diarrhea: characteristic?
- Stool leukocytes?
- Protein v Antigen: Gluten or Gliadin?
- Antibodies pathogenic?
- Intestine macro: location and appearance?
- Intestine micro: result?
- Malabsorption of fats, vitamins, minerals?
- Associated condition?
- Complication?



Congratulations on completing the celiac challenge!

- Diarrhea: **steatorrhea**
- Stool leukocytes: **non-inflammatory** (no WBC)
- Protein: **Gluten** v Antigen: **Gliadin**
- Antibodies pathogenic: **No (tissue transglutaminase)**
- Intestine macro: **D/J w/ blunting of villi**
- Intestine micro: **flattened villi, lymphocytic infiltrate**
- Malabsorption of fats, vitamins, minerals: **All**
- Associated condition: **Dermatitis herpetiformis**
- Complication: **NHL**

Gluten → Gliadin

↓

Deamidated/presented to APC

↓

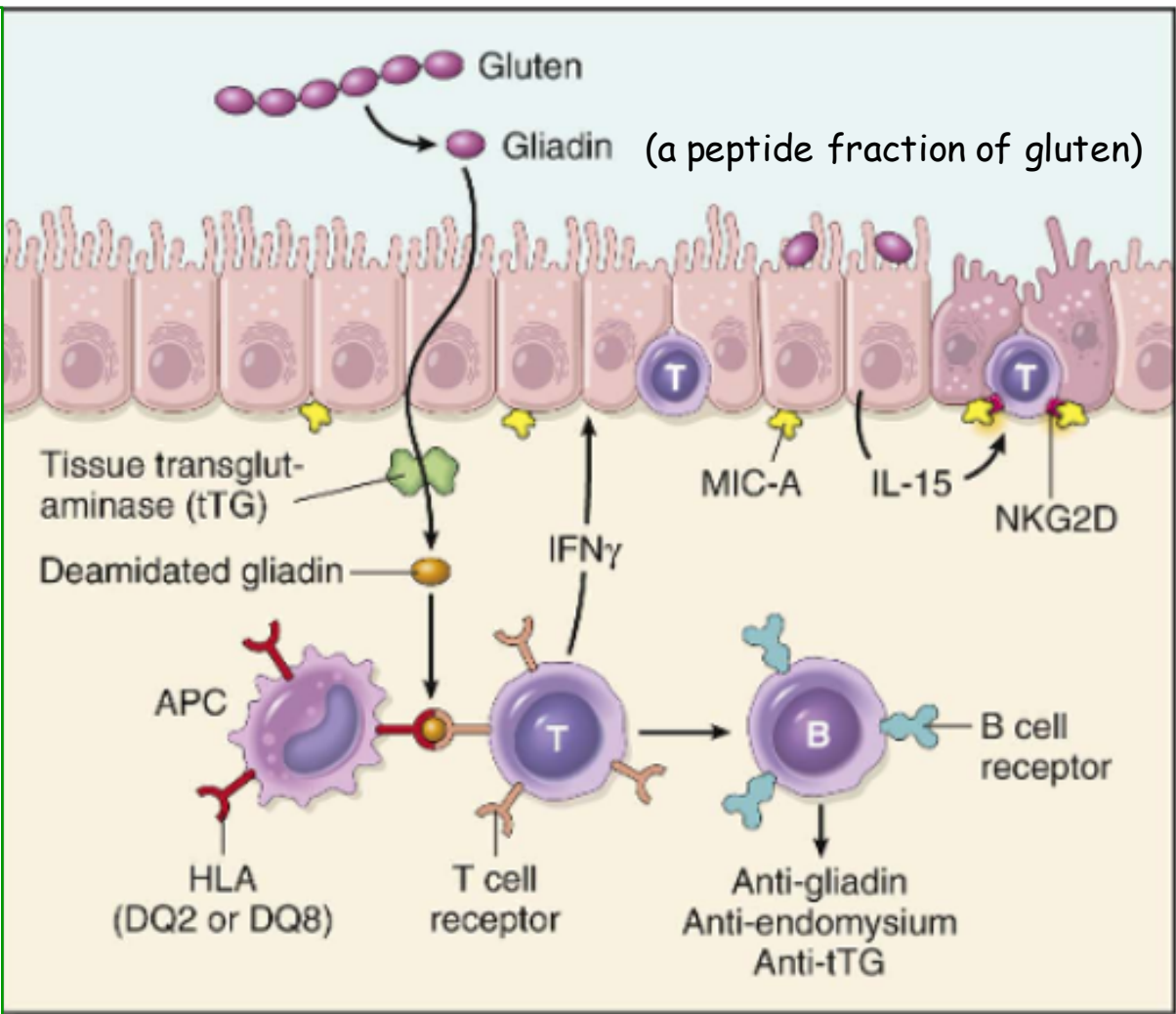
Genetic Susceptibility (DQ)

↓

T-lymphocyte

↓

B-cell (antibodies)
Cytokines (TNF, IFN)



Genetic susceptibility

Lymphocytic Infiltrate

Disease Marker (Aby)

Villous Blunting

Malabsorption

Celiac (Sprue) Disease (Gluten Enteropathy)

- Autoimmune disorder occurring in genetically susceptible persons exposed to gluten.
 - Gluten, primary storage protein of wheat.
 - Gliadin is the alcohol-soluble portion of digested gluten
- Antibodies are directed against the gliadin fraction of gluten
- Associated w/ other autoimmune disorders: **dermatitis herpetiformis**, thyroiditis, PBC, DM1, IgA deficiency

Footprints of malabsorption plus pruritic, vesicular rash...

Malabsorption

Celiac (Sprue) Disease (Gluten Enteropathy)

- Autoimmune disorder occurring in genetically susceptible persons exposed to gluten.
 - Gluten, primary storage protein of wheat.
 - Gliadin is the alcohol-soluble portion of digested gluten
- Antibodies are directed against gliadin fraction of gluten
- Associated w/ other autoimmune disorders: dermatitis herpetiformis, thyroiditis, PBC, DM1, IgA deficiency
- Pathogenesis: **Tissue transglutaminase...**
 - **Deamidates** absorbed gliadin yielding negatively charged peptides
 - These are phagocytized in lamina by Ag-presenting cells and presented (with MHC **DQ2/8**) to CD4 T-helper cells
 - CD4Th produce cytokines (γ -IFN & TNF- α) that destroy tissue **in susceptible patients**. Anti-tTG ab do not appear to be causative.

