

Author(s): Rebecca W. Van Dyke, M.D., 2012

License: Unless otherwise noted, this material is made available under the terms of the **Creative Commons Attribution – Share Alike 3.0 License**:
<http://creativecommons.org/licenses/by-sa/3.0/>

We have reviewed this material in accordance with U.S. Copyright Law **and have tried to maximize your ability to use, share, and adapt it.** The citation key on the following slide provides information about how you may share and adapt this material.

Copyright holders of content included in this material should contact open.michigan@umich.edu with any questions, corrections, or clarification regarding the use of content.

For more information about **how to cite** these materials visit <http://open.umich.edu/education/about/terms-of-use>.

Any **medical information** in this material is intended to inform and educate and is not a tool for self-diagnosis or a replacement for medical evaluation, advice, diagnosis or treatment by a healthcare professional. Please speak to your physician if you have questions about your medical condition.

Viewer discretion is advised: Some medical content is graphic and may not be suitable for all viewers.

Attribution Key

for more information see: <http://open.umich.edu/wiki/AttributionPolicy>

Use + Share + Adapt

{ Content the copyright holder, author, or law permits you to use, share and adapt. }



Public Domain – Government: Works that are produced by the U.S. Government. (17 USC § 105)



Public Domain – Expired: Works that are no longer protected due to an expired copyright term.



Public Domain – Self Dedicated: Works that a copyright holder has dedicated to the public domain.



Creative Commons – Zero Waiver



Creative Commons – Attribution License



Creative Commons – Attribution Share Alike License



Creative Commons – Attribution Noncommercial License



Creative Commons – Attribution Noncommercial Share Alike License



GNU – Free Documentation License

Make Your Own Assessment

{ Content Open.Michigan believes can be used, shared, and adapted because it is ineligible for copyright. }



Public Domain – Ineligible: Works that are ineligible for copyright protection in the U.S. (17 USC § 102(b)) *laws in your jurisdiction may differ

{ Content Open.Michigan has used under a Fair Use determination. }



Fair Use: Use of works that is determined to be Fair consistent with the U.S. Copyright Act. (17 USC § 107) *laws in your jurisdiction may differ

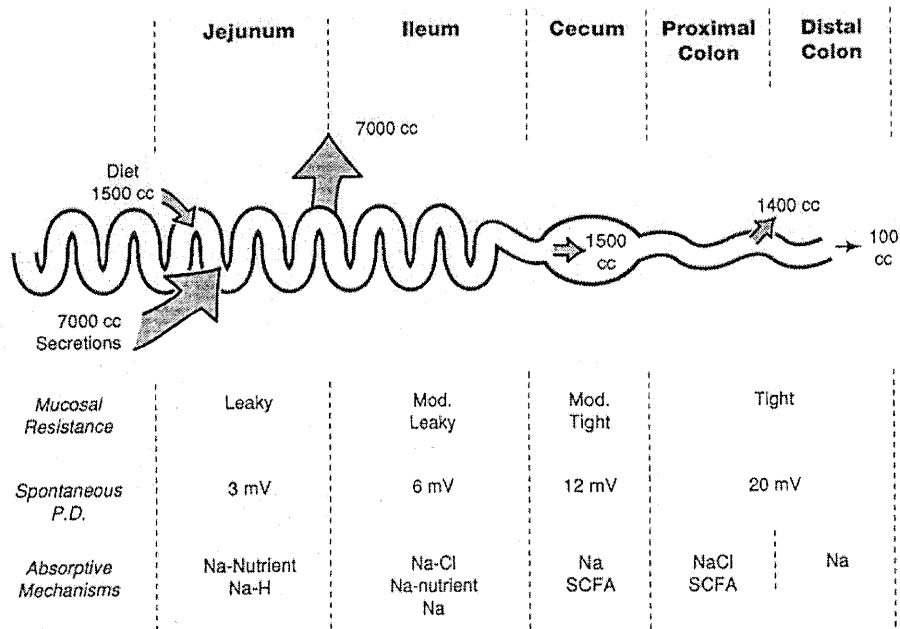
Our determination **DOES NOT** mean that all uses of this 3rd-party content are Fair Uses and we **DO NOT** guarantee that your use of the content is Fair.

To use this content you should **do your own independent analysis** to determine whether or not your use will be Fair.

