Systemic Sclerosis Gastrointestinal Manifestations: Practical Tools for its Assessment and Management

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Disclosure

- I have no financial disclosures or commercial relationships.

Overview

- Review how gastrointestinal tract symptoms are assessed in Systemic Sclerosis (SSc).
- Highlight common gastrointestinal tract conditions in SSc.
  - Gastroesophageal reflux disease (GERD)
  - Gastroparesis
  - Food Allergy and Intolerance
- Discuss special management considerations for SSc-related gastrointestinal conditions.

Systemic Sclerosis Gastrointestinal Tract (SSc-related GIT)

Importance:

- The GIT is the most commonly involved internal organ in SSc.
- GIT involvement is the presenting feature in 10% of SSc patients
- GIT involvement occurs during disease course in up to 95% of SSc patients.

Challenges:

- SSc –related GIT clinical presentation and disease course varies.
- Symptoms often precede laboratory or anatomical abnormalities.
- Absence of symptoms does not exclude esophageal dysfunction.

Gyger G. Curr Rheumatol Rep 2012; Forbes A. Rheumatol. 2009; Hansi N. Clinical and Experimental Rheumatology. 2014.

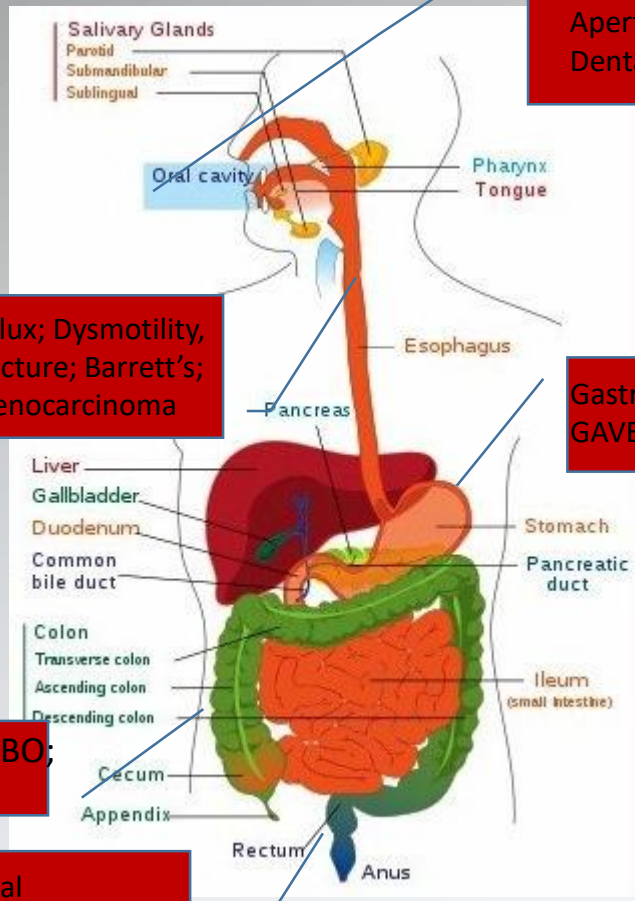
Prevalence by Organ Involvement

Symptom Assessment:

- Questionnaires
- Categorical Severity
- Objective GIT testing

Testing:

- Laboratory
- Direct tissue visualization
- Motility
- Imaging



Small Oral Aperture; Sicca; Dental issues

Reflux; Dysmotility, Stricture; Barrett's; Adenocarcinoma

Gastroparesis; ulcer; GAVE

Pseudo-obstruction; SIBO; Diverticuli; Megacolon

Fecal incontinence; rectal prolapse

Gyger. Curr Rheumatol Rep. 2012; Bae. Clin Exp Rheumatol. 2013

Gastro-esophageal Symptoms: Assessment by Questionnaire

Upper Tract Symptoms	Patient Burden
GERD-Q[1]*	6 Questions
UCLA SCTC GIT 2.0[2]	8 Questions
NIH PROMIS[3]* • Reflux • Disruptive Swallowing • Nausea and Vomiting	 8-13 Questions 7 Questions 3-4 Questions

*link calculates scores: http://www.soapnote.org/digestive-system/gerdq; http://www.healthmeasures.net

[1]Jonasson. Aliment Pharmacol Ther. 2013; [2]Khanna. Arthritis Rheum. 2009; [3]Spiegel. Am J Gastroenterol.2014

THE UCLA SCTC GIT 2.0 QUESTIONNAIRE

Table 1. The GerdQ questionnaire … ymptoms over the previous week

Question		… ts) for symptom … days	4–7 days
1. How often did y			3
2. How often did y throat or mout			3
3. How often did y			0
4. How often did y			0
5. How often did y heartburn and/			3
6. How often did y regurgitation, Rolaids, Maalo			3

	In the past 1 week, how often did you …	(CHECK ONE RESPONSE FOR EACH QUESTION) No Days[0]	1-2 Days[1]	3-4 Days[2]	5-7 Days[3]
REFLUX	1. … have difficulty swallowing solid food?	☐	☐	☐	☐
	2. … have an unpleasant stinging or burning sensation in your chest (heartburn)?	☐	☐	☐	☐
	3. … have a sensation of bitter or sour fluid coming up from your stomach into your mouth (acid reflux)?	☐	☐	☐	☐
	4. … have heartburn on eating 'acidic' foods such as Tomatoes & Oranges?	☐	☐	☐	☐
	5. … regurgitate (throw up or bring up small amounts of previously eaten food)?	☐	☐	☐	☐
	6. … sleep in a 'raised' or an 'L shaped' position?	☐	☐	☐	☐
	7. … feel like vomiting or throwing up?	☐	☐	☐	☐
	8. … vomit or throw up?	☐	☐	☐	☐

Gastroesophageal Reflux

PROMIS Scale v1.0 – Gastrointestinal Reflux 13a

Think of the area behind your breastbone (the area extending from the base of your throat to mid-chest). In the past 7 days…

7 GISX14 How often did you feel burning in the red area shown in the picture — that is, behind the breastbone?

- ☐ 1 Never
- ☐ 2 One day
- ☐ 3 2-6 days
- ☐ 4 Once a day
- ☐ 5 More than

8 GISX21 How often did you feel burning in your throat?

- ☐ 1 Never
- ☐ 2 Rarely
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Always

