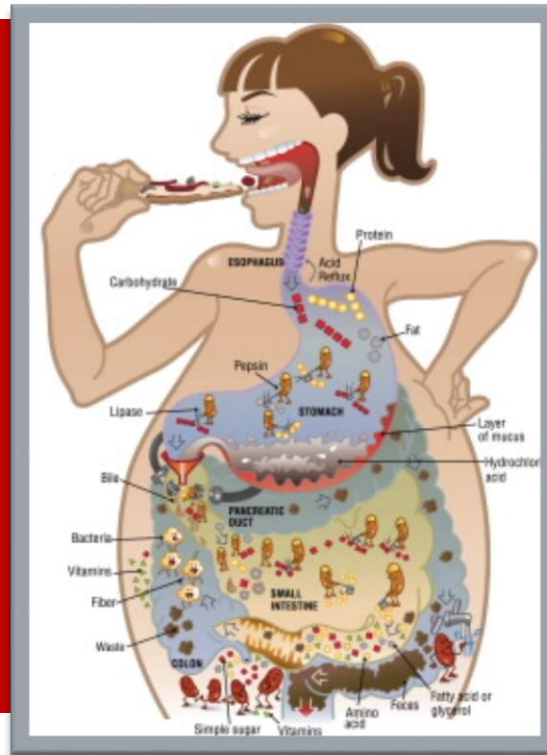




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Management Challenges of the Gastrointestinal Tract (GIT) in Systemic Sclerosis (SSc)



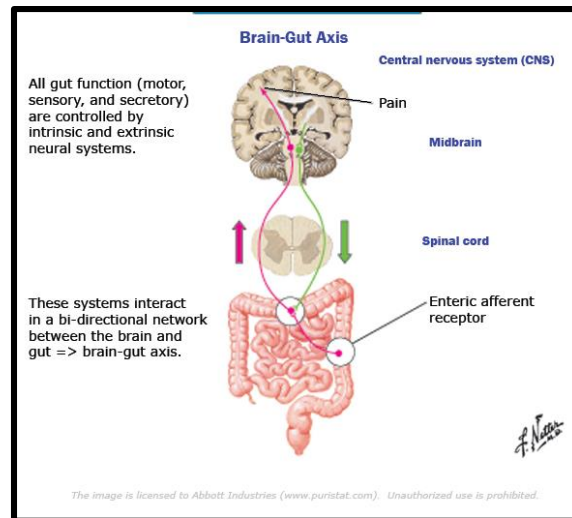
Presented by:
Tracy M. Frech, MD, MS
April 2016

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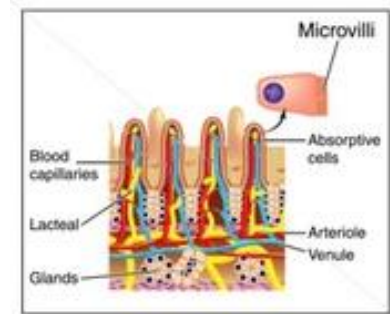
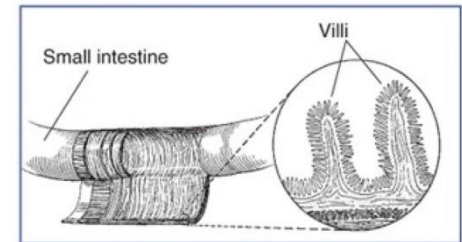
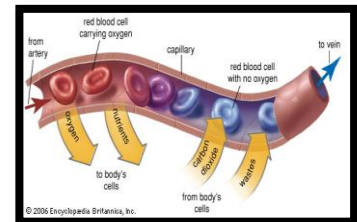
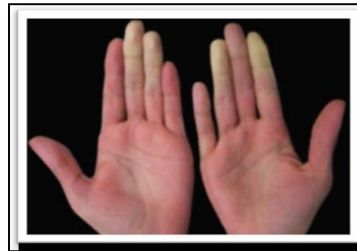
WHY GASTROINTESTINAL SYMPTOMS MATTER TO THE RHEUMATOLOGIST

- The gastrointestinal tract is the largest immune compartment of the human body.
- The major function of the intestinal immune cells is to maintain the integrity of the body at the huge interface between external stimuli:
 - Medications
 - Nutrition
 - Intestinal microflora
 - Brain-gut axis



SSc IS A PROGRESSIVE DISEASE OF THE MICROVASCULATURE

- Vascular dysfunction
- Swelling
- Decreased oxygen and nutrient delivery to tissues
- Tissue death
- Immune dysregulation
- Scarring



CRITERIA FOR SYSTEMIC SCLEROSIS DO NOT CAPTURE GIT DISEASE

2013 ACR / EULAR Criteria For The Classification Of Systemic Sclerosis (Scleroderma)*

Item	Sub-items(s)	Weight/score †
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints (<i>sufficient criterion</i>)	-	9
Skin thickening of the fingers (<i>only count the higher score</i>)	Puffy fingers	2
	Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints)	4
Fingertip lesions (<i>only count the higher score</i>)	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia	-	2
Abnormal nailfold capillaries	-	2
Pulmonary arterial hypertension and/or interstitial lung disease (<i>maximum score is 2</i>)	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon	-	3
SSc-related autoantibodies (anticentromere, anti-topoisomerase I [anti-Scl-70], anti-RNA polymerase III) (<i>maximum score is 3</i>)	Anticentromere 3	3
	Anti-topoisomerase I	
	Anti-RNA polymerase III	

* The criteria are not applicable to patients with skin thickening sparing the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (e.g., nephrogenic sclerosing fibrosis, generalized morphea, eosinophilic fasciitis, scleredema diabeticorum, scleromyxedema, erythromyalgia, porphyria, lichen sclerosis, graft-versus-host disease, diabetic cheiroarthropathy).