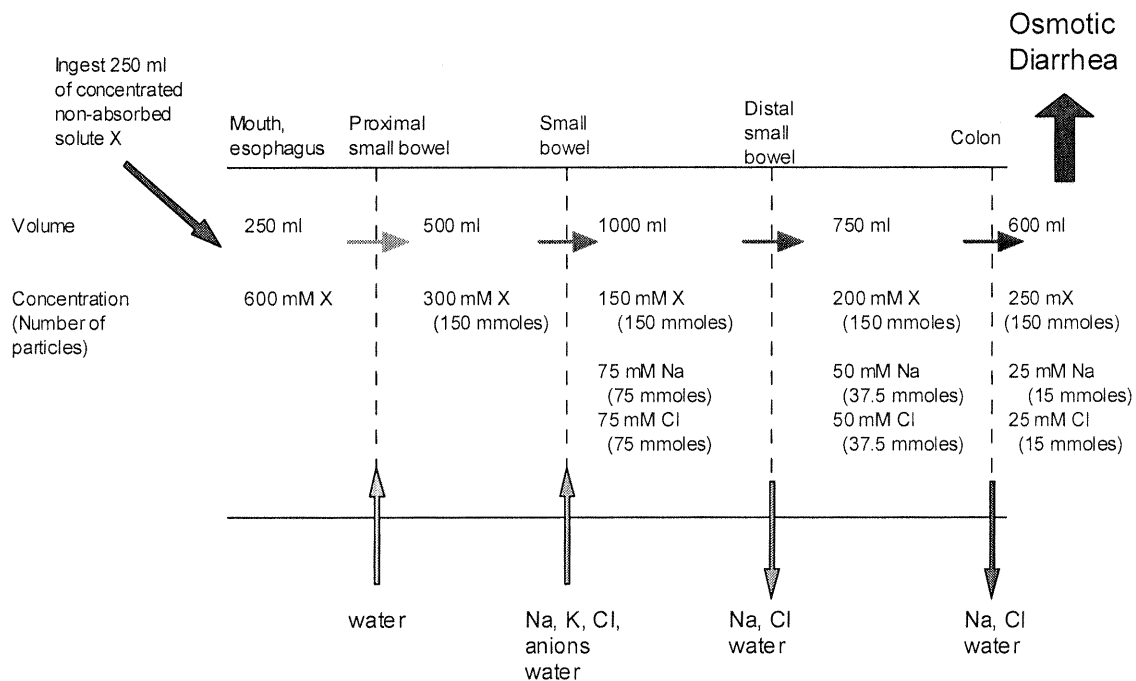
Supplementary information to accompany the lecture and assigned readings.

This material is included for those who find it useful in better understanding diarrhea and malabsorption.

1. Fluid Movement in Normal Intestinal Tract:



2. Pathophysiology of Osmotic Diarrhea:



3. Evaluation of Stool Electrolytes

Fecal Electrolytes - Normal Versus Secretory Diarrhea

	<u>Normal</u>	<u>Secretory Diarrhea</u>
Na ⁺ (mEq/l)	~20-40	~80-110
K ⁺ (mEq/l)	~90	~40
Cl ⁻ (mEq/l)	~15	~60
HCO ₃ ⁻ (mEq/l)	~30	~50
Anions (SO ₄ ⁻² , PO ₄ ⁻³ , fatty acids)	~85	~30
Other (Mg ⁺²)	<15-20	<10
Volume (liters/day)	<1	5-10

Fecal Electrolytes - Three types of diarrhea

<u>Solute (mEq/l)</u>	<u>Normal</u>	<u>Secretory</u>	<u>Malabsorption (Carbohydrate)</u>	<u>Osmotic (Mg salt)</u>
Na ⁺	~40	~90	~40	~20
K ⁺	~90	~40	~40	~20
Cl ⁻	~15	~60	~10	~60
HCO ₃ ⁻	~30	~50	~10	~20
Anions (SO ₄ ⁻² , PO ₄ ⁻³ , fatty acids)	~85	~30	~80	~100
Other (Mg ⁺²)	<15-20	<10	10	~70
Sugars (mM)	0	0	~100	0
Volume (liters/day)	<1	5-10	1-3	1-3
Osmolality (mOsm/l)	~290	~290	~290	~290
2 (Na+K)	~260	~260	~160	~80
Fecal osmotic gap	~30	~30	~100	~200

* Measured osmolality of stool can be greater than plasma osmolality if unabsorbed carbohydrates are present and stool sits at room temperature for hours, allowing bacterial fermentation.