In the past 7 days…

9 GISX22 How often did you burp?

- ☐ 1 Never → **If Never, go to #11**
- ☐ 2 One day
- ☐ 3 2-6 days

GERD has 4 specific symptom clusters:

1) Liquid and food sensation
2) Painful sensations
3) Belching and hiccups
4) Head and neck sensations

11 GISX25 How often did you have hiccups?

- ☐ 1 Never
- ☐ 2 Rarely
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Very often

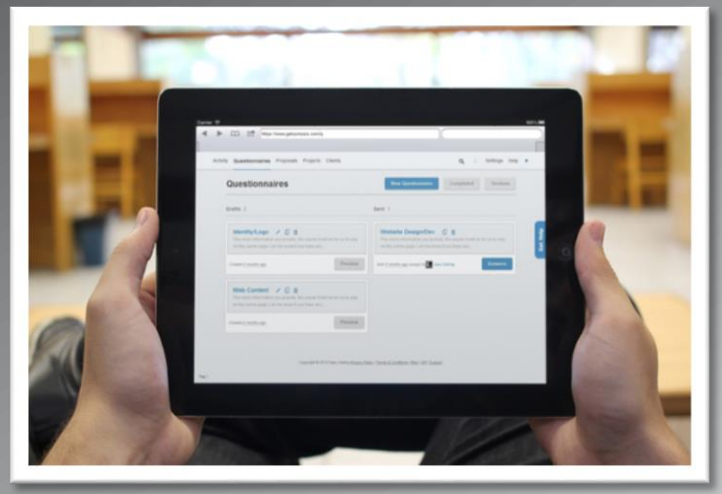
12 GISX28	How often did you feel like there was a lump in your throat?

- ☐ 1 Never → **If Never, you are finished.**
- ☐ 2 Rarely
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Very often

13 GISX30	How much did having a lump in your throat bother you?

- ☐ 1 Not at all
- ☐ 2 A little bit
- ☐ 3 Somewhat
- ☐ 4 Quite a bit

Practical Aspect of Using Questionnaires



Goal is for symptom identification.

Minimal patient time burden.

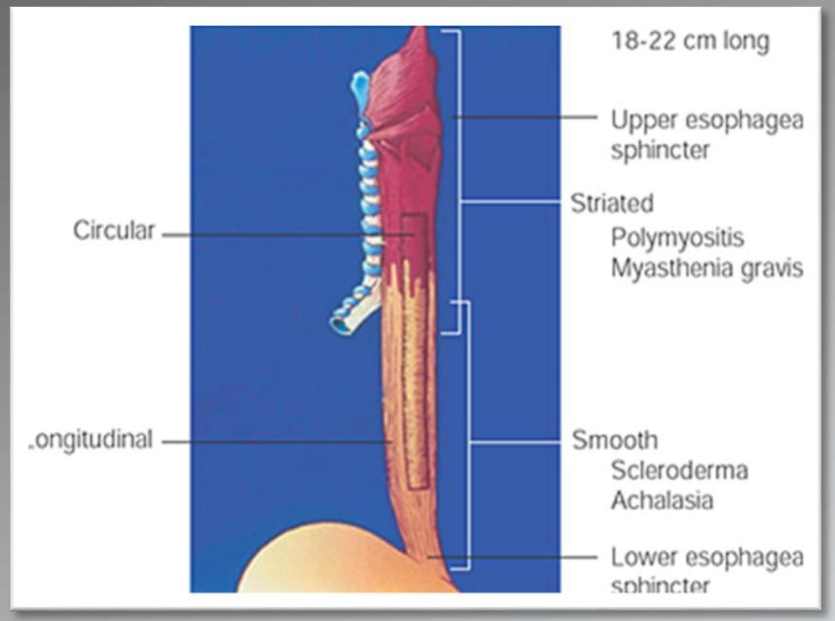
With no cost, can guide care decisions.

Not clear if improves patient satisfaction.[1]

[1]*Almario. Am J Gastroenterol. 2016*

Assessing Heartburn and Difficulty Swallowing

90% prevalence of esophageal symptoms in SSc patients.



Heartburn	Is the patient adhering to behavioral interventions?
	Is the patient on treatment?
	Is the patient considering surgical intervention?
Difficult swallowing	Liquids?
	Solids?
	Regurgitation?

GERD Management Considerations

Behavioral	Invasive

• Smaller meals
• No eating 4 hours before bedtime
• Elevate head of the bed
• Avoid esophageal irritants
• Avoid tight fitting clothes
• Avoid alcohol and tobacco
	• Medications
	  • Coating
	  • Sulfacrate/carafate
	  • Acid suppression
	  • Acid neutralization
	  • Pro-motility
	
	Procedure:
	• Partial Nissen

Current Management Strategies for GERD

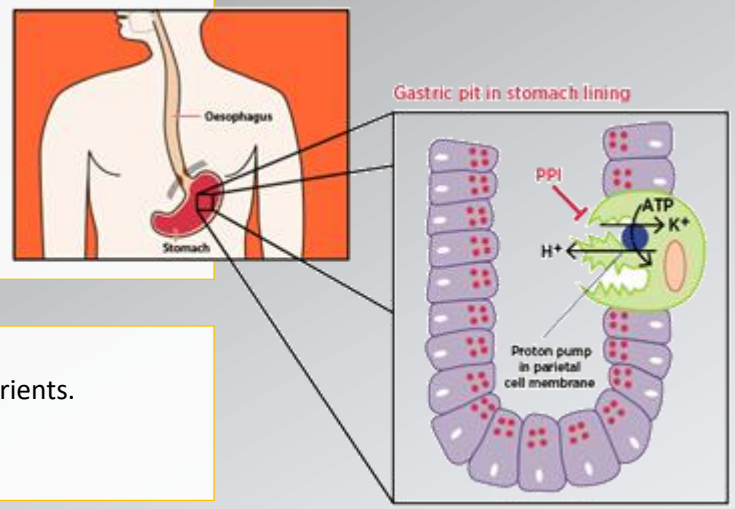
- Rely on empiric trials of acid suppression as both therapeutic and diagnostic tools.

- The PPI test:
  - Patients are started on a single-dose proton pump inhibitor (PPI).
  - Patients that fail single-dose PPI are increased to twice daily.
  - Sensitivity 80% for GERD diagnosis
  - Specificity 74% for GERD diagnosis
  - Not studied in patients with complex symptoms.
  - Long-term management has not been adequately studied.

Proton Pump Inhibitor Acid Suppression

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

Histamine (H2) Blockers Acid Suppression

H2 Blockers

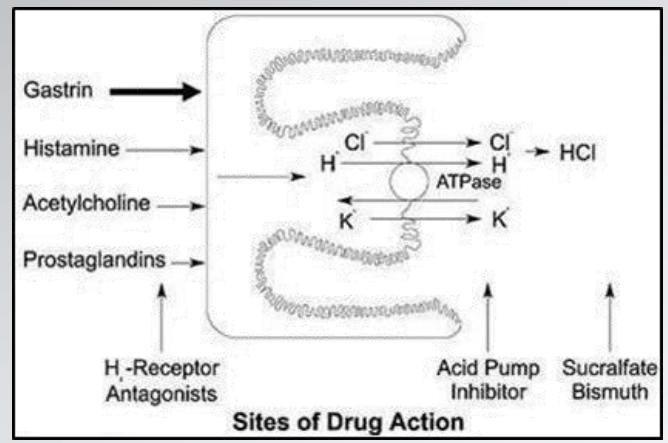
- Ranitidine (Zantac)
- Famotidine (Pepcid)

Cautions

- Many drug interactions, including calcium channel blockers.

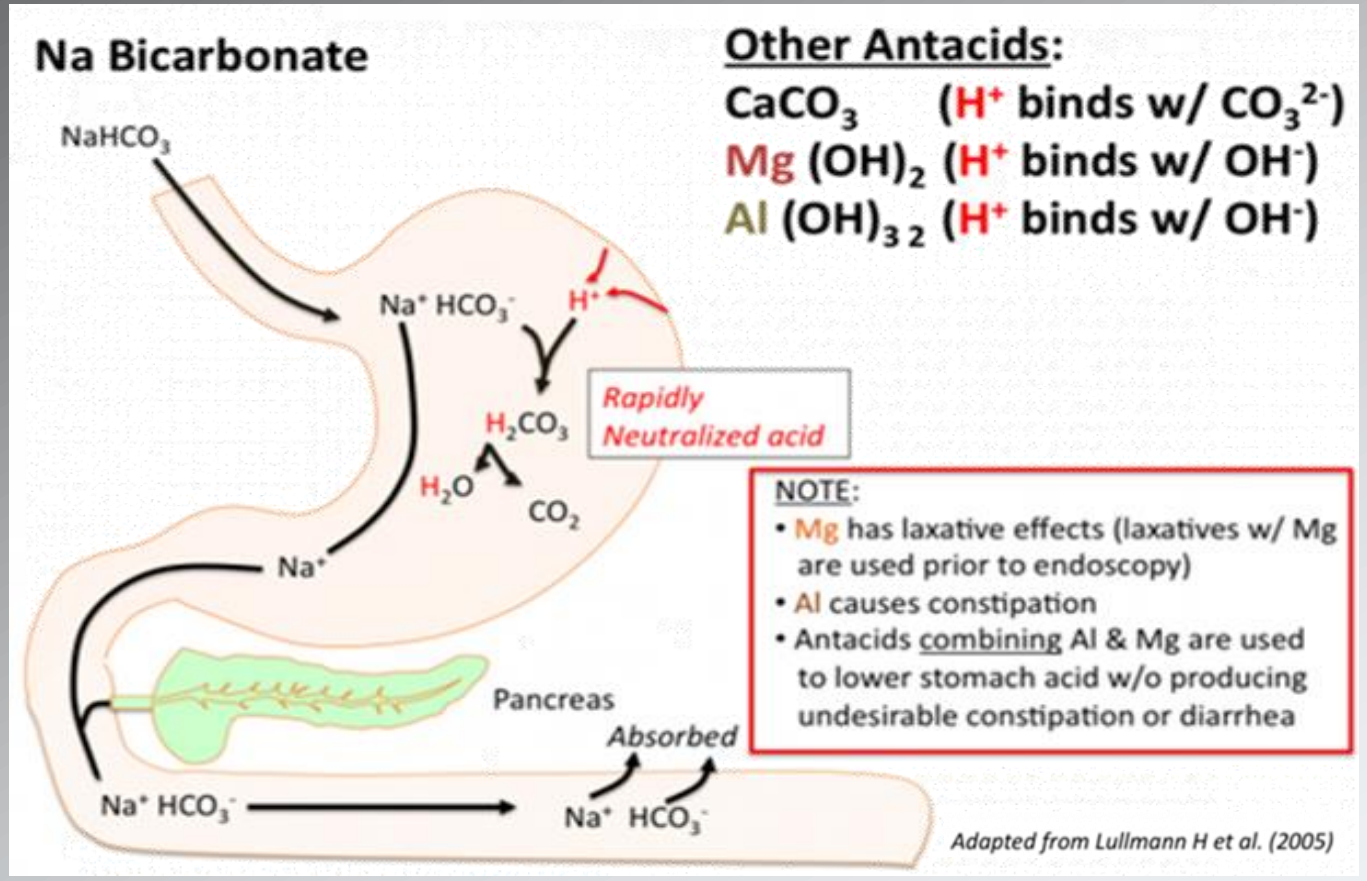
Indications

- Peptic ulcer disease
- GERD



Sites of Drug Action

Acid neutralization with Antacids



Radiographic Assessment: Barium Swallow

Swallow evaluation with speech language pathologist

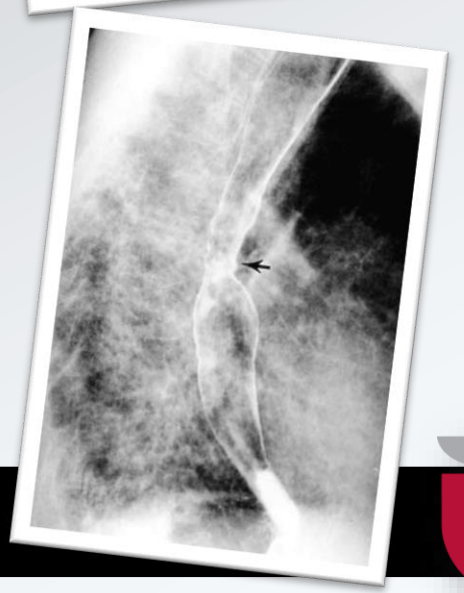
- Ordered for concern for aspiration.

Upper GI series or sine esophagram

- Single contrast provides information on stricture.
- Double contrast provides information on mucosal abnormalities:
  - Erosive esophagitis, hiatal hernia, cancer, and abnormal motility.

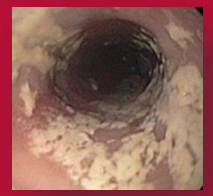
Practical Considerations:

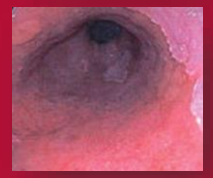
- Not useful for making a diagnosis of GERD.
- Time:~15 minutes to 1 hour
- Cost: ~$305 (with speech therapy $516)



Esophagogastroduodenoscopy (EGD)

Diagnostic:





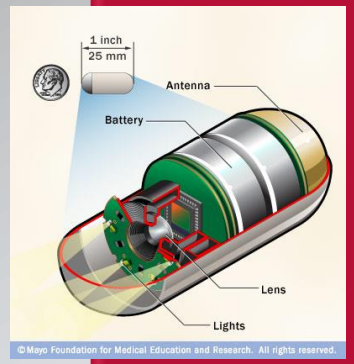
- Esophagitis:
  - Infectious
  - Pill-induced
  - GERD-related
  - Barrett's
  - Eosinophilic
- GAVE
- Celiac

Therapeutic

- Stricture dilation

Practical Considerations:

- Preparation: ~12 hours
- Time: ~ 2 hours (with recovery)
- Cost: $1,170 to $2,400.



Alternative wireless capsule

- Indicated for identification of occult bleeding in small bowel.
- Contraindications:
  - Stricture
  - Gastroparesis
- Time: ~30 hours
- Cost: ~$1,400

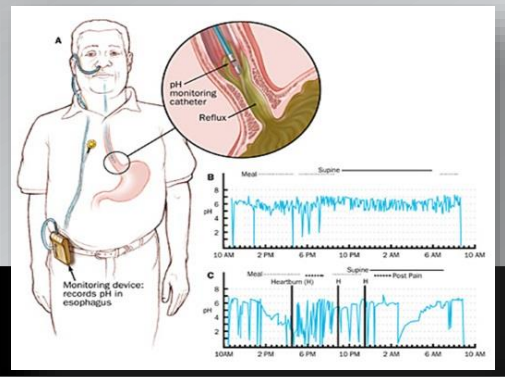
GERD Monitoring

pH-monitoring in SSc:

- Assessing symptom relationship to reflux
- Assessing efficacy of therapy
- Indicated before surgical referral

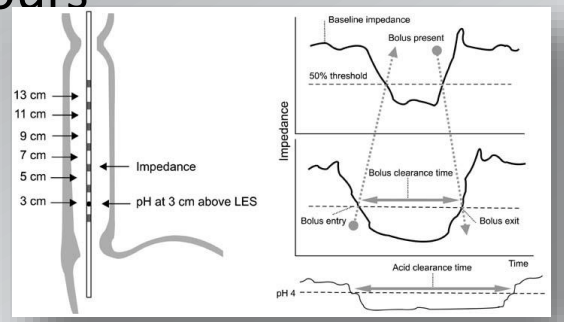
Catheter-based:

- Assessing if reflux reaching pharynx
- Composite score:
  - % time pH < 4
  - # of reflux episodes
  - # of episodes > 5 minutes
- Time: 24-48 hours
- Cost: $225-1500



pH-Impedance

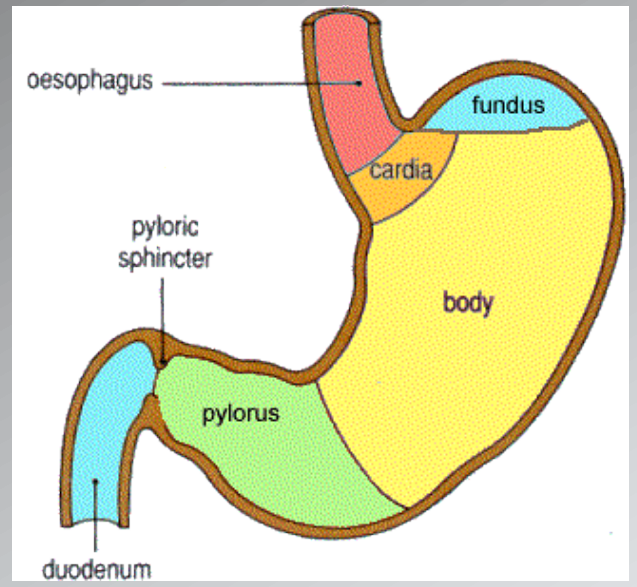
- Assessing non-acid reflux
- Time: ~24 hours
- Cost: $450



Wireless:

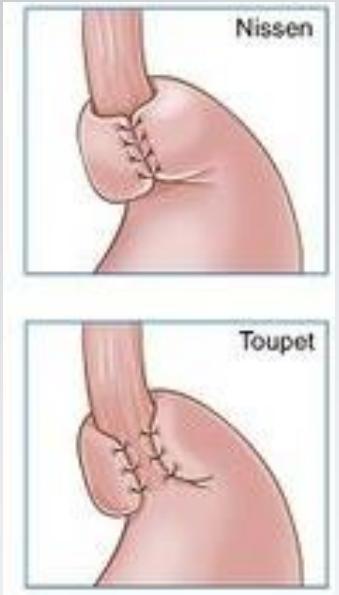
- Cannot assess pharyngeal reflux
- Time: 48-96 hours
- Cost: $1,000

GERD Surgical Options



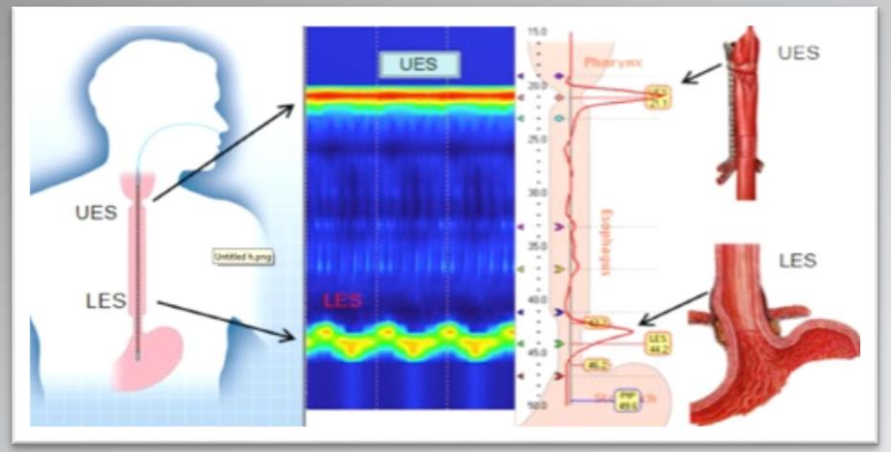
Patients with Normal Motility

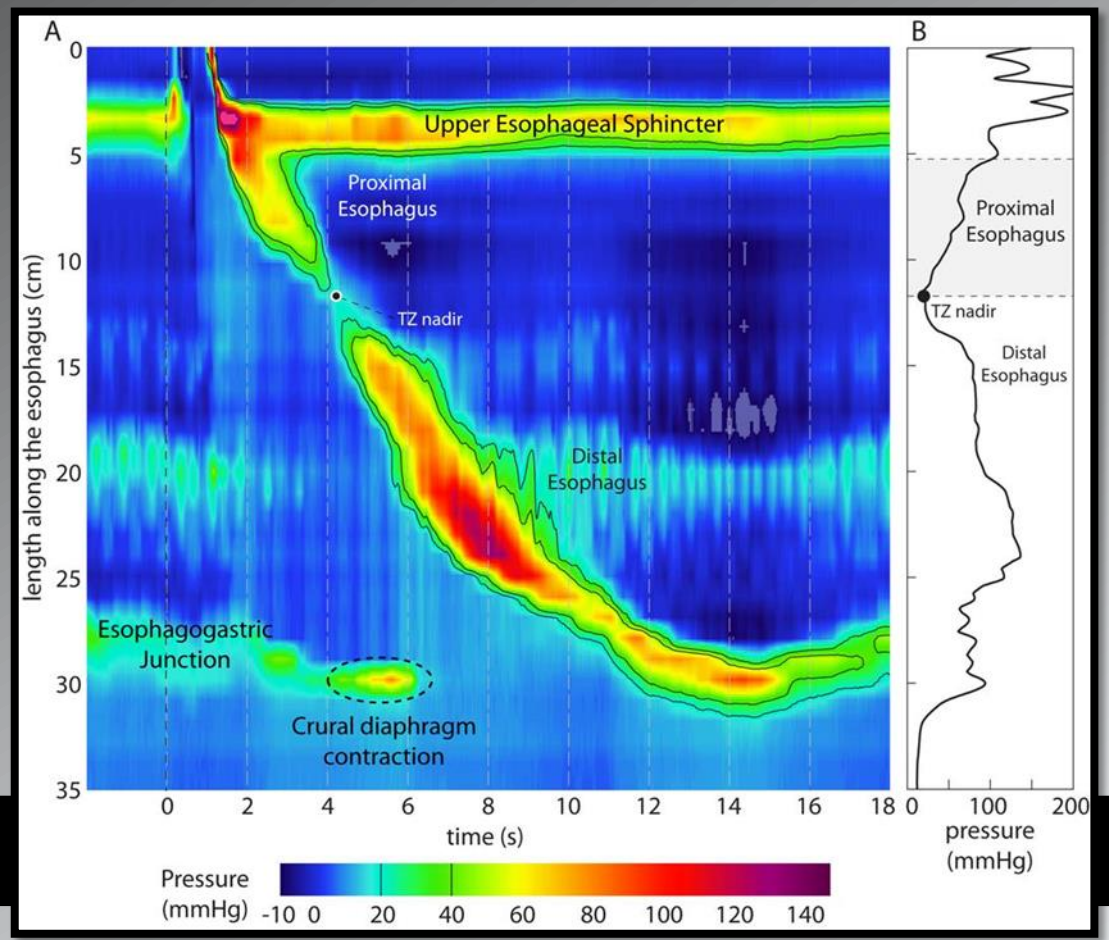
- Nissen Laproscopic Fundoplication
- Toupet Partial Fundoplication

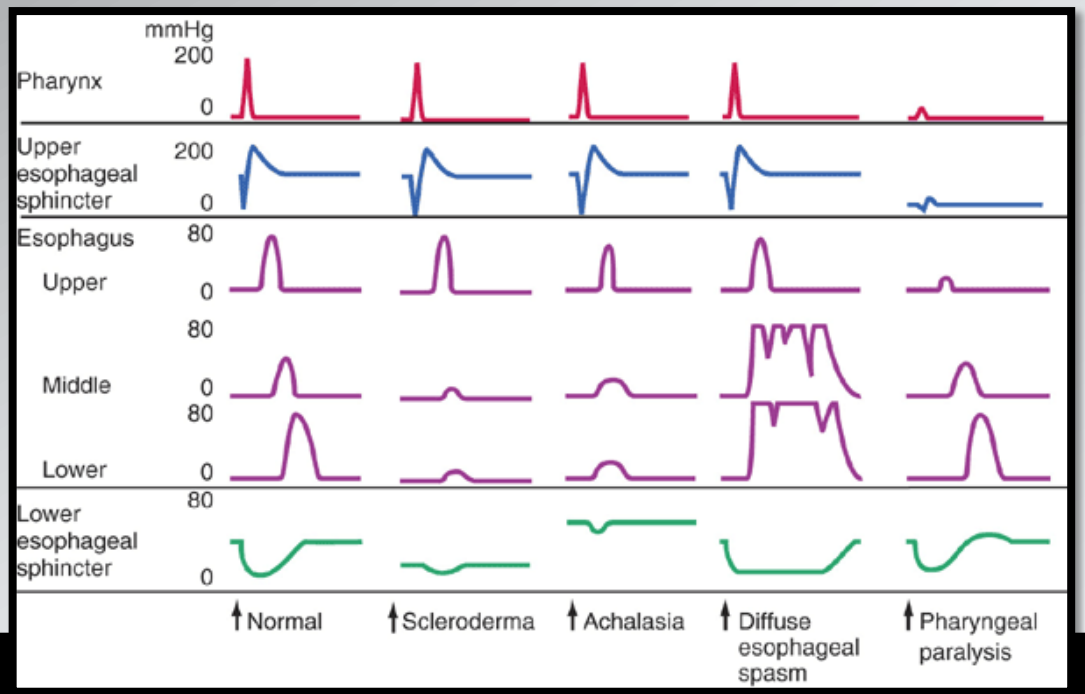


Motility assessment: Manometry

- Indicated if reflux testing normal
- Practical Considerations:
  Time: ~30-40 minutes
  Costs: ~$500-1500







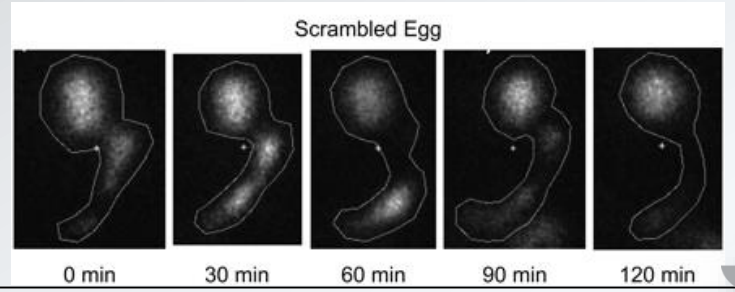
Nausea, Vomiting and Abdominal Distention

Abdominal Imaging: Pseudo-obstruction

- Indicated if acute mechanical obstruction suspected.
- Practical consideration:
  - Outpatient: Abdominal radiograph
  - Inpatient: CT without contrast
  - Outcomes[1]:
    - 70% resolution
    - 9% surgical resection
    - 16% mortality

Motility testing: Gastric Emptying Study[2]

- Intestinal dysmotility occurs in 40-90%.
- Indicated if gastroparesis suspected.
- Obtain prior to initiation of pro-kinetics[3].
- Practical considerations:
  - Time: ~5 hours
  - Cost: $2800



[1]Mecoli C. *J Rheumatol*. 2014;[2]Klingensmith WC. *J Nucl. Med. Technol*. 2008;[3]Camilleri M. *Am J Gastroenterol*. 2013

Gastroparesis Management

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

Treatment Options

- Metoclopromide (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

Botulinum toxin injections are not recommended

Camilleri. Am J Gastroenterol. 2013

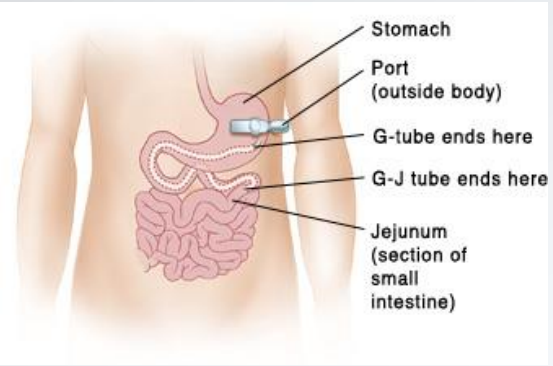
Surgical Options: Gastroparesis

Gastric Electrical Stimulation

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

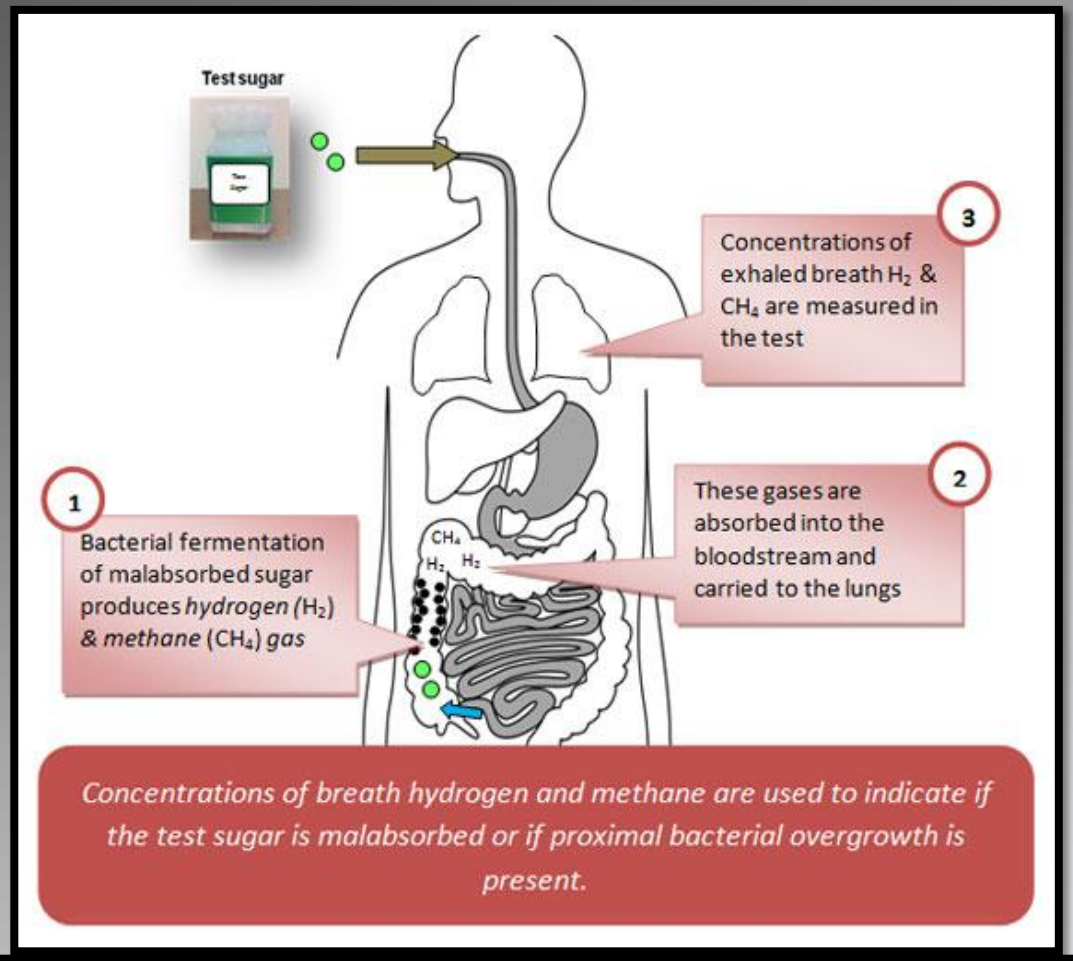
Feeding Tube

- Usually inserted directly into the small intestine through the abdomen



Camilleri. Am J Gastroenterol. 2013

Assessing Abdominal Pain and Distention



Is small intestinal bacterial overgrowth (SIBO) suspected[1]?

- Effects 50% of SSc patients.
- Breath testing[2]:
  - Sensitivity ranges form 65-70%
- Laboratories:
  - Serum[3]: carotene, vitamin D-25OH, B12, iron.
  - Fecal calprotectin[4]

[1]Marie. Rheumatology. 2007; [2]Ghoshal. Eur J Gastroenterol Hepatol. 2014; [3]Nagaraja. Current Treatment Options in Rheumatol. 2015; [4]Marie. Autoimmun Rev. 2015

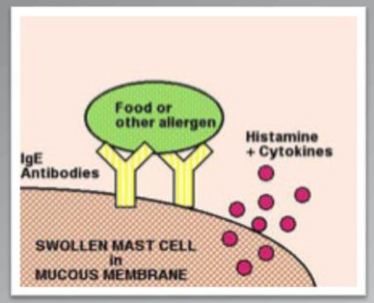
Small Intestinal Bacterial Overgrowth

Characteristics	Behavioral	Therapeutics

• Abdominal Pain
• Distention
• Diarrhea
	• Minimize certain medications
	  • Hormone replacement
	  • PPI dose
		• Pro-motility drugs
		• Initiate or cycle antibiotics
		• Probiotic
		
		• Nutrition

Food Allergies and Intolerance

- Food allergy is an urgent, severe reaction that can be identified by allergy testing.
  - Skin prick testing
  - Atopy patch testing
  - Blood RAST testing



- Food intolerance or sensitivity has less severe symptoms, but is very uncomfortable and can be associated with pain and distention.
  - Lactose
    - Lactose-free products.
  - Fructose
    - Limit fruit (including juices and dried), honey, high-fructose corn syrup, and alcohol.

Nutritional Considerations

- The physical ability to digest food including chewing, elimination
- ith dietary lifestyle

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.

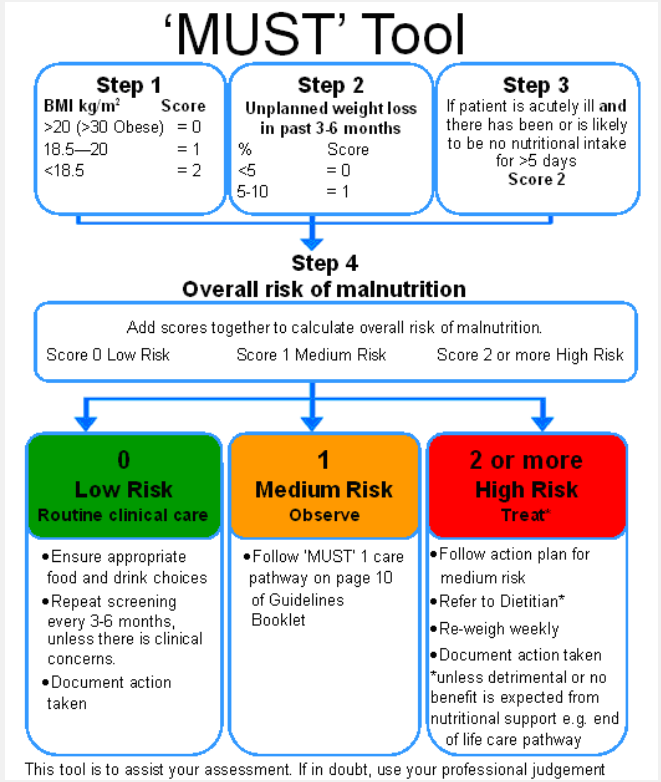
https://stanfordhealthcare.org/content/dam/SHC/for-patients-component/programs-services/clinical-nutrition-services/docs/pdf-lowfodmapdiet.pdf

http://www.med.monash.edu/cecs/gastro/fodmap/iphone-app.html

FODMAP Education

- Low FODMAP education consists of initially eliminating FODMAPs from the diet for 6-8 weeks.
- Following symptom resolution, gradual reintroduction of foods to determine individual tolerance.
- FODMAP dietary education should be provided by a trained dietician.

Weight Loss and Nutritional Issues



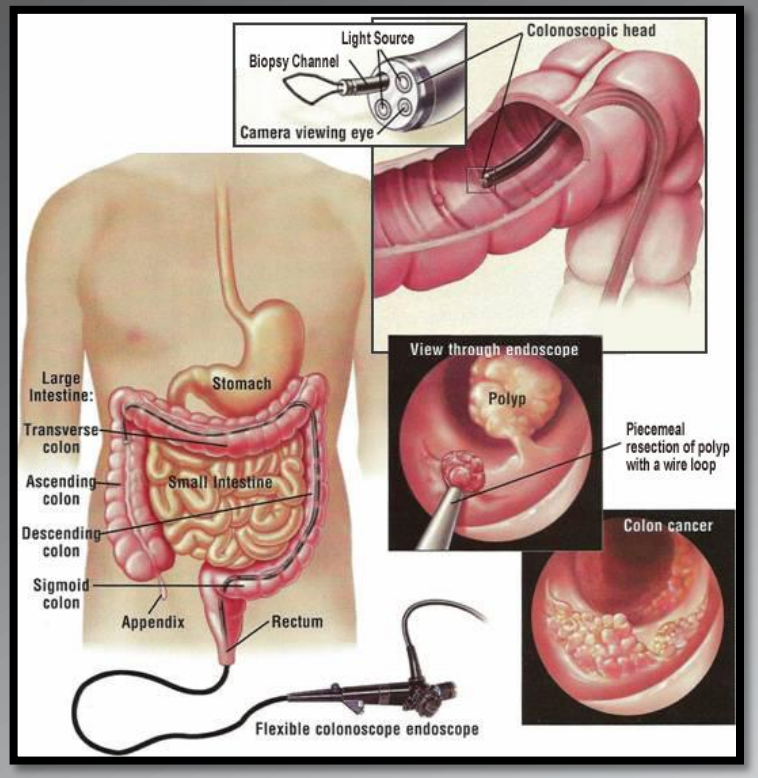
Prevalence of malnutrition in 18-25% of SSc patients.

Malnutrition occurs across BMI or dietary self-report.

Clinical assessment tools:

- Malnutrition universal screening tool
- Laboratory: Serum carotene, folate, pre-albumin.

Prevalence of colon and anorectal disorders

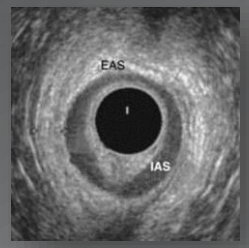


- Colonic involvement is seen in up to 20-50% of SSc patients.
- Anorectum is involved in 50-70%.
- Fecal incontinence occurs in over 20%.
- Digital rectal exam is first step in evaluation.
- Colonoscopy:
  - All fecal incontinence patients.
  - All SSc patients > age 50.
  - Diagnostic and therapeutic.
  - Cost:

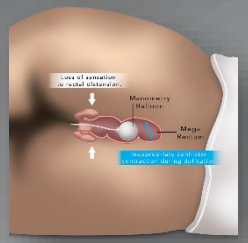
Franck-Larsson. J Gastroenterol Hepatol. 2009; Mawdsley. Rheumatology. 2006

Assessment of Incontinence

Gastroenterology/Colorectal Surgeon

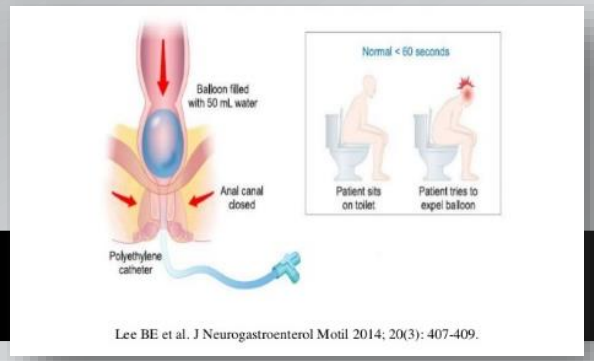


- Endo-sonography:
  - Time: 45 minutes
  - Cost: $175



- Manometry:
  - Time: 60 minutes
  - Cost: $ 600-1500

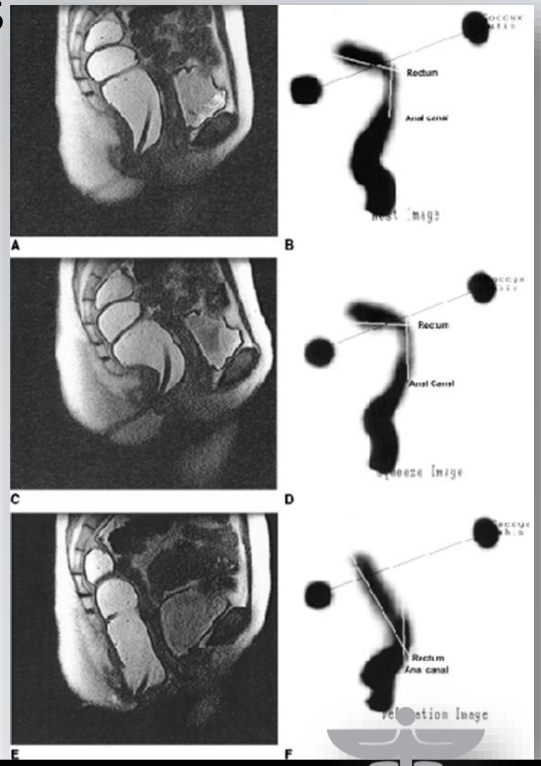
- Balloon Expulsion test:
  - Cost: $275



Lee BE et al. J Neurogastroenterol Motil 2014; 20(3): 407-409.

Radiographic Assessment:

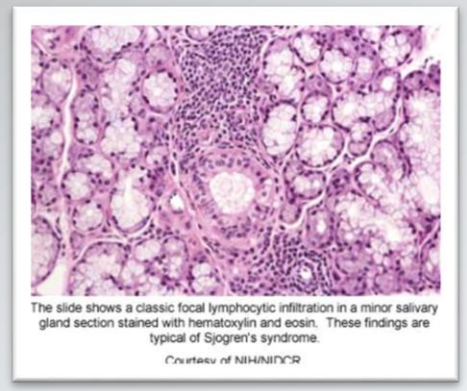
- Scintigraphic Defecography:
  - Time: ~ 3 hours
  - Cost: $500
- Dynamic MRI:
  - Time: ~1 hour
  - Cost: $750



Additional Considerations: Oral-Facial Assessment

- Increase incidence of Sjögren's syndrome in SSc[1].
  - Practical assessment: Documentation of dentition in clinical assessment for dental coverage.

Gold standard diagnosis:
- >50 lymphocytes around a salivary gland duct is defined as a focus.
- ≥ 1 focus/4mm^2 is diagnostic



- Sub-lingual frenulum changes[2].
  - Practical assessment: Clinical assessment of sublingual frenulum may assist in speech therapy evaluation.

[1]Tseng CC, et al. Autoimmunity. 2015; [2]Frech TM, et al. JCR. 2015

SSc-related GIT Management Care Team

Components

- Team based care with Rheumatology, Gastroenterology, Social Work.
- Care coordination for access to specialists.
- Outcome measures to guide research.

Domains

- Transdisciplinary approach.
- Scheduling based on complexity.
- Quantification of processes and outcomes.

Key Elements

- Close liaison amongst providers.
- Dedicated schedulers and medical assistants with iterative flexibility.
- System to identify clinical care gaps.

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Prevalence and Practical Assessment Conclusions:

It is essential to ask SSc patients questions in order to understand symptoms.	Questionnaires allows both severity grading and proper test ordering.
The ordering of a GIT test should be guided by burden on patient and cost.	The role of symptom relief versus prevention not yet clear.
Oral and nutritional assessment can support ancillary services for SSc patients.	All SSc patients should be assessed for malnutrition risk.
True prevalence and best practice for management for SSc-related GIT will only be possible with collaboration.	

Acknowledgements and Questions

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