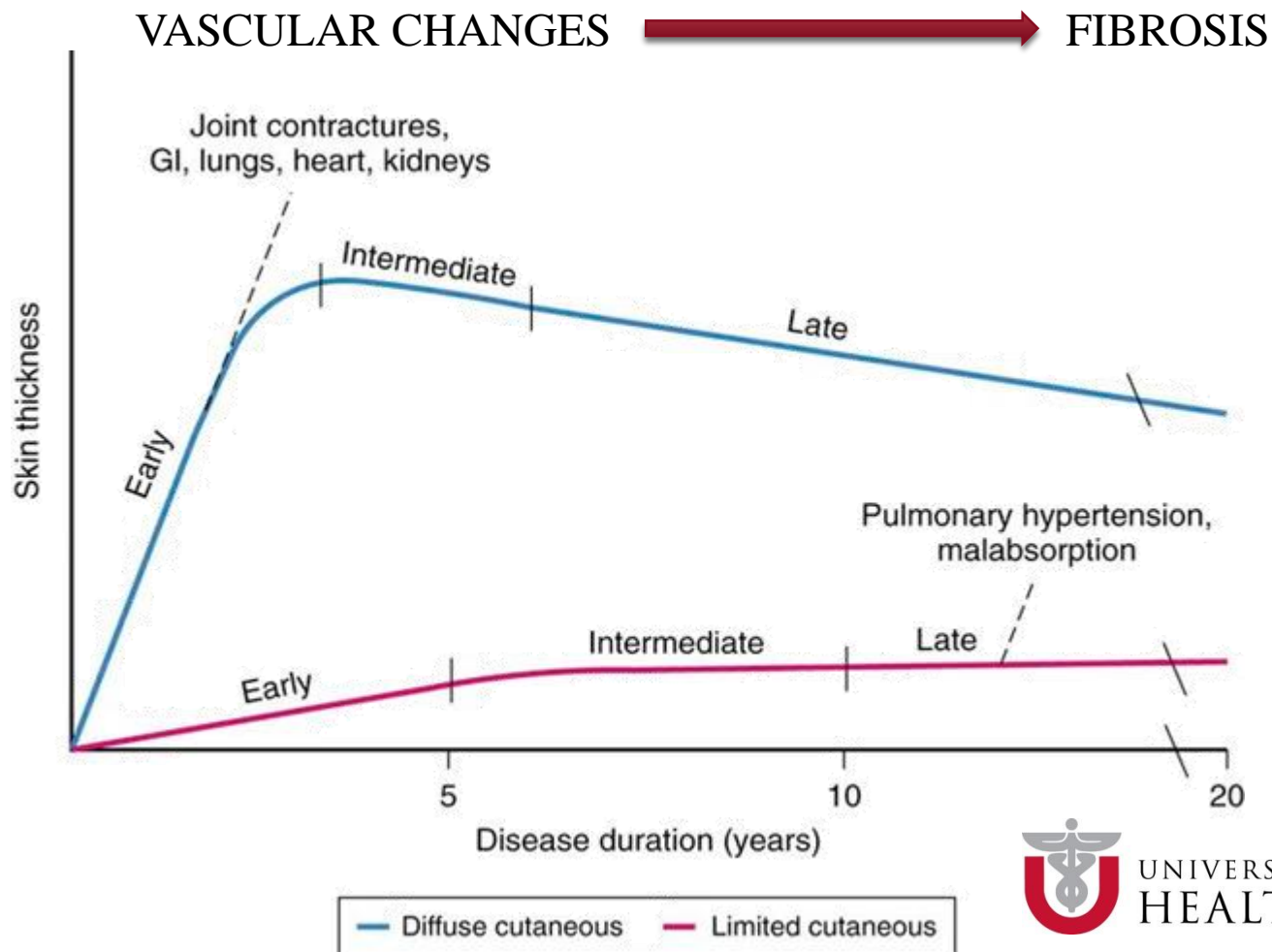
† The total score is determined by adding the maximum weight (score) in each category.
Patients with a total score of ≥ 9 are classified as having definite scleroderma.

Sensitivity 91% Specificity 92%

Van den Hoogen et al. 2013 Classification Criteria for Systemic Sclerosis. Arthritis and Rheumatism. Vol. 65, No. 11, November 2013, pp 2737–2747



SSc CHANGES OVER TIME



SYSTEMIC SCLEROSIS (SSc)-GIT: BASICS

Patients present
in 3rd or 4th
decade of life

In adults,
women are at
greater risk,
ratio 4:1

Except for skin,
GIT is most
common organ
system involved
in SSc

GIT is the
presenting
feature in 10%
of patients

Over the course
of the disease,
GIT affects up
to 90% of
patients*

**At the University of Utah, 99%.*

Gyger G, *Current Rheumatology Reports* 2012.

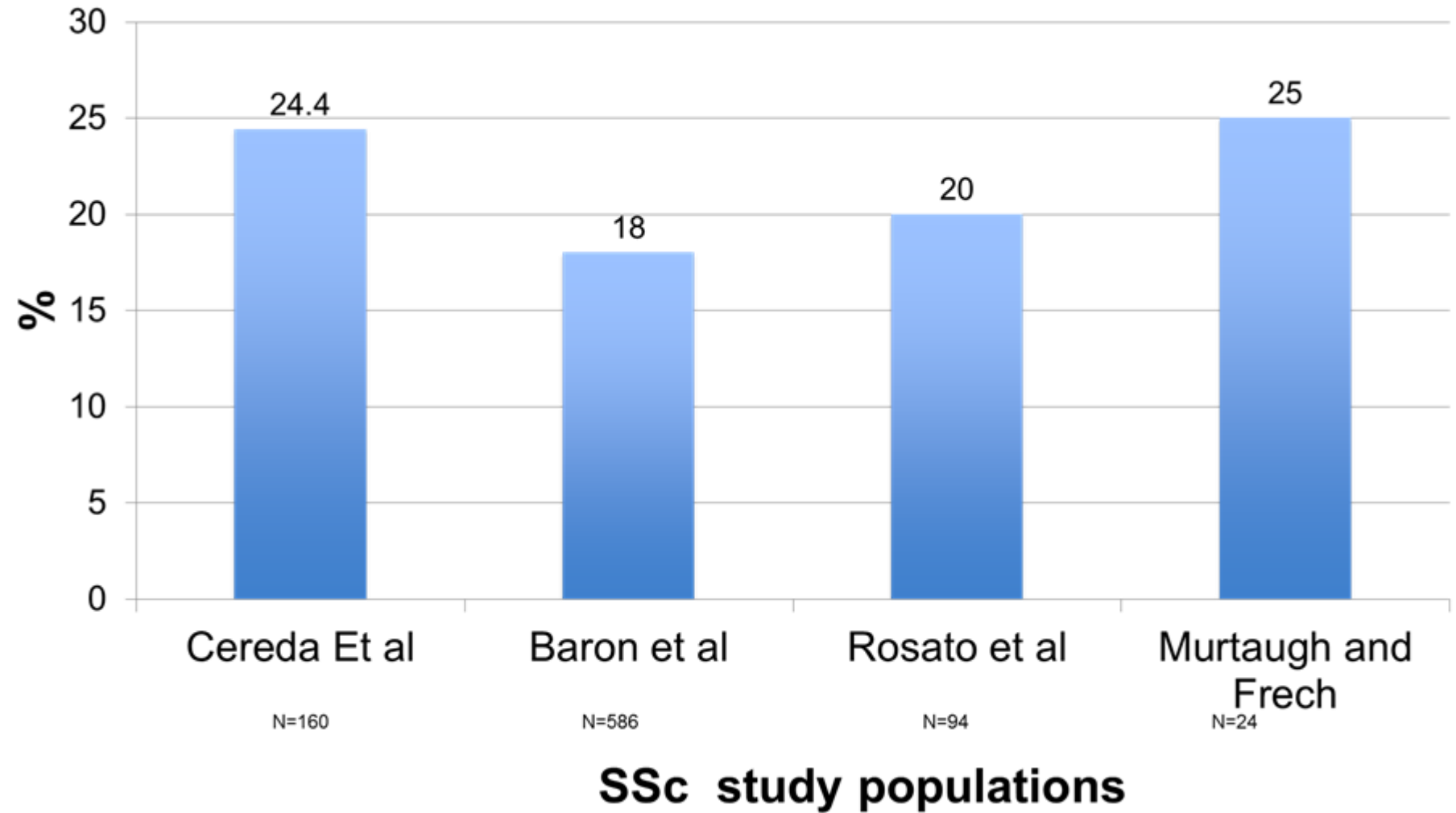
Steen VD, *Arthritis and Rheumatism* 2000.

Hansi N, *Clinical and Experimental Rheumatology* 2014.