OSMOTIC GAP

Question: Are there osmotically active molecules in stool that should not be there?

Cations + anions + neutral molecules ~ 300 mM

Cations = anions (electroneutrality)

Na and K are the usual stool cations and are easily measured.

Anions are a mixed bag (Cl, bicarbonate, sulfate, phosphate, fatty acids) and are NOT easily measured.

Neutral molecules and unmeasured cations are also a mixed bag but usually constitute < 30mM.

Equation for measurable molecules in stool:

$$2(\text{Na}+\text{K}) \sim 270\text{-}290 \text{ mM (equal to plasma osmolality)}$$

Thus the osmotic gap (osmotically active molecules that cannot be accounted for) can be calculated as:

$$\text{Osmotic gap} \sim 300 - 2(\text{Na}+\text{K}) \quad \sim 10\text{-}30 \text{ mM for normal stool}$$

An osmotic gap of >> 50 is abnormal and suggests osmotic diarrhea

4. Treatment of Large Volume Watery Diarrhea with Oral Rehydration Solutions:

The WHO (World Health Organization) solution is optimal for watery diarrhea, however several other commercially available products are reasonable substitutes as shown in the following chart. Gatorade, sodas and fruit juices are not acceptable substitutes as they contain too much glucose (or sucrose or fructose) and too little electrolyte to promote water absorption.

The rationale for use of these solutions was reviewed in the lecture - frequently in secretory diarrheas, although electrolyte secretion has been markedly stimulated, absorptive mechanisms for organic solutes, often in conjunction with electrolytes, remain fully functional and may be exploited to force sufficient absorption of electrolytes and water to compensate for losses due to secretion. The patient therefore remains hydrated until the underlying cause of the secretory diarrhea can be removed.

You may wish to keep a copy of this table for your Pediatric rotation

Composition of Oral Replacement Solutions for the Treatment of Diarrhea

SOLUTION	Na mmol/L	K mmol/L	Cl mmol/L	BICARBONATE or CITRATE mmol/L	GLUCOS E mmol/L (g/L)	OSMOLAL -ITY mosms/L
Rehydration						
WHO solution	90	20	80	30	110 (20)	310
Pedialyte RS	75	20	65	30	139 (25)	329
Pedialyte	45	20	35	30	139 (25)	250
Resol	50	20	50	34	111 (20)	270
Lytren	50	25	45	30	111 (20)	290
Infalyte	50	20	40	30	111 (20)	270
CeraLyte available online at CeraProductsInc.com	70-90	20	60	30	40 gm rice digest	265-275
Clear Liquids						
Gatorade	23.5	<1	17	---	(40)	?
Coca-Cola	1.6	<1	---	13.4	(100)	750
Apple juice	<1	25	?	---	(120)	~730
Orange juice	<1	50	---	50	(120)	~800
Chicken broth	250	8	250	0	0	450

Homemade version: 1 liter (1 quart) boiled water
 2 tablespoons sugar or honey
 ¼ teaspoon salt (NaCl)
 ¼ teaspoon baking soda (NaHCO₂)

Mix and drink at least 1 cup (250 ml) every 15 minutes until hydrated and then give 1.5 liters (1.5 quarts) for every liter (quart) of stool produced.

5. Antidiarrheal Agents: Know the categories and a few names.

DRUG	MECHANISM OF ACTION IN HUMANS	SIDE EFFECTS
Bismuth subsalicylate Pepto-Bismol	Anti-inflammatory, but mechanism not known, also has some bactericidal activity	Salicylate toxicity, Black stools
Opiates Paregoric Deodorized tincture of opium Codeine Diphenoxylate with atropine Loperamide	Decreases motility and peristalsis of small bowel and colon. Increases bowel transit time and thus increases opportunity for absorption of salt and water. May have anti-secretory effects as well. Work via endogenous opiate receptors in gut.	In inflammatory diarrheas may enhance bacterial invasion, and prolong excretion of pathogens. Opiates may cause CNS and respiratory depression. Addiction potential (except loperamide which does not pass the blood-brain barrier)
Anticholinergics Atropine	Alter motility and slow bowel transit Generally not as effective as opiates	Same as above but minus addiction and CNS/respiratory depression Can cause urinary retention, dry mouth/dry eyes, blurred vision. Difficult to tolerate at effective doses.
Cholestyramine	Binds bile acids	Binds medications and vitamins, may cause steatorrhea when used in large doses for long periods
Bulk-forming agents Psyllium Methylcellulose	Hydroscopic, partially nonabsorbed bulk (cellulose) added to stool. Alters bacterial cell mass	Few side effects. Some patients note increased flatus as these are non-absorbed carbohydrates
Octreotide (somatostatin)	Suppresses hormone secretion from neuroendocrine cells, mild antisecretory effect, decreases motility	Suppresses pancreatic secretion, delays gallbladder emptying, suppresses insulin secretion
5-ASA derivatives (azulfadine, mesalamine etc.)	Anti-inflammatory	Abdominal pain, headaches (sulfa moiety of azulfadine)