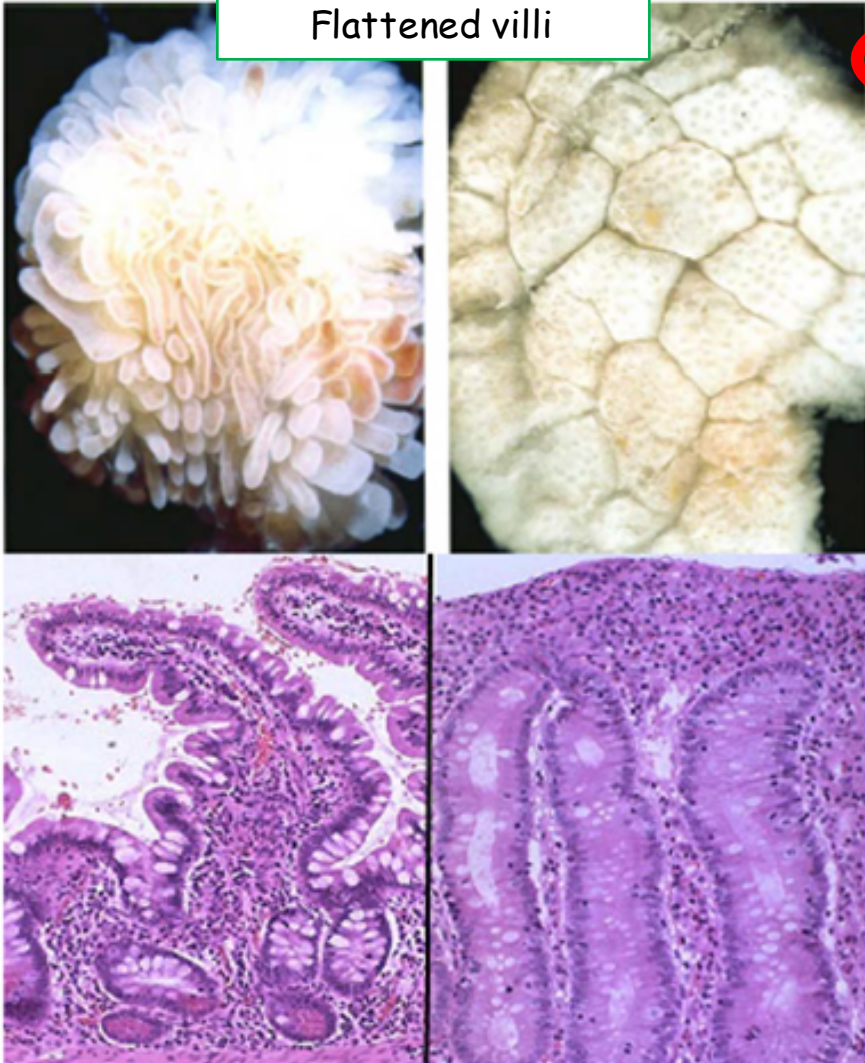
- Presentation: diarrhea, wt loss, anemia, DH, vitamin/mineral deficiencies, ↑ AST/ALT
- Diagnosis:
 - Antibodies
 - Anti-IgA tissue transglutaminase aby
 - Anti-endomysial (EMA) aby (expensive)
 - Anti-gliadin aby (insufficient sensitivity)
 - EGD/Bx (D/J):
 - Villous atrophy (flattening; blunting)
 - Intense lymphocytic infiltrate in lamina
 - Crypt hyperplasia

Vocabulary: Diarrhea PLUS Vit/Min deficiency +/- anemia, wt loss, vesicular rash = Celiac

Morphology

...a bx of the jejunum
is shown...

Flattened villi



2nd part of the duodenum or proximal jejunum

- ▶ Higher exposition to gliadin

Histologic features:

- ▶ Inflammation
 - ▶ Intraepithelial lymphocytes (CD8+ T cells)
 - ▶ Lamina propria plasma cells, mast cells, and eosinophils
- ▶ Crypt hyperplasia
 - ▶ Increased rates of epithelial turnover
 - ▶ Limited differentiation of enterocytes
 - ▶ Defects in terminal digestion and transepithelial transport

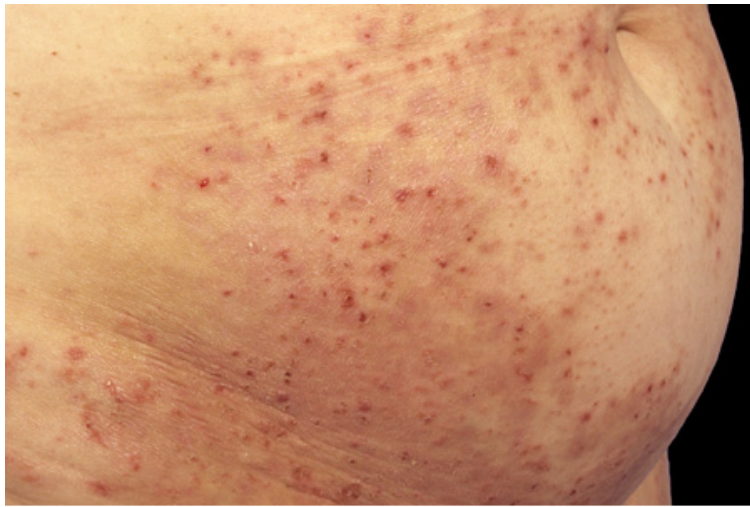
Villous atrophy - Enterocyte failure

- ▶ Accounts for the malabsorption
- ▶ Blunting and flattening of villi
- ▶ Mucin depletion of enterocytes
- ▶ Loss of mucosal and brush-border surface

Dermatitis Herpetiformis

- **Characteristic Lesions**
 - Papulovesicular eruption on trunk and extremities, especially extensor surfaces.
 - Symmetric and extremely pruritic.
- “Common” in patients with celiac disease (1:400)
- Patients with DH need to be evaluated for celiac disease as the majority are gluten sensitive
- Pathology:
 - Dermal papilla with neutrophils/fibrin and IgA deposits on unaffected subepidermal basement membrane.