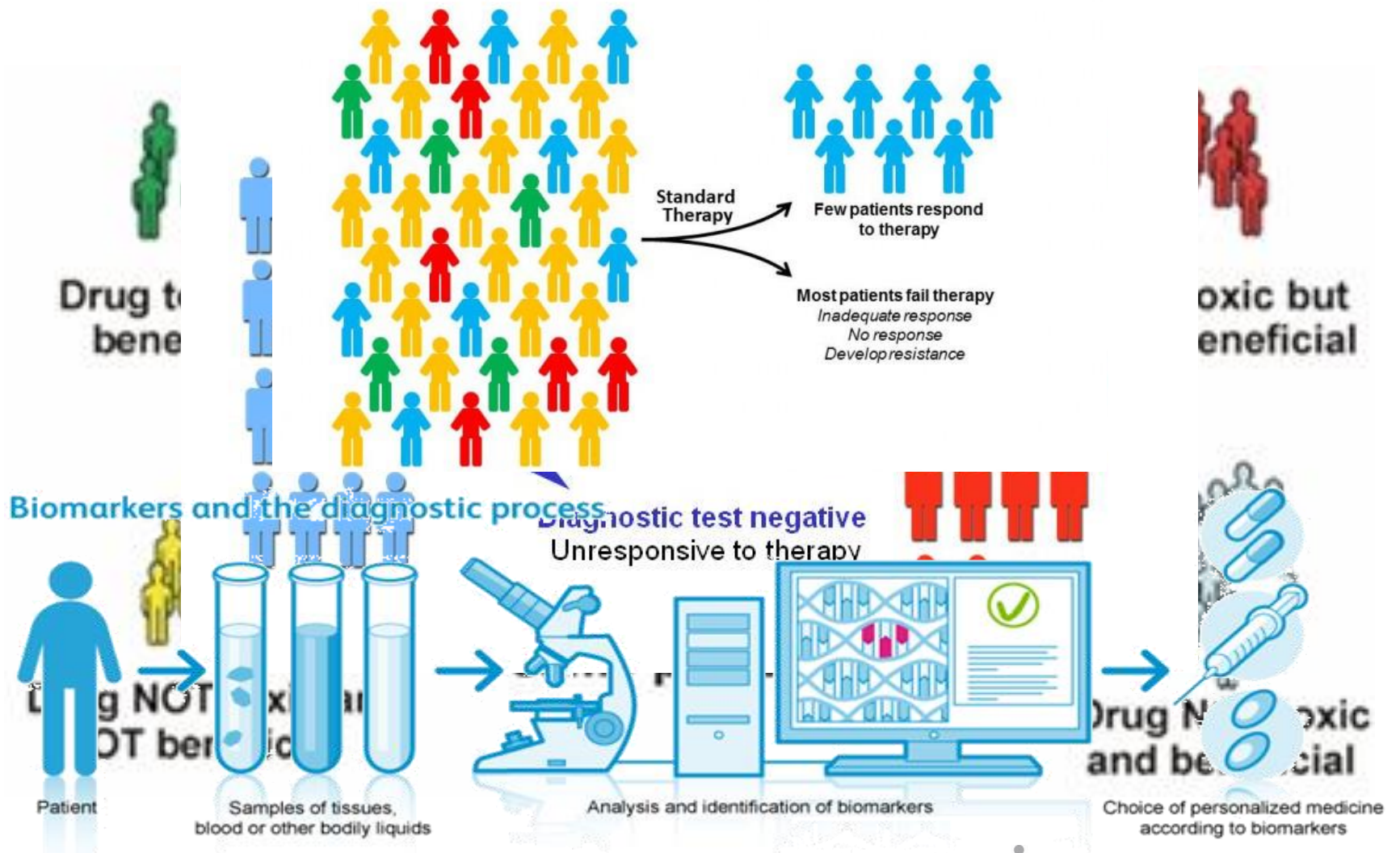


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PREVALENCE OF MALNUTRITION IN SSc



CURRENT PRACTICE



CHALLENGE OF PERSONALIZED SS_c-GIT

Upper tract and lower tract

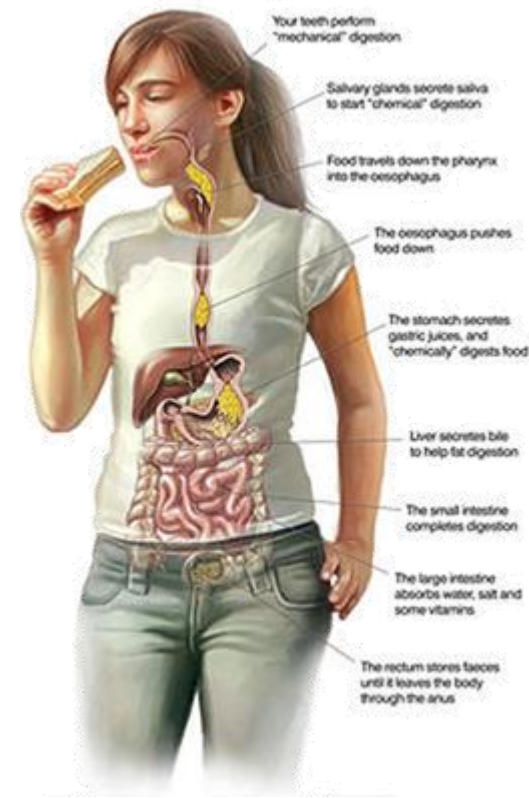
- The GIT is 30 feet long

Digestion

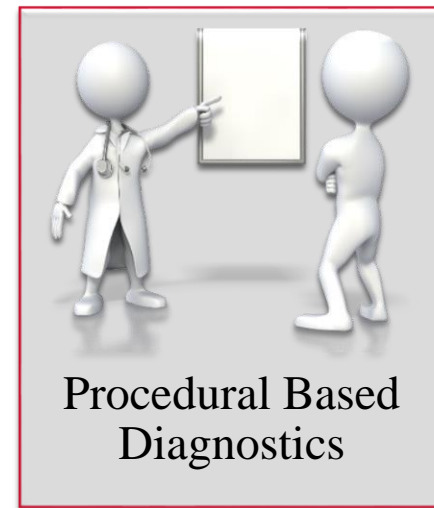
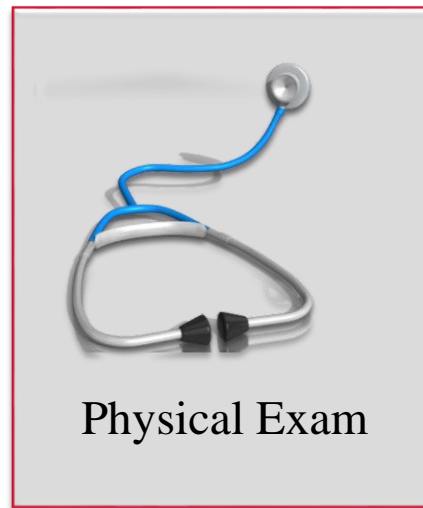
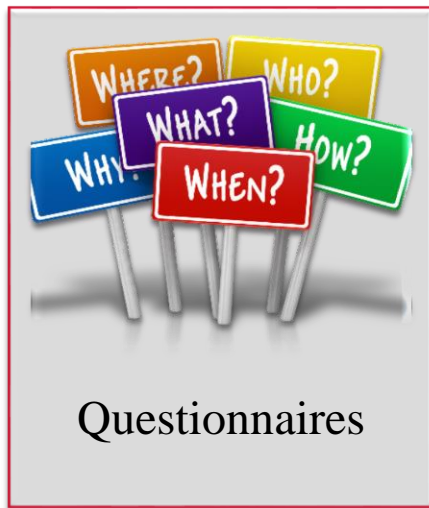
- Mechanical digestion
- Chemical digestion
- Detoxification system
- All the chemicals (neurotransmitters) found in the brain, are also found in the GIT.

Immune Function

- The largest immune organ in the body.
- Continually exposed to substances from the outside world.
- Has extremely thin lining providing the barrier between the internal body and the external world.



LIMITATIONS OF CLINICAL ASSESSMENT



The UCLA SCTC GIT 2.0

Questionnaire

The following questions ask about your gastrointestinal (gut, GI) symptoms and how they affected your life over the last 7 days. Answer every question by selecting the answer as indicated. Most questions have 4 choices: "No Days", "1-2 Days", "3-4 Days", or "5-7 Days". Questions 15 and 31 have 2 choices only: "Yes" or "No". If you are unsure about how to answer a question, please give the best answer you can.

In order to score the instrument, all questions must be answered.