6. Malabsorbed substances commonly found in foods and medications:

This will be very useful when you are working with patients:

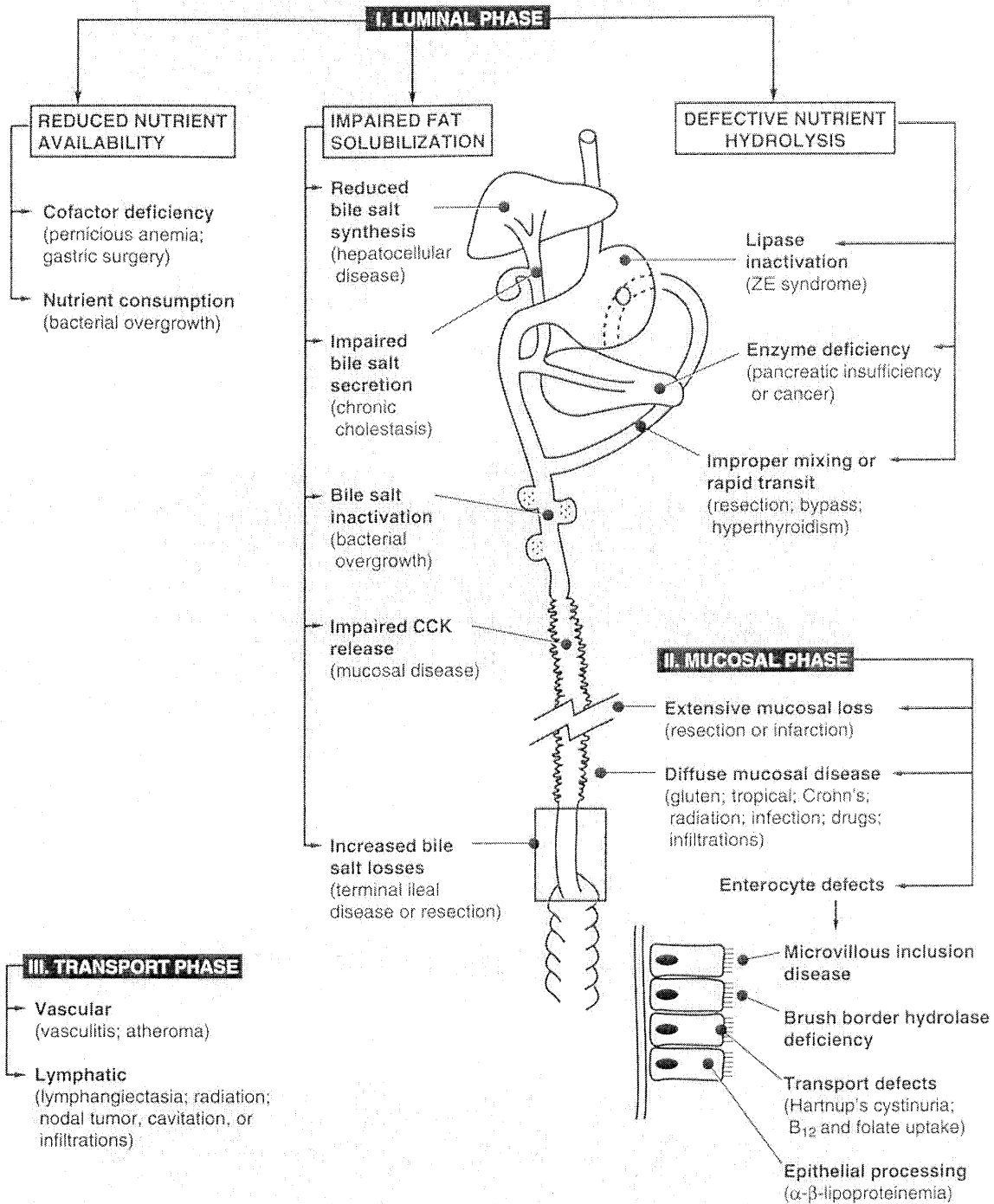
<u>Food</u>	<u>Substance</u>
Milk	lactose
Dried beans/legumes	raffinose, melitose, stachyose
Mushrooms	trehalose
Fiber	cellulose or other plant-derived complex carbohydrates
Dietetic or diabetic foods	sorbitol, fructose
Corn syrup in sweetened soft drinks	fructose
Fruit juices	fructose, sorbitol

