

Medical Report



National
Scleroderma
Foundation

Digestive System Involvement

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After the skin, the digestive system is the most commonly affected organ system in people with scleroderma, affecting about 75 to 90 percent of all patients (Table 1 and Figure 1).

The majority of people with gut involvement experience symptoms that interfere with their day-to-day activities and quality of life.

The function of the gut is to push the food and liquid down from the mouth to the large intestine (or colon), extract and absorb nutrients, and excrete the waste in the form of stool. It does so by well-orchestrated and rhythmic motions of the gut muscles (also known as peristalsis). The primary events that cause trouble in the scleroderma gut are due to a decrease in the blood supply to the nerves, which are needed to stimulate the bowel. There is also some evidence that nerve damage may occur due to an autoimmune process. With decreased stimulation, there is progressive weakening of muscle strength and tone and resultant slowing and disorganized motion of the gut. Virtually every gut symptom is the result of weakening of the gut muscle. The weakening starts in the esophagus (food pipe) and stomach, and works its way down to the small and large intestine.

This article will explain the reasons for the gastrointestinal symptoms and discuss treatments as well.

Oropharyngeal (Mouth)

Approximately 20 percent of people with scleroderma develop secondary Sjogren's syndrome, a syndrome associated with dry eyes and dry mouth. This may cause difficulty swallowing, gum disease or cavities. If people have symptoms of dry mouth, they should see a dentist at least every six months (for some, a visit every four months may be required). In

Table 1: Frequency of GI symptoms
(from 209 patients)

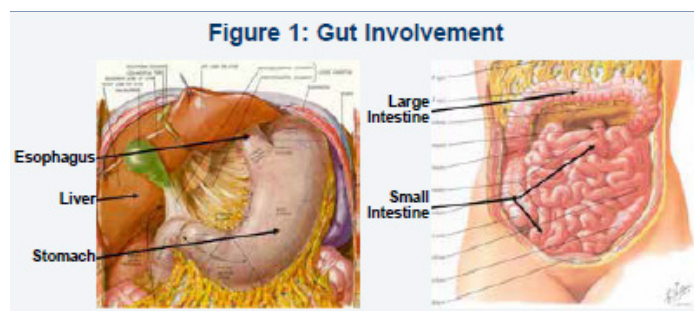
Prevalence	Symptom (%)
Heartburn	71
Trouble Swallowing	52
Bloating	80
Diarrhea	51
Constipation	51
Fecal Incontinence	35

National Scleroderma Foundation survey 2010

addition, use sugar free lozenges to keep your mouth moist and use over the counter dry mouth products such as Biotene® mouthwash and oral gel (more information available at www.biotene.com). Other available over-the-counter therapies include xylitol containing products. Seeing