Reflux				
	(Check one response for each question)			
	No Days	1-2 Days	3-4 Days	5-7 Days
1	In the past one week, how often did you have difficulty swallowing solid food?			
2	In the past one week, how often did you have an unpleasant stinging or burning sensation in your chest (heartburn)?			
3	In the past one week, how often did you have a sensation of bitter or sour fluid coming up from your stomach into your mouth (acid reflux)?			
4	In the past one week, how often did you have heartburn on eating 'acidic' foods such as Tomatoes & Oranges?			
5	In the past one week, how often did you regurgitate (throw up or bring up small amounts of previously eaten food)?			
6	In the past one week, how often did you sleep in a 'raised' or an 'L shaped' position?			
7	In the past one week, how often did you feel like vomiting or throwing up?			
8	In the past one week, how often did you vomit or throw up?			

Distension / Bloating				
	(Check one response for each question)			
	No Days	1-2 Days	3-4 Days	5-7 Days
9	In the past one week, how often did you feel bloated (a sensation of gas or air in the stomach)?			
10	In the past one week, how often did you notice an increase in your belly, sometimes requiring you to open your belt, pants or shirt?			
11	In the past one week, how often did you feel full after eating a small meal?			
12	In the past one week, how often did you pass excessive gas or flatulence?			

uclascleroderma.researchcore.org

Soilage				
	(Check one response for each question)			
	No Days	1-2 Days	3-4 Days	5-7 Days
13	In the past one week, how often did you accidentally soil (dirty) your underwear before being able to get to a bathroom?			

Diarrhea				
	(Check one response for each question)			
	No Days	1-2 Days	3-4 Days	5-7 Days
14	In the past one week, how often did you have loose stools (diarrhea)?			
	(Check one response for each question)			
	Yes		No	
15	In the past one week, have you noticed your stools becoming watery?			

Constipation				
	(Check one response for each question)			
	Yes		No	
16	In the past one week, have you noticed your stools becoming harder?			
	(Check one response for each question)			
	No Days	1-2 Days	3-4 Days	5-7 Days
17	In the past one week, how often were you constipated or unable to empty your bowels?			
18	In the past one week, how often did you have hard stools?			
19	In the past one week, how often did you have pain while passing your stools?			

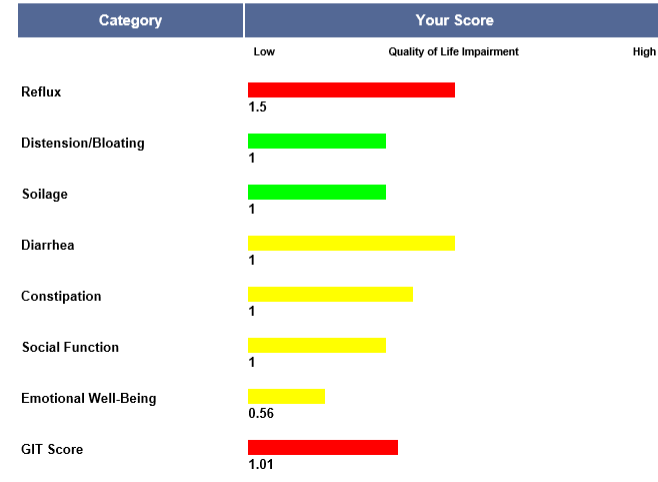
The UCLA SCTC GIT 2.0 Questionnaire

Your total GIT score is **1.008**. Your individual section scores are detailed in the table below and after each section in the questionnaire.

[Click here](#) for a printable version of your results.

Social Function				
(Check one response for each question)				
	No Days	1-2 Days	3-4 Days	5-7 Days
20	In the past one week, how often did nausea interfere with social activities such as visiting friends or relatives?			
21	In the past one week, how often did vomiting interfere with social activities such as visiting friends or relatives?			
22	In the past one week, how often did stomach aches or pain interfere with social activities such as visiting friends or relatives?			
23	In the past one week, how often did diarrhea interfere with social activities such as visiting friends or relatives?			
24	In the past one week, how often did the fear of accidentally soiling your underwear interfere with social activities such as visiting friends or relatives?			
25	In the past one week, how often did bloated sensations interfere with social activities such as visiting friends or relatives?			

Emotional Well-Being				
(Check one response for each question)				
	No Days	1-2 Days	3-4 Days	5-7 Days
26	In the past one week, how often did you feel worried or anxious about your bowel problems?			
27	In the past one week, how often did you feel embarrassed because of your bowel symptoms?			
28	In the past one week, how often did you have problems with sexual relations because of your bowel symptoms?			
29	In the past one week, how often did you fear not being able to find a bathroom?			
30	In the past one week, how often did you feel depressed or discouraged due to your bowel symptoms?			
31	In the past one week, how often did you avoid or delay traveling because of your bowel symptoms?			
32	In the past one week, how often did you feel angry or frustrated as a result of your bowel symptoms?			
33	In the past one week, how often did you have problems with your sleep as a result of your bowel symptoms?			
34	In the past one week, how often did you feel 'stress' or an upset mood worsens your bowel symptoms?			



GIT Score: **1.008**

Severity of GIT involvement: **Severe-to-Very Severe**

Reflux Score: **1.5**

Severity of GIT involvement: **Severe-to-Very Severe**

Distension/Bloating Score: **1**

Severity of GIT involvement: **None-to-Low**

Soilage Score: **1**

Severity of GIT involvement: **None-to-Low**

Diarrhea Score: **1**

Severity of GIT involvement: **Moderate**

Constipation Score: **1**

Severity of GIT involvement: **Moderate**

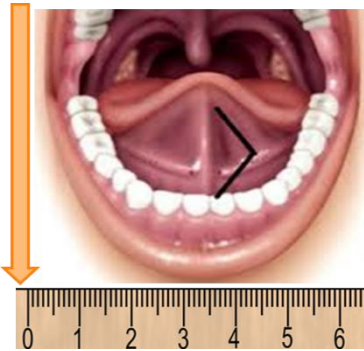
Social Function Score: **1**

Severity of GIT involvement: **Moderate**

Emotional Well-Being Score: **0.556**

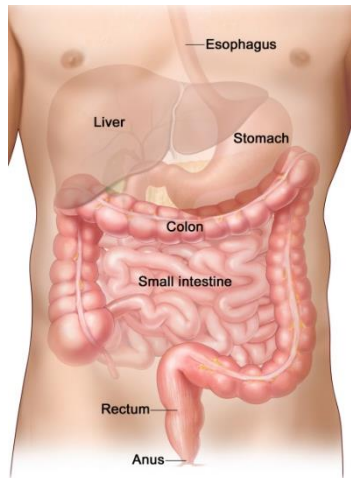
Severity of GIT involvement: **Moderate**

PHYSICAL EXAM: CAN IT HELP US?



Oral

- Exam can guide referrals
- Dental
- Speech and swallow



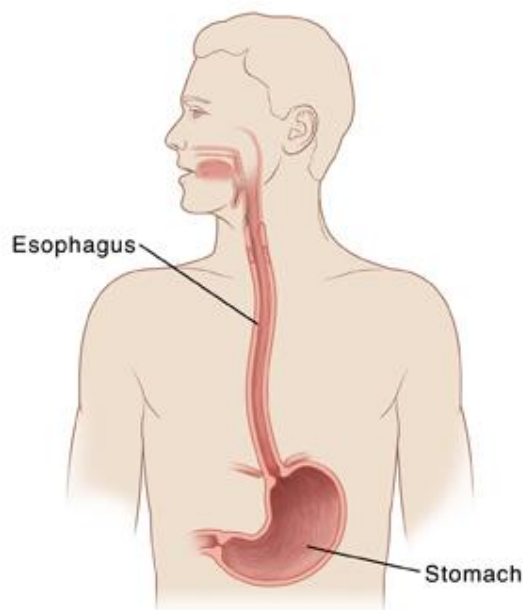
Abdominal

- Exam is limited
- Pain
- Distention

Rectal

- Exam is usually only performed for prostate assessment

INVESTIGATIONAL PROCEDURES: UPPER GIT



Esophageal Motility

- Modified barium swallow
- Manometry
- Impedance
- pH monitoring
- Scintigraphy

• Tissue Evaluation

- Endoscopy
 - Traditional
 - Capsule

Stomach Motility

- Scintigraphy
- Electrogastrography
- Gastric Emptying
- Breath test
- Single Photon Emission CT
- Wireless pH monitoring
- MRI

• Tissue evaluation

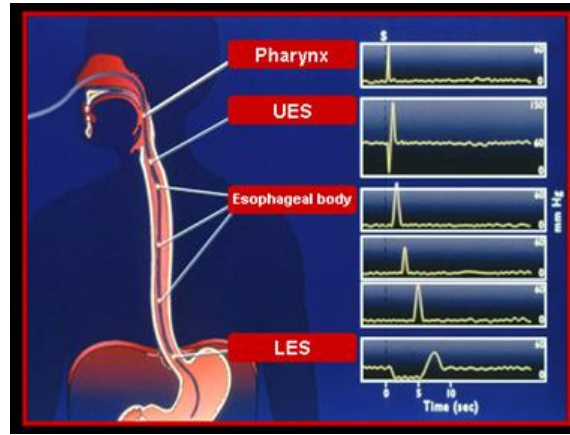
- Endoscopy
 - Traditional
 - Capsule



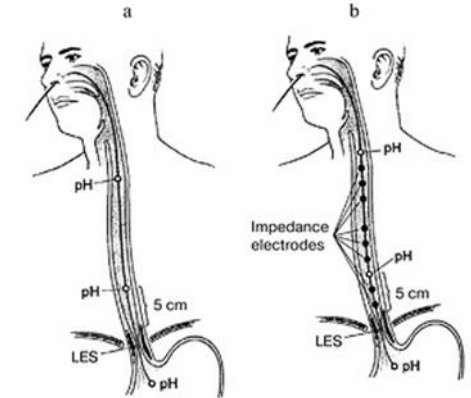
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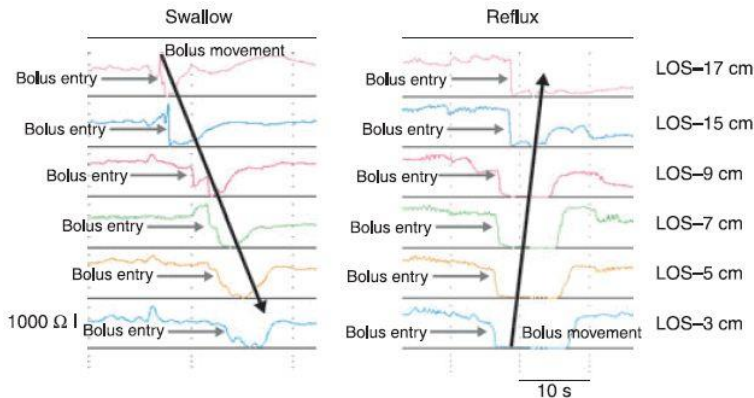
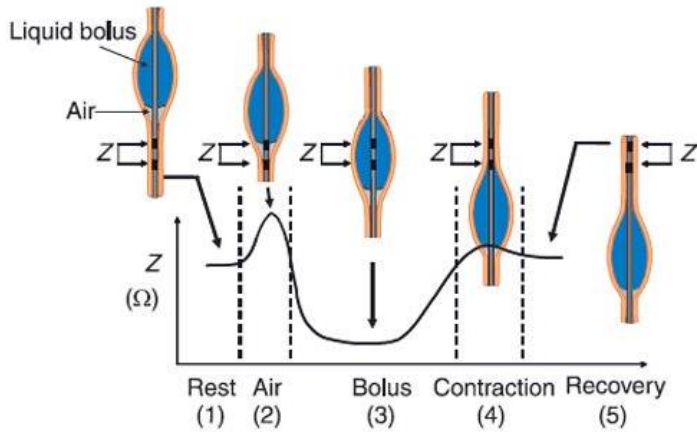
Modified Barium Swallow



Manometry



Impedance-pH monitoring



Impedance



Scintigraphy



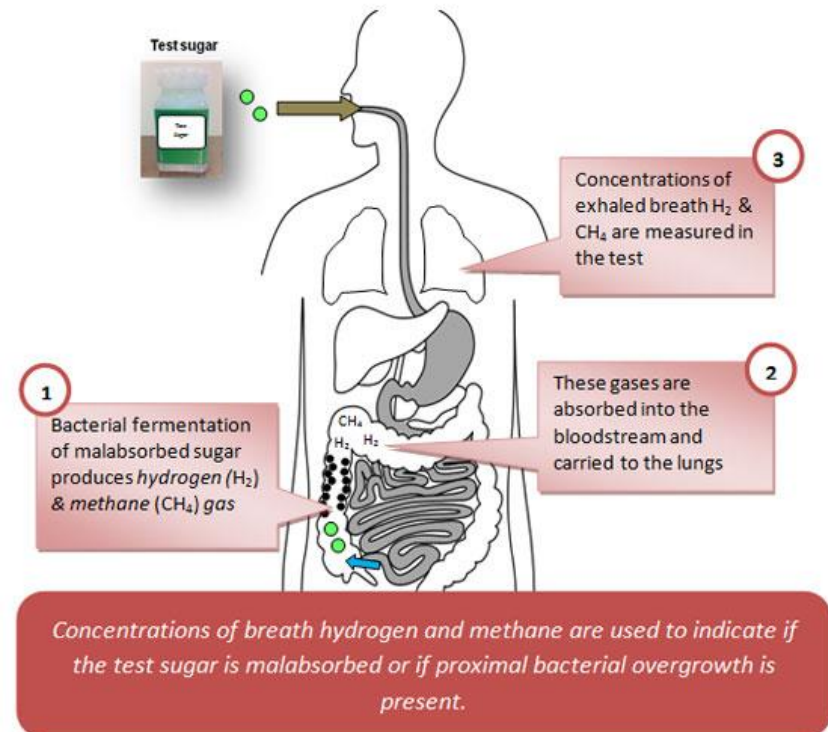
Capsule



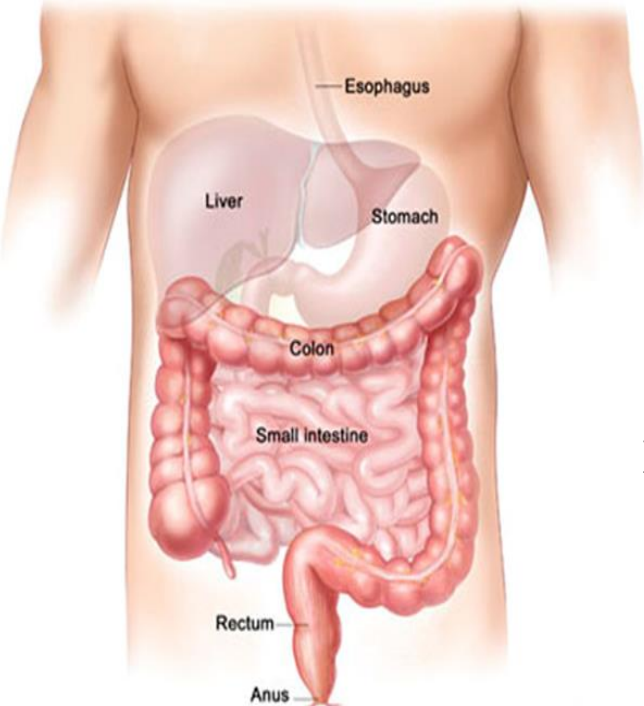
Endoscopy

SMALL INTESTINE BACTERIAL OVERGROWTH TESTING

- Breath Testing
 - Abnormal glucose hydrogen breath test
 - Abnormal lactulose hydrogen breath test
- Endoscopy
 - Jejunal aspiration
- Small bowel motility study



INVESTIGATIONAL PROCEDURES: LOWER GIT



Small Bowel Motility

- Manometry
- Scintigraphy
- Breath Testing
- MRI

Tissue Evaluation

- Enteroscopy
- Capsule

Large Bowel Motility

- Radio-opaque Markers
- Scintigraphy
- Wireless Motility Capsule
- MRI

Tissue evaluation

- Colonoscopy
- Capsule

Anorectal

- Manometry
- Endosonography
- Scintigraphy
- Electromyography
- Dynamic MRI
- Defecography
- Balloon Expulsion Test

Tissue evaluation

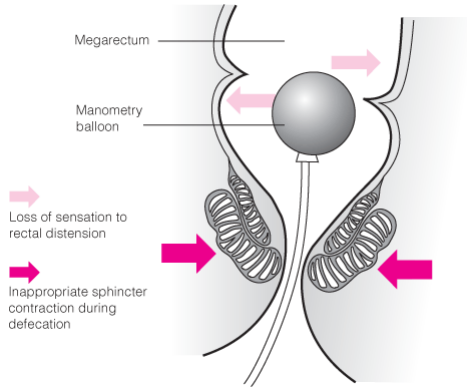
- Colonoscopy

National Cancer Institute

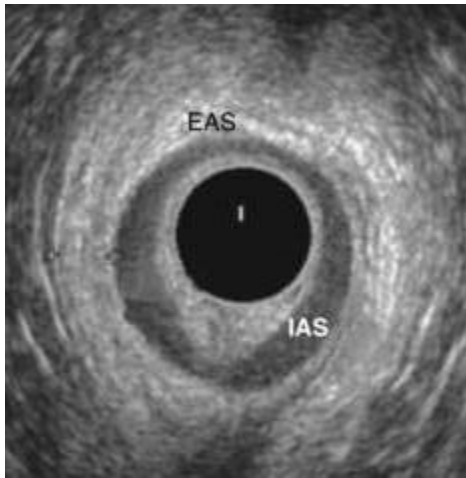


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Anorectal manometry



Anal endosonography



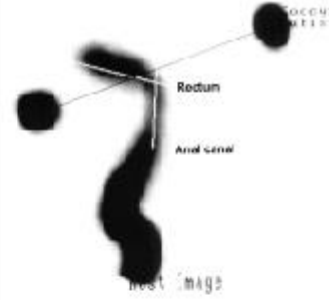
Electromyography



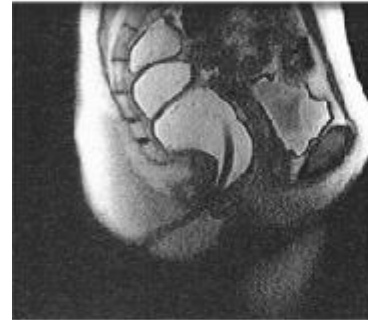
MR fluoroscopic and scintigraphic defecography



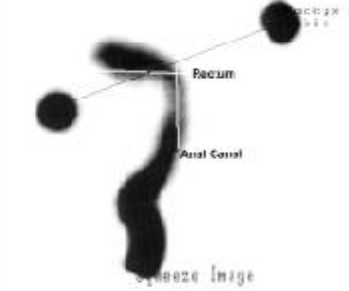
A



B



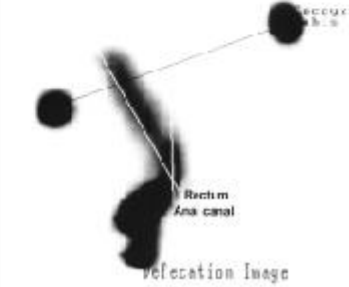
C



D



E



F

THE PROBLEM WITH GIT PROCEDURES

Invasive

Expensive

Often times do not provide guidance:

- “Findings consistent with Systemic Sclerosis”

Empiric treatments often the standard of care

HEARTBURN

Behavioral

- Smaller meals
- No eating 4 hours before bedtime
- Elevate head of the bed
- Avoid esophageal irritants
- Avoid tight fitting clothes
- Avoid alcohol
- Avoid tobacco

Invasive

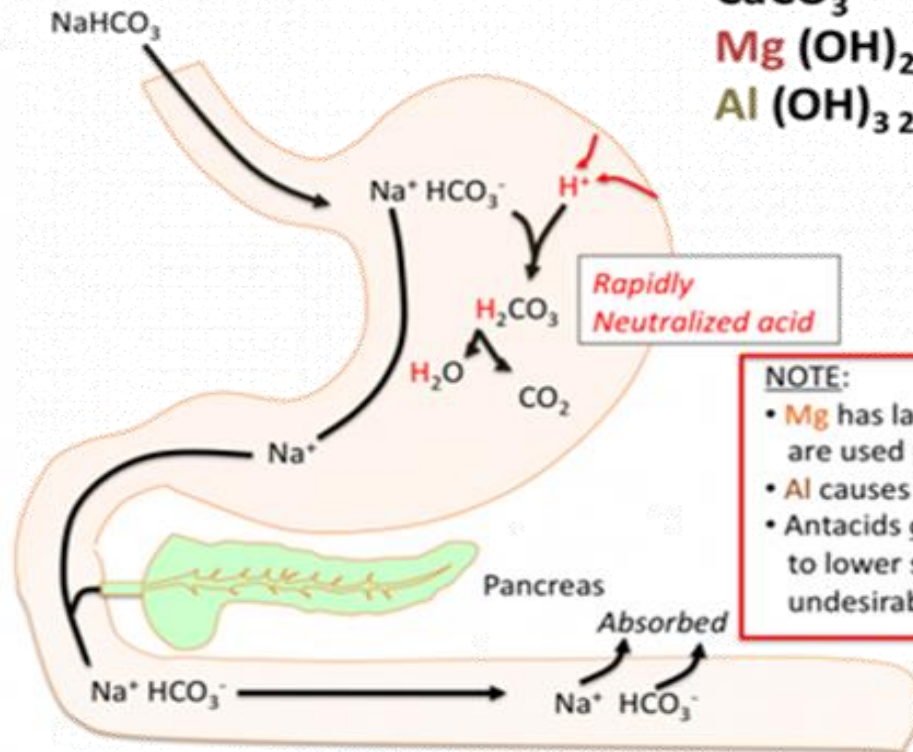
- Medications
 - Coating
 - Sucralfate/carafate
 - Acid neutralization
 - Acid suppression
 - Pro-motility

Procedure:

- Partial Nissen

ANTACIDS

Na Bicarbonate



Other Antacids:

CaCO_3 (H^+ binds w/ CO_3^{2-})

$\text{Mg}(\text{OH})_2$ (H^+ binds w/ OH^-)

$\text{Al}(\text{OH})_3$ (H^+ binds w/ OH^-)

NOTE:

- **Mg** has laxative effects (laxatives w/ Mg are used prior to endoscopy)
- **Al** causes constipation
- Antacids combining Al & Mg are used to lower stomach acid w/o producing undesirable constipation or diarrhea



Product	Alkaline ion	Aluminum	Calcium	Magnesium	Potassium	Sodium
Alka-selzer	bicarbonate				X	X
Andrews Antacid	bicarbonate		X			
Equate	bicarbonate	X	X	X		
Maalox (liquid)	bicarbonate	X		X		
Maalox (tablet)	bicarbonate	X				
Milk of Magnesia	hydroxide			X		
Pepto-Bismol	bicarbonate		X			
Rennie (tablets)	bicarbonate		X	X		
Rolaids	bicarbonate		X	X		
Tums	carbonate		X			
Mylanta	hydroxide	X		X		
Eno	bicarbonate					X
Gaviscon	bicarbonate		X			X
Droxygel	hydroxide	X		X		
Gelusil	hydroxide	X		X		

ACID SUPPRESSION: PPI

Proton Pump Inhibitors

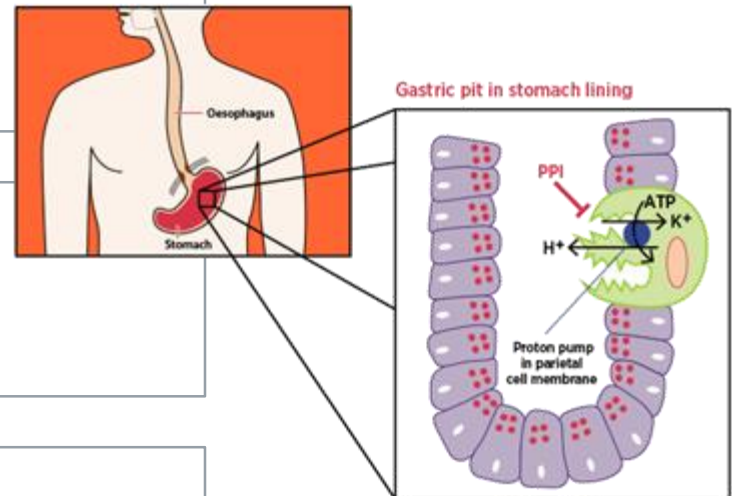
- Omeprazole (Prilosec, Zegrid)
- Lansoprazole (Prevacid)
- Dexlansoprazole (Dexilant)
- Esomeprazole (Nexium)
- Pantoprazole (Protonix)
- Rabeprazole (Acidphex)

Cautions

- Gastric acid is important for breakdown of food and release of micronutrients.
- High dose and/or long-term use, increased risk of bone fractures.
- Small bacterial overgrowth.

Indications

- Symptomatic GERD
- Peptic ulcer disease
- As part of *Helicobacter pylori* eradication therapy
- Barrett's esophagus
- Eosinophilic esophagitis
- Laryngopharyngeal reflux causing laryngitis and chronic cough



ACID SUPPRESSION: H2 BLOCKERS

H2 Blockers

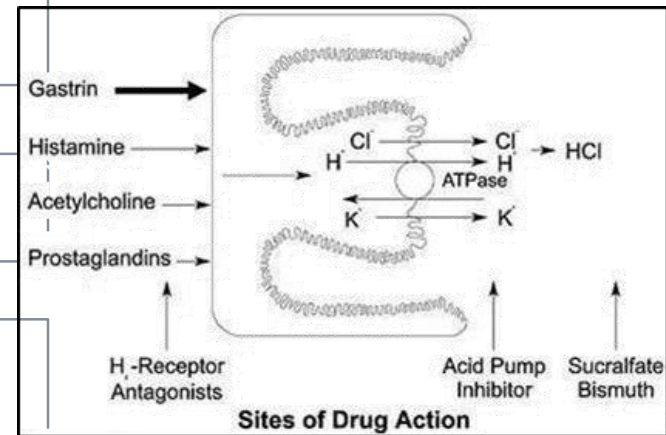
- Ranitidine (Zantac)
- Famotidine (Pepcid)

Cautions

- Many drug interactions, including calcium channel blockers.

Indications

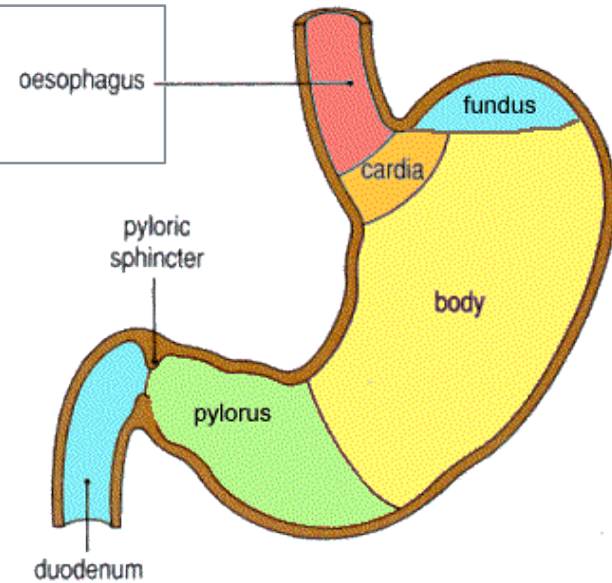
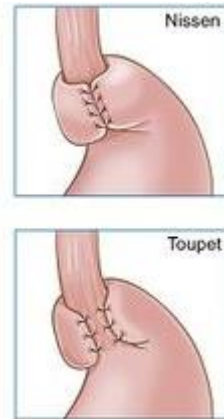
- Peptic ulcer disease
- GERD



SURGICAL OPTIONS: REFLUX

Patients with Normal Motility

- Nissen Laproscopic Fundoplication
- Toupet Partial Fundoplication



PRO-MOTILITY: UPPER GIT

Behavioral

- High-fiber foods can make gastroparesis worse
 - Oranges, broccoli, apple with the skin on, wheat, beans, nuts, kale, and red cabbage.
- Fatty foods can make gastroparesis worse
 - Butter, cheese, processed meats, canned goods, and any fried meat.
- Minimize exacerbating medications:
 - Narcotic
 - Tricyclic antidepressants
 - Calcium channel blockers
 - Clonidine
 - Dopamine agonists
 - Lithium
 - Nicotine
 - Progesterone

US Medication Options

- Metoclopramide (Reglan®)
- Erythromycin (low dosages, not antibiotic dosing levels)
- Domperidone (Motilium®, now only under special FDA protocols)
- Tegaserod (Zelnorm®, Zelmac®, now only available under special FDA protocols)

Mechanism:

- Speeds up stomach emptying and movement of the upper intestines.
- Caution: Cardiac toxicity

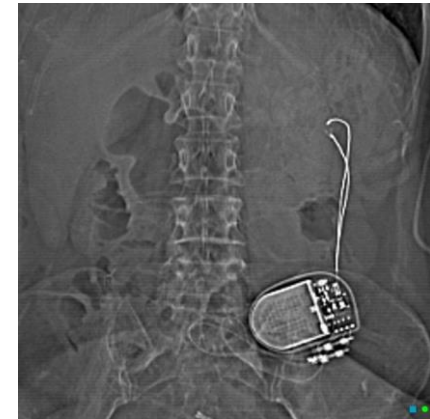
Treatment of nausea



SURGICAL OPTIONS: GASTROPARESIS

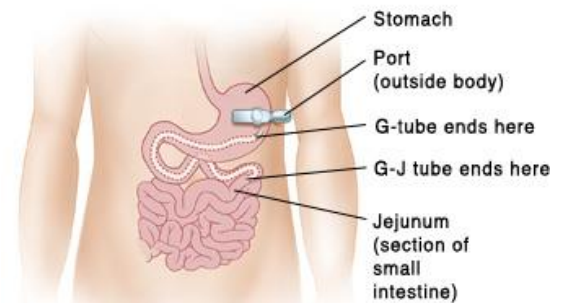
Gastric Pacemaker

- Battery-operated device is implanted into the abdomen
- Sends electrical pulses to the muscles of the abdomen to increase gastric emptying



Feeding Tube

- Usually inserted directly into the small intestine through the abdomen



SMALL INTESTINAL BACTERIAL OVERGROWTH

Characteristics

- Abdominal Pain
- Distention
- Diarrhea

Behavioral

- Minimize medications
 - Hormone replacement
 - PPI

Therapeutics

- Pro-motility drugs
- Initiate or cycle antibiotics
- Probiotic

- Nutrition

CONSTIPATION

Behavioral

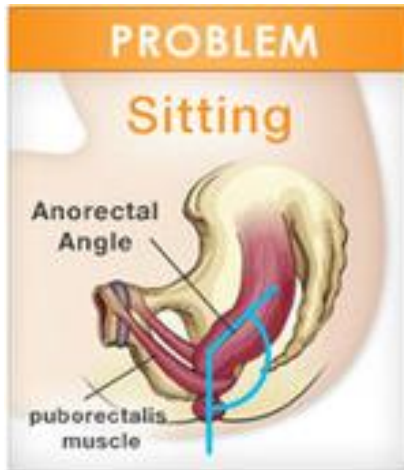
- Physical activity
- Adequate fluid intake
- Stop constipating medications

Therapeutics

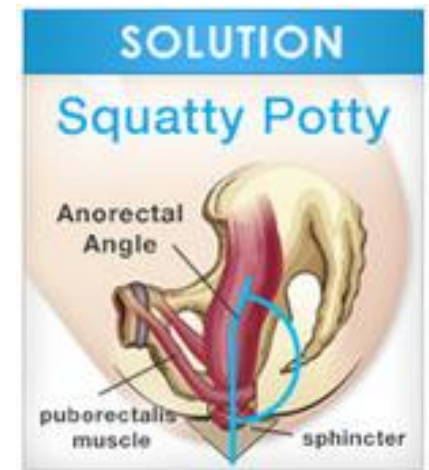
- Osmotic Laxatives
- Stimulants:
 - Lubiprostone
 - Linaclotide
- Pro-motility:
 - Pyridostigmine
- Biofeedback
- Sacral Nerve Stimulation

TECHNIQUE

How it works



THE PUBORECTALIS MUSCLE
"CHOKES" THE RECTUM
MAINTAINING CONTINENCE



SQUATTING RELAXES THE
PUBORECTALIS MUSCLE ALLOWING
EASIER ELIMINATION

DIARRRHEA & SOILAGE

Important Considerations

- Medication review:
 - Magnesium
 - Cholesterol-lowering
 - Gout medication
 - Anti-inflammatories
 - Metformin
 - Thyroid medication
- Recent antibiotics:
 - C. Difficile toxin
- Travel:
 - Giardia antigen
 - Ova/ parasites

Behavioral

- Pelvic floor exercises
- Biofeedback

Therapeutics

- Octreotide
- Bile acid sequestrants
- Anti-depressants

Dietary Considerations

- Lactose intolerance
- Sugar substitutes
- Food allergies
 - Gluten



NUTRITIONAL CONSIDERATIONS

- The physical ability to digest food including chewing, swallowing, absorption,

F	Fermentable	
O	Oligosacchrides	Fructans
D	Disaccharides	Lactose
M	Monosaccharides	Fructose
A	And	
P	Polyols	Sorbitol

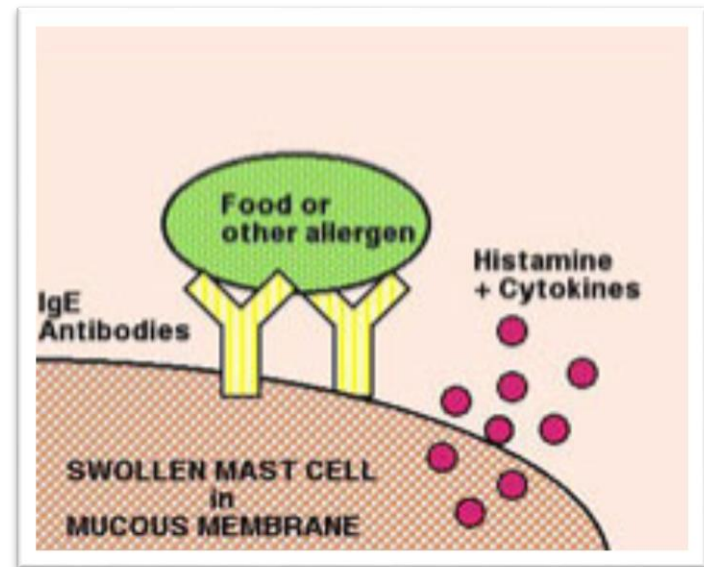
FODMAP Diet:

- Short-chain carbohydrates
- Poorly absorbed
- Osmotically active
- Rapidly fermented
- Result in symptoms of abdominal bloating and pain.

lifestyle changes.

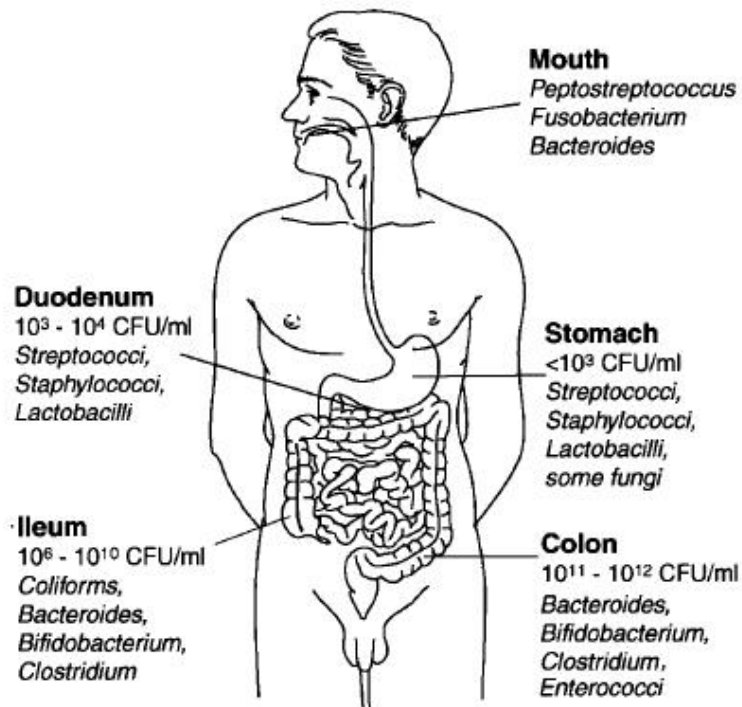
ALLERGEN TESTING

- The role of food allergy in SSc is unclear.
- Immunologic methods used in evaluating food allergies may include:
 - Skin prick testing
 - Atopy patch testing
 - Blood RAST testing
- Goal is to identify trigger and restore gut balance.



GOOD GUT BACTERIA

Figure 1. Micro-organisms in the GI Tract



- Changes in the distribution or composition of the GIT microbiota may alter intestinal physiology and immunity.
- Environmental, nutritional, and gut-derived triggers that cause microbiome perturbations can drive an abnormal overload of dysbiosis, influencing gut barrier.
- The change in composition of the GIT biofilm communities in response to immunosuppressive therapies has not been well-characterized.

SSc-GIT HOMEOSTASIS

Probiotics

- Live microorganisms that, when administered in adequate amounts, have shown potential benefits in SSc patients.

Prebiotics

- Non-absorbed carbohydrate polymers that promote metabolic activity and expansion of presumed beneficial gut bacteria.

Rifaximin

- Non-absorbable antibacterial activity, including prevention of gut mucosal adherence and bacterial translocation.

Fecal Microbiota

- Recipients following transplantation becomes more diverse and more similar to the donor profile.

In Summary

- GIT symptoms in SSc are common.

- A personalized approach to each patient and a focus on nutrition is critical.

- Improved use of questionnaires, bedside testing, and biopsy specimens will improve management.

- The role of dysbiosis and immune dysfunction in SSc-GIT needs to be defined in management.

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QUESTIONS?