Medication

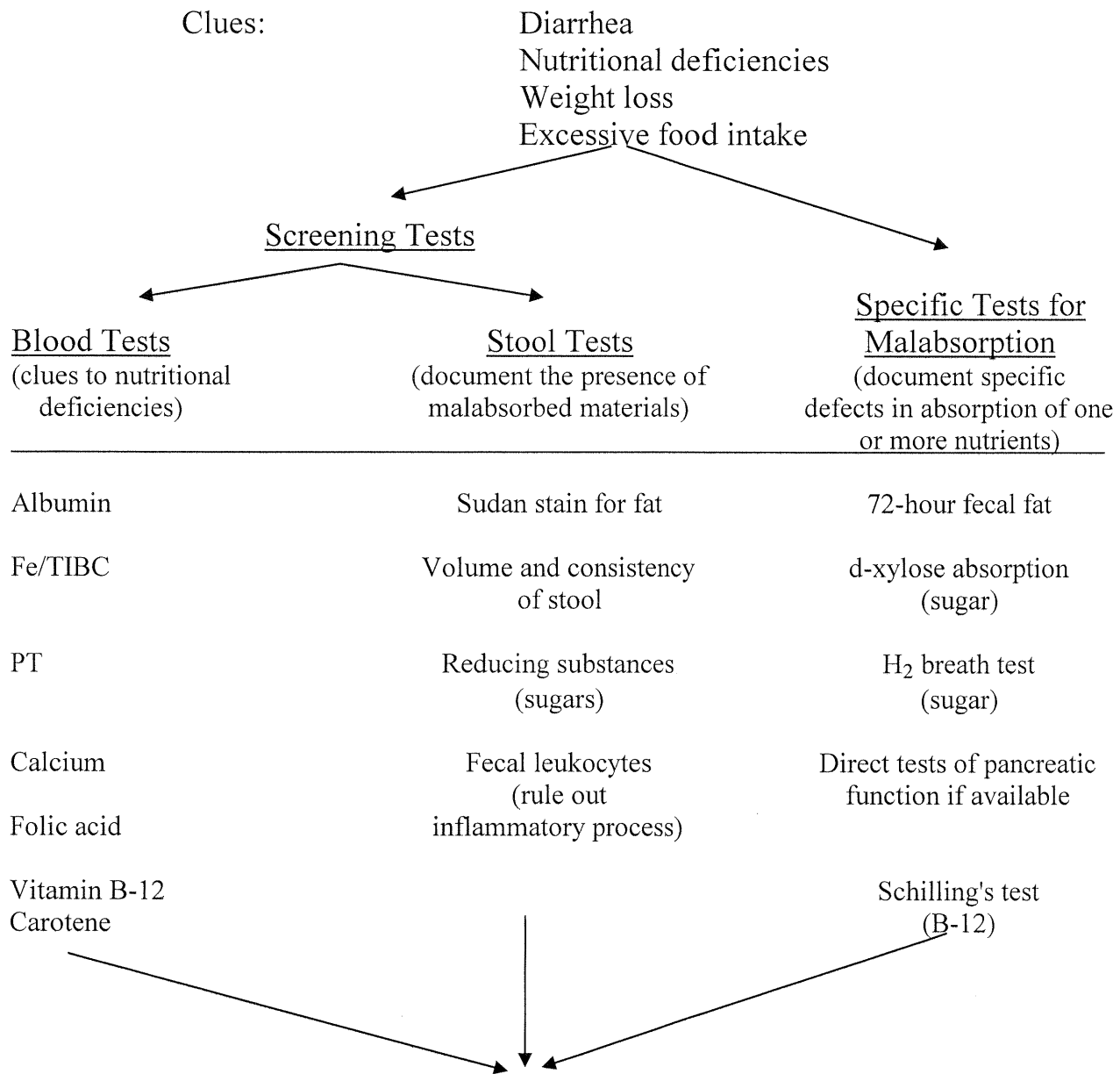
Antacids	magnesium hydroxides
Laxatives	magnesium citrate
Lactulose	lactulose

7. Mechanisms of Malabsorption: A Pathophysiologic Diagram –

This outline of almost all potential mechanisms may help give perspective to this topic, however don't spend time memorizing all the details.