Source: Wolff K, Johnson RA: *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 6th Edition*: <http://www.accessmedicine.com>
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IgA on unaffected subdermal basement membrane



Source: Wolff K, Johnson RA: *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 6th Edition*: <http://www.accessmedicine.com>
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Never see vesicles, just
excoriations!

Celiac disease in a nutshell:

- Diarrhea: steatorrhea
- Stool leukocytes: non-inflammatory
- Protein: Gluten v Antigen: Gliadin
- Antibodies pathogenic: No (tissue transglutaminase)
- Intestine macro: D/J w/ blunting of villi
- Intestine micro: flattened villi, lymphocytic infiltrate
- Malabsorption of fats, vitamins, minerals: **All**
- Associated condition: Dermatitis herpetiformis
- Complication: NHL

Malabsorption II

Whipple's disease

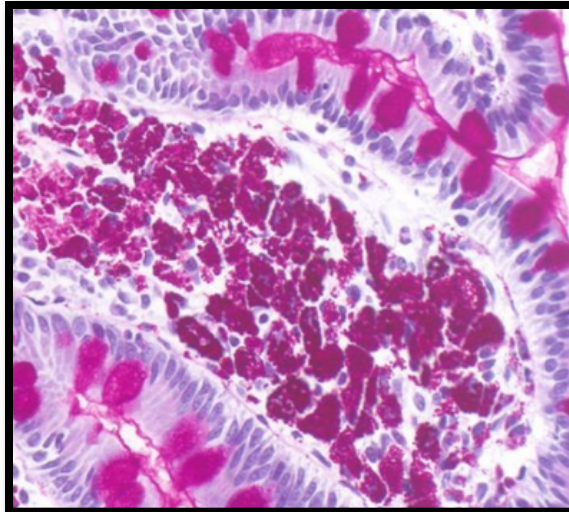
- Presentation, **multisystem**:
 - **Steatorrhea**, fever, recurrent **polyarthrititis**, **LAN**, skin pigmentation & **neuropsych symptoms** seen in older, white males.

Malabsorption II

Whipple's disease

- Presentation, **multisystem**:
 - **Steatorrhea**, fever, recurrent **polyarthritits**, **LAN**, skin pigmentation & **neuropsych symptoms** seen in older, white males.

Whipple questions will be multisystem involvement PLUS...



PAS (+) MΦ

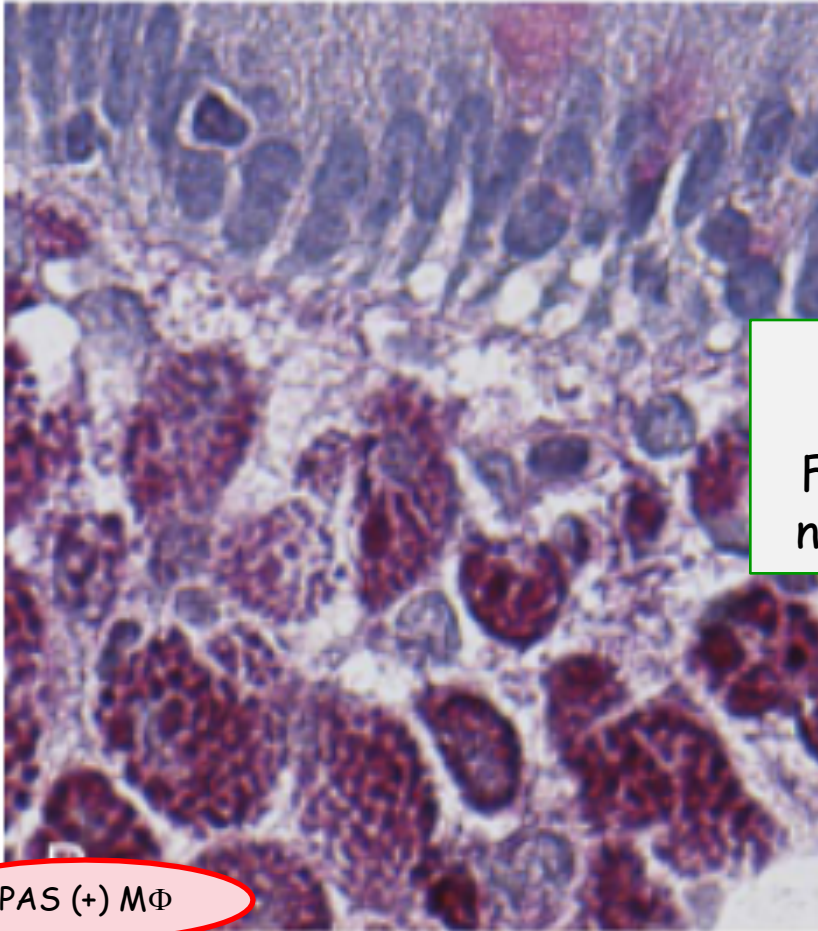
Malabsorption II

Whipple's disease

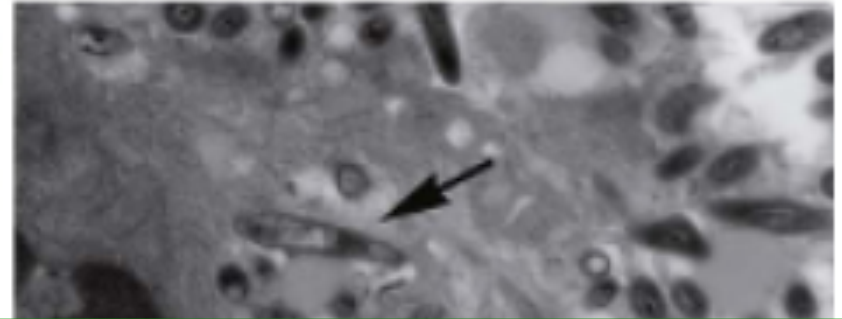
- Presentation, multisystem:
 - Steatorrhea, fever, recurrent polyarthritides, LAN, skin pigmentation & neuropsych symptoms seen in older, white males.
- Caused by infectious G (+) bacillus:
 - Tropheryma whippelii (PCR, EM)
- Pathology:
 - Villous blunting
 - Distended lamina propria with foamy, PAS-positive MΦ
 - Obstruct lymphatics leading to fat malabsorption

Organism not seen on LM.
What is seen instead?

Diarrhea from obstruction and villous blunting

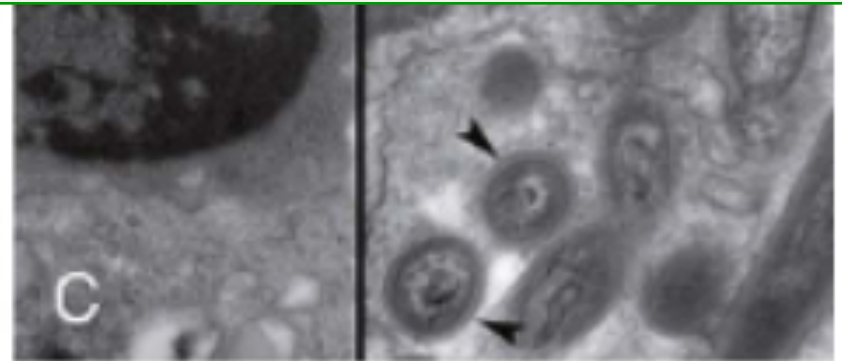


PAS (+) MΦ



Intracellular organism (i.e. MΦ)

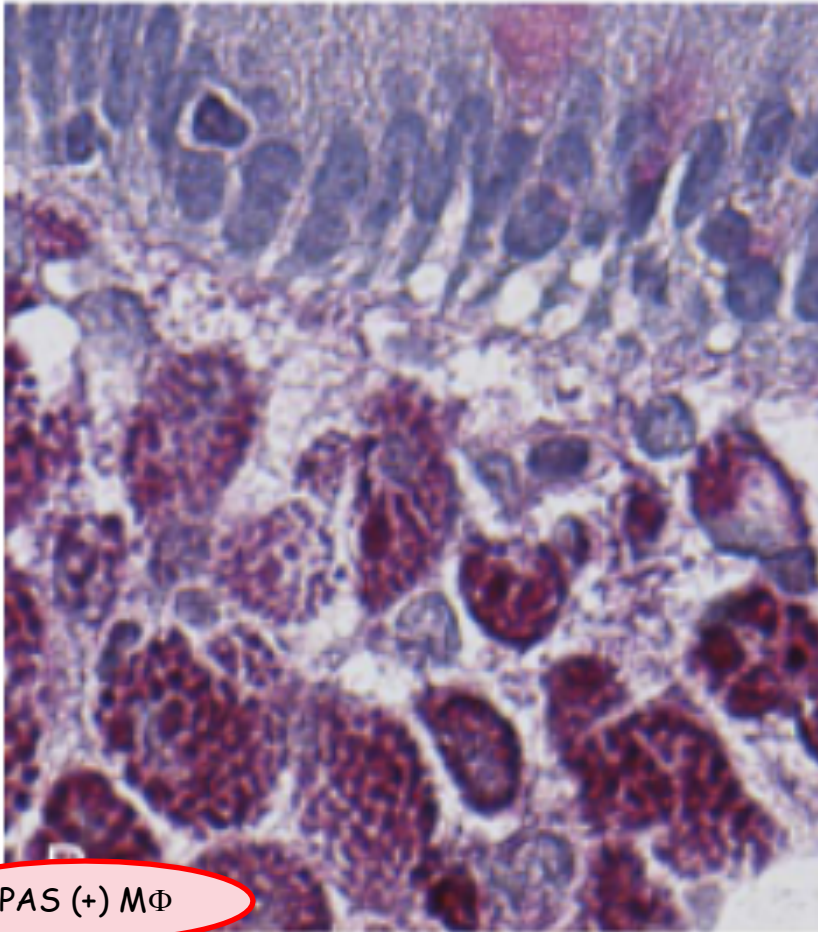
FYI: Given intracellular location, does not provoke an inflammatory response



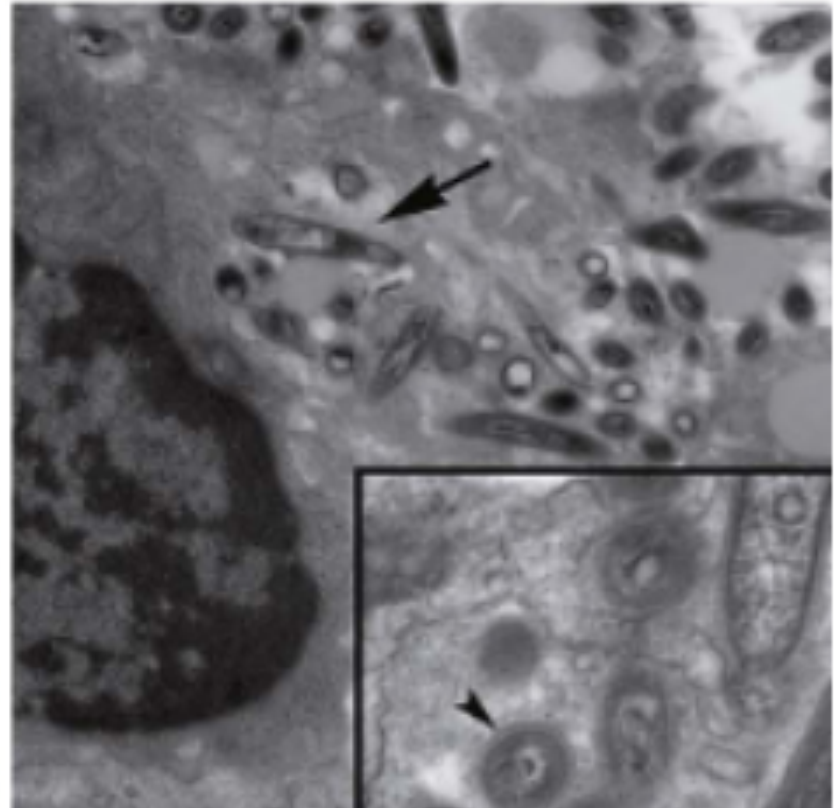
What is PAS staining???

Glycogen, Glycoproteins, Glycolipids

Diarrhea from obstruction and villous blunting



PAS (+) MΦ

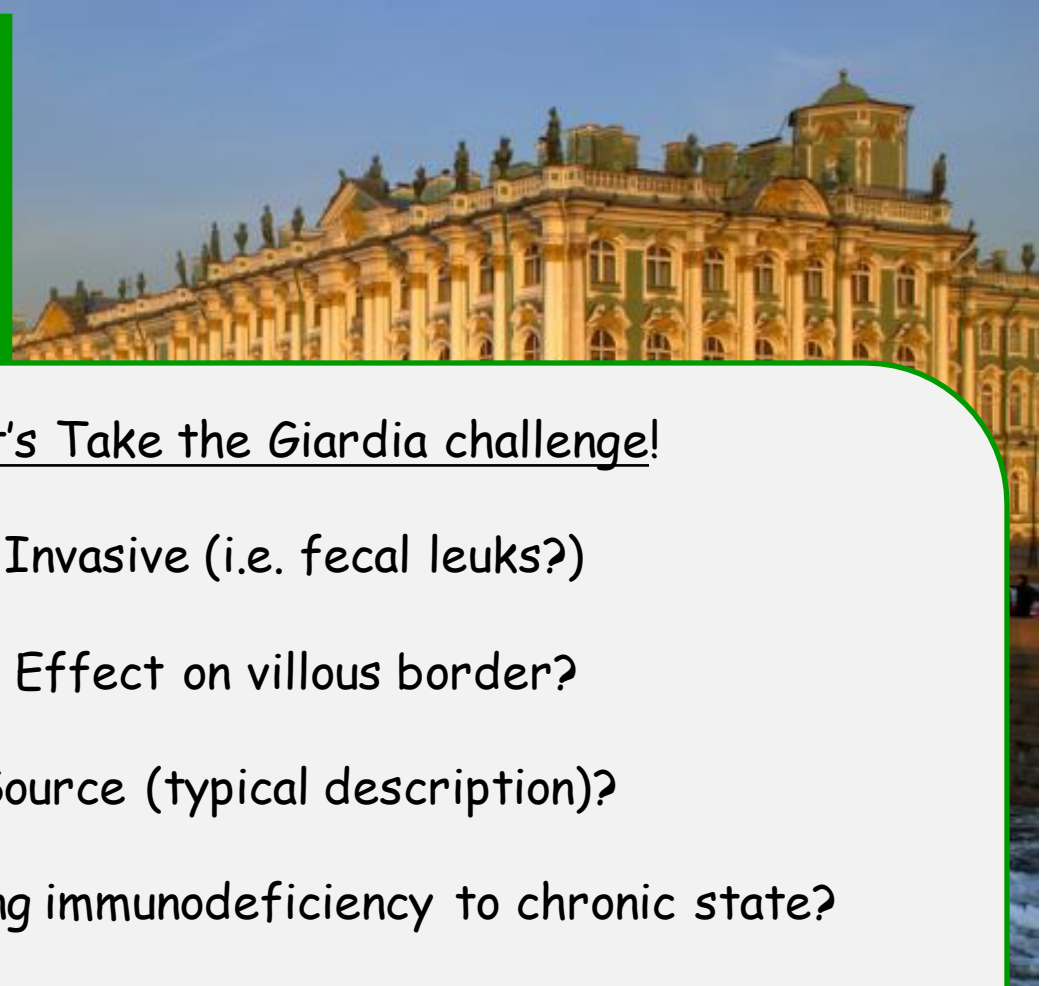


Rx: Abx (TTC, Sulfa)

St Petersburg: the Venice of the North



St Petersburg: the Venice of the North



Let's Take the Giardia challenge!

Invasive (i.e. fecal leuk?)

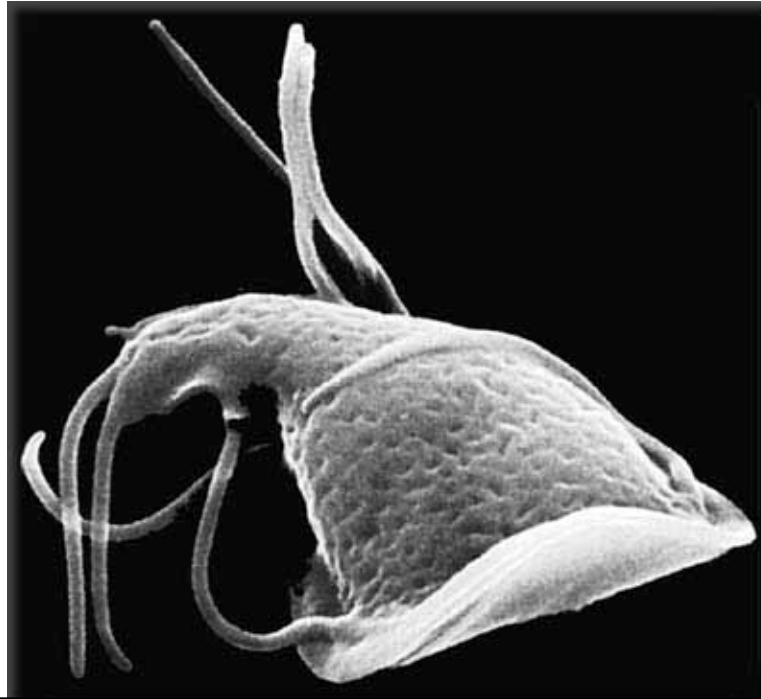
Effect on villous border?

Source (typical description)?

Predisposing immunodeficiency to chronic state?

Manifestions?

How to kill the little bugger?

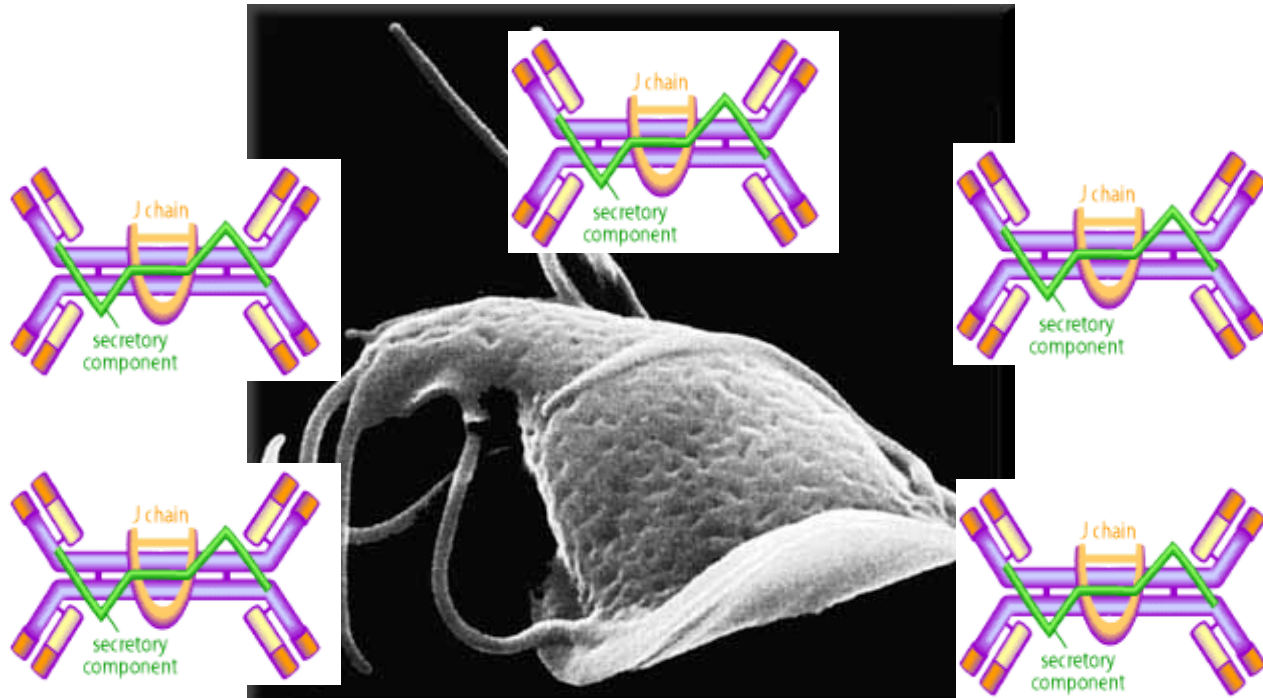


Invasive (i.e. fecal leuko?): **No**

Effect on villous border?: **Villous blunting**

Source (typical description)? Diarrhea PLUS **camping, hiking, Colorado...**

Predisposing immunodeficiency to chronic state?
(i.e. which antibody associated w/ GI lymphatics?)



Invasive (i.e. fecal leuko?): No

Effect on villous border?: Villous blunting

Source (typical description)? Diarrhea PLUS camping, hiking, Colorado...

Predisposing immunodeficiency to chronic state:
(i.e. which antibody associated w/ GI lymphatics?)

Secretory IgA (dimeric form protected from degradation)

Guaranteed to see this photo.

The question will be a hiker develops diarrhea.

You will know it is *Giardia* BUT they will ask either about the pathologic change (**disrupted villi**), the **LACK** of inflammatory cells in **stool**, **IgA deficiency** or **malabsorption** - type questions.



Transmitted by ingestions of **cysts** in food/water.

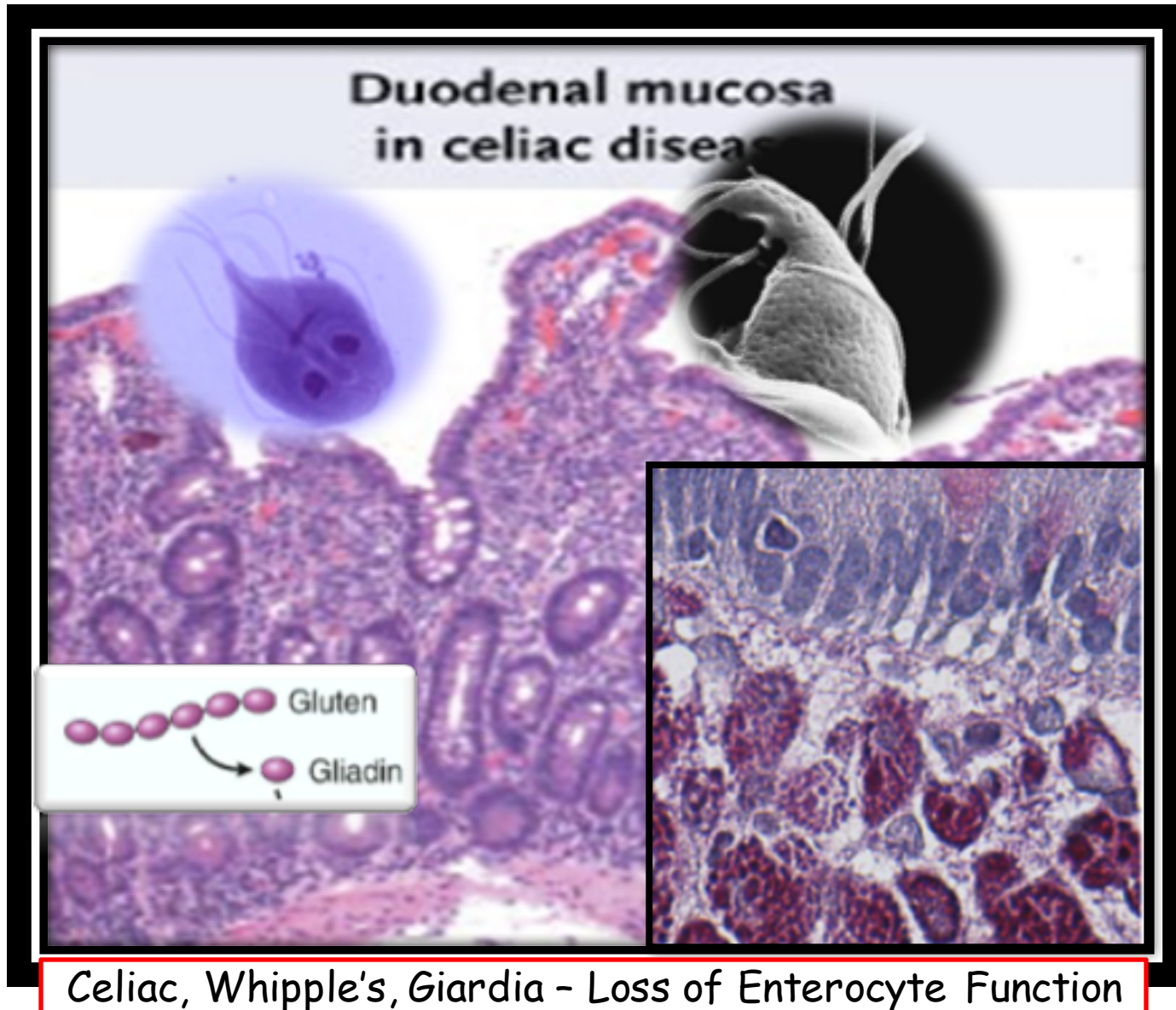


Giardia Cysts

Young patient w/ recurrent diarrhea. Stool specimen reveals the following. Which cellular or humoral deficiency is most likely?



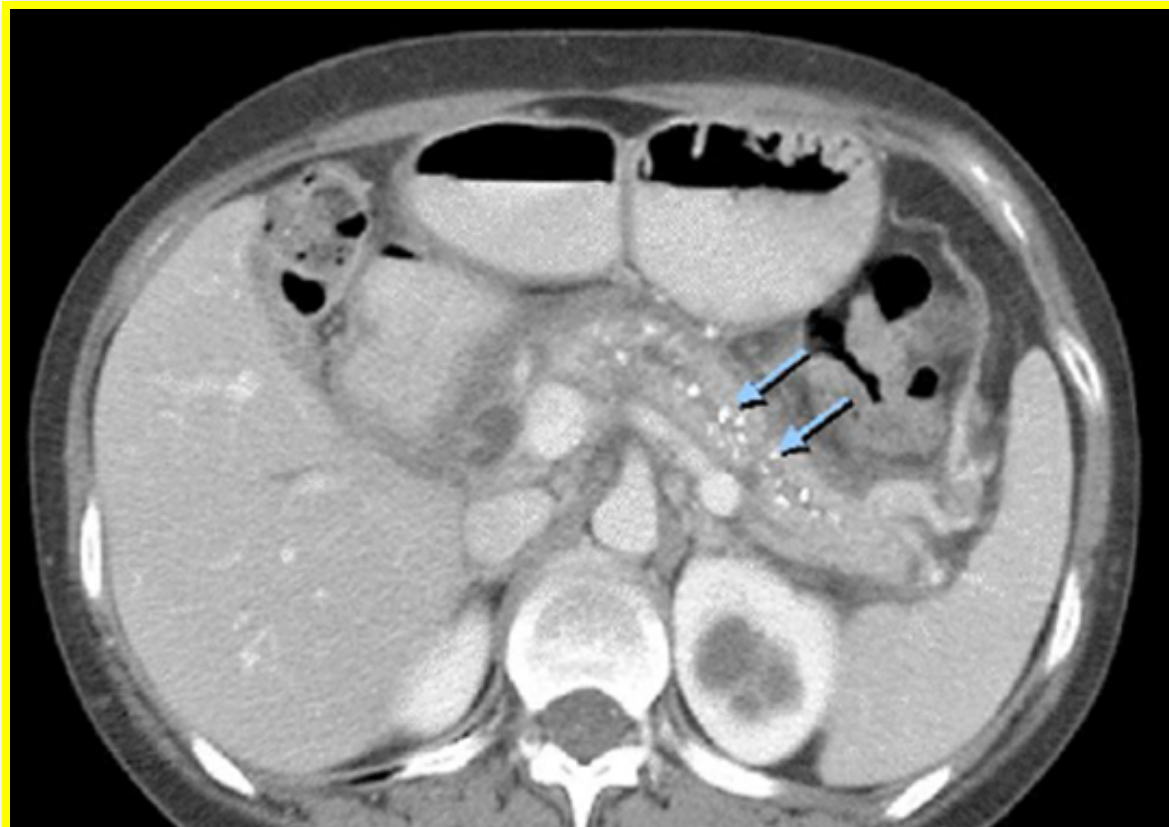
When you lose villi & microvilli...



Pancreatic Exocrine Insufficiency and Malabsorption

Symptoms: Failure of Lipase (and others)

Diagnostic: Failure of HCO_3^-



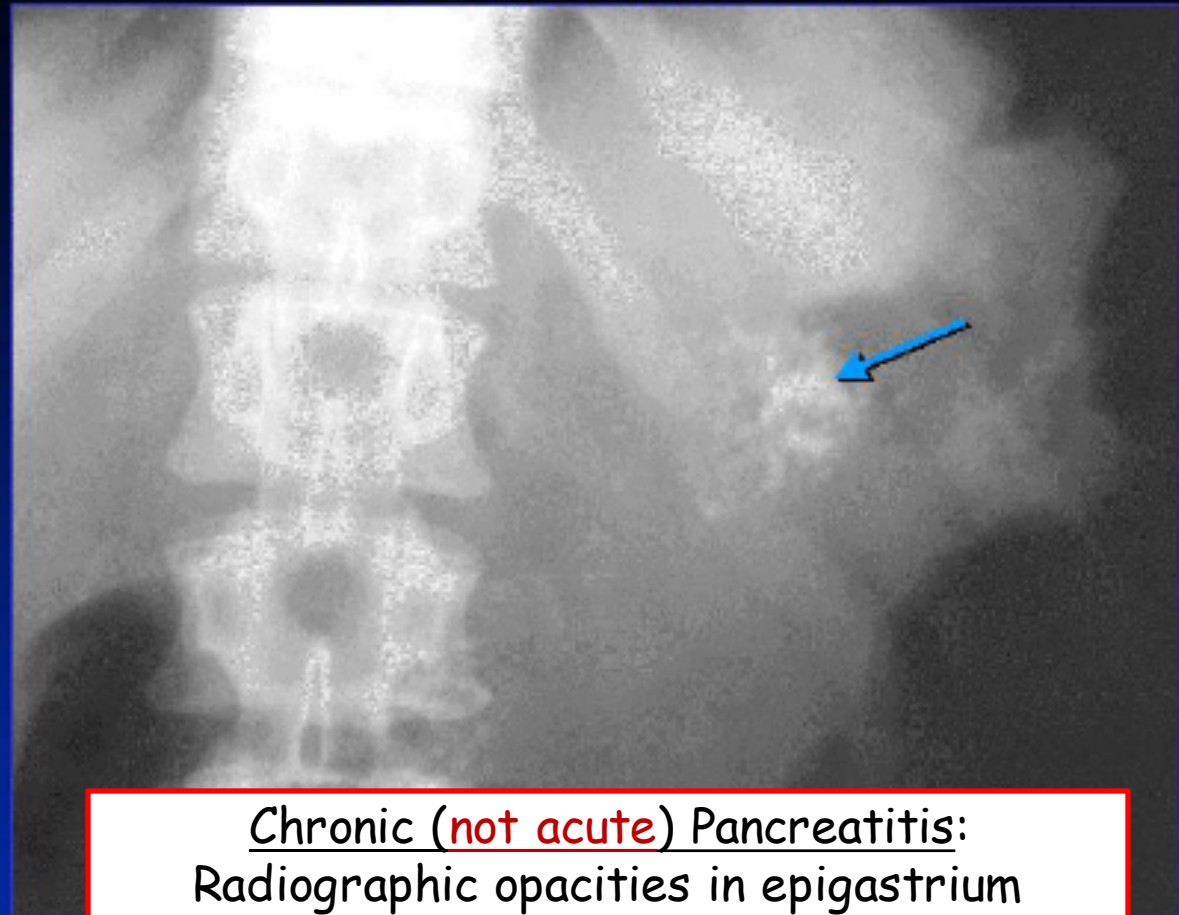
Alcoholic with 'opacities' in epigastrium

Pancreatic Insufficiency, Exocrine

- Background
 - Failure of digestive enzymes, especially **colipase/lipase** (fats), amylase (starch), trypsin (protein), **~HCO₃~**
- Key Conditions
 - Alcohol → chronic pancreatitis
 - Cystic fibrosis → chronic pancreatitis
 - Comorbid bile salt failure in advanced disease (biliary cirrhosis)
- Clinical presentation
 - Steatorrhea: 'greasy stool that floats'
 - Nutritional deficiencies
 - Fat-soluble vitamins, macrocytic anemia

Chronic Pancreatitis

Calcifications



Chronic (not acute) Pancreatitis:
Radiographic opacities in epigastrium

Diagnostic clue...a footprint for recurrent episodes

Pancreatic Insufficiency, Exocrine

- Diagnostic testing
 - Fecal stool studies:
 - Qualitative (Sudan black → fat/triglyceride globules)
 - Quantitative (72 h collection)
 - Secretin stimulation test
 - S-cells in duodenum stimulate HCO_3 release
 - Nutritional deficiencies

12 y.o. with recurrent respiratory infections, absence of vas deferens and chronic diarrhea presents with bilateral foot tingling. PE reveals abnormal vibratory sensation. Appropriate labs ordered:

A1c	5.7%
Lyme titre	negative
HCT	34%
Haptoglobin	low
MCV	84 fL

What is the most likely cause of his condition?

1. Thiamine deficiency
2. Vitamin A deficiency
3. Iron deficiency
4. Vitamin D deficiency
5. Cobalamin deficiency
6. Vitamin E deficiency
7. Folate deficiency

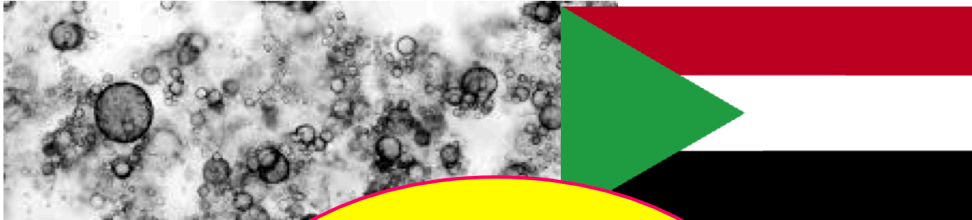
12 y.o. with recurrent respiratory infections, **absence of vas deferens** and **chronic diarrhea** presents with bilateral foot tingling. PE reveals **abnormal vibratory sensation**. Appropriate labs ordered:

A1c	5.7%
Lyme titre	negative
HCT	34%
Haptoglobin	low
MCV	84 fL

What is the most likely cause of his condition?


1. Thiamine deficiency:
 - Neuropathy but no hemolysis or absence of vas deferens
2. **Vitamin A deficiency: hyperkeratosis and nyctalopia**
3. Iron deficiency: low MCV
4. **Vitamin D deficiency: low calcium, bone pathology**
5. Cobalamin deficiency: high MCV
6. **Vitamin E deficiency: hemolysis, neuromuscular findings**
7. Folate deficiency: high MCV

Podcast (Video Recorded Lecture Series):
Malabsorptive Diarrhea for the USMLE Step One Exam



Fat Absorption
- How to absorb fats

Fat Malabsorption
- Symptoms
- Causes
- Consequences



The image contains several elements: a microscopic view of numerous small, clear fat droplets; the Sudanese flag (red, white, green, and black horizontal stripes); a map of Sudan and its neighbors (Libya, Egypt, Saudi Arabia, Chad, Eritrea, Ethiopia, C.A.R., Congo DRC, Uganda, Kenya); and a microscopic view of larger, red-stained fat droplets.

Howard J. Sachs, MD
www.12DaysinMarch.com
Email: Howard@12daysinmarch.com