8. Approach to Diagnosis when there is a Suspicion of Malabsorption



Define whether the problem is one of specific malabsorption of one or only a few nutrients or whether there is generalized malabsorption of many nutrients and then select the appropriate specific diagnostic tests to determine the exact disease. These may include:

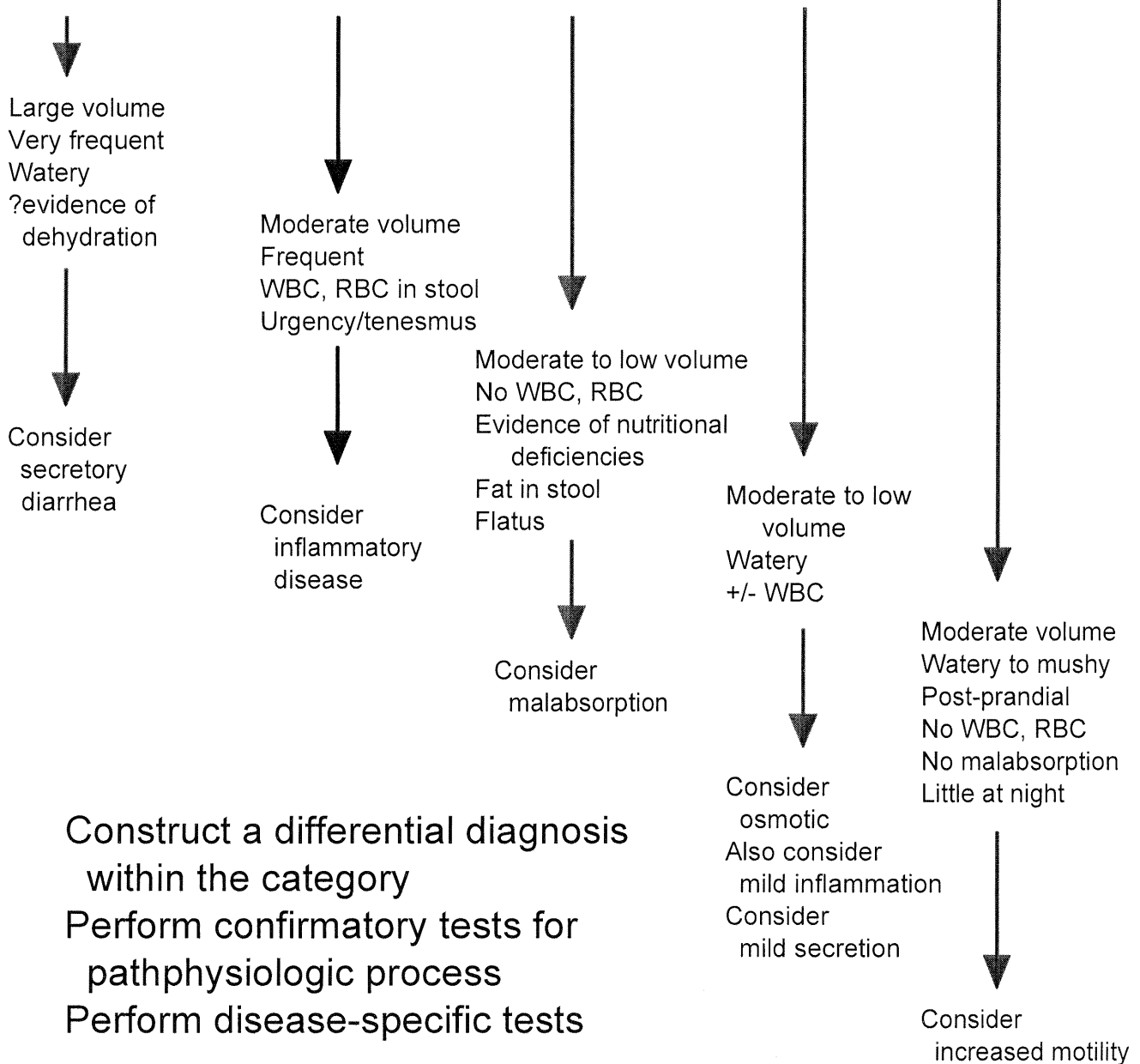
- Small bowel biopsy
- Small bowel quantitative bacterial culture
- Small bowel/pancreatic x-rays
- Endoscopic retrograde cholangiopancreatography (ERCP) or pancreatic secretion tests
- Therapeutic trials such as effects of pancreatic enzyme supplementation on steatorrhea.

Overall Algorithm:

Chronic Diarrhea

Analyze:

Patient description of stool (volume, consistency, frequency)
Clinical findings (weight loss, malnutrition, bleeding, fever)
Laboratory testing (fecal WBC, RBC, electrolytes, osmotic gap, evidence of dehydration, inflammation, malnutrition)



Interpretation of Patient Cases:

1. This is acute diarrhea that is voluminous without any evidence of a major inflammatory process. Although the differential diagnosis includes a number of elements, a secretory process due to a toxin from a bacteria is the most likely. The evaluation should focus on treating symptoms and looking for complications (such as dehydration) as most infectious diarrheas resolve quickly.
2. This baby also has an acute, likely infectious, diarrhea. The fever is typical of infectious processes. The diarrhea may be due to a bacterial infection with production of a secretory toxin and/or with components of a mild inflammatory process as well as loss of small bowel surface area from viral infection. Like in case #1, the underlying disease is probably self-limited. In this small child treatment of dehydration (which the patient exhibits) is the most important aspect of care.
3. A chronic history of diarrhea requires full evaluation as this is unlikely to get better on its own. The WBC in the stool and modest diarrhea suggest a moderate inflammatory process in the colon is most likely. Inflammatory bowel diseases such as mild ulcerative colitis/proctitis, microscopic colitis or even mild colonic Crohn's disease are possibilities.
4. This elderly patient probably has diarrhea due to decreased surface area in the colon. Bowel slowing agents to allow more contact time between colon contents and the absorptive epithelial cells will likely control these symptoms.
5. Diarrhea occurring soon after eating is often seen in hypermotility disorders. Eating stimulates the gastrocolic reflex which is exaggerated in patients with rapid motility. The other symptoms may be signs of hyperthyroidism (see Endocrine sequence in the spring).
6. This patient could have any one of many causes of diarrhea, although the story sounds more like mild secretory or osmotic, rather than inflammatory. Mild hypermotility is also possible. However an important clue is the history that he is using large amounts of magnesium-containing antacids each day. A clinical trial of stopping the antacids could provide a quick and easy answer to the problem. If the diarrhea does not stop within a day or so, then a very thorough investigation is warranted. In this case, stopping the large doses of Maalox was curative.
7. Given the large (documented) weight loss, change in stool consistency and presence of flatus and fat in the stool, malabsorption (especially of fats and carbohydrates) would be an important part of the differential diagnosis. The laboratory studies give evidence of loss of other nutrients (iron) as well, thus generalized malabsorption may be present. The differential diagnosis includes celiac sprue (probably the most common explanation in this patient) as well as severe extensive small bowel Crohn's disease, bacterial

overgrowth (you would have to look for a structural reason for this), or Whipple's disease (very rare). Pancreatic insufficiency could be present but usually doesn't result in clinically significant carbohydrate insufficiency (and excess flatus).

8. This patient is similar to #7 – weight loss, altered stools, low albumin (evidence for malnutrition), low carotene/cholesterol and fat globules in the stool as well as an elevated osmotic gap, consistent with fat malabsorption and osmotic diarrhea (perhaps from carbohydrates). Generalized malabsorption due to bacterial overgrowth (in the long limb of duodenum excluded by a gastrojejunostomy) or celiac sprue are likely. Pancreatic insufficiency is possible, however less likely to cause carbohydrate malabsorption of this magnitude.

9. Flatus and watery diarrhea on only a few days per week suggests ingestion of malabsorbed carbohydrates – a good dietary history may elicit frequent use of foods sweetened with sorbitol/fructose in someone trying to diet. A similar pattern could be seen in lactase-deficient individuals who take in sufficient lactose on a few days per week and lactase may slowly disappear from the bowel with age – he just got old enough to have symptoms! However, if a short clinical trial of avoiding these foods does not quickly eliminate the diarrhea and excess flatus, a much more thorough evaluation for true malabsorption will be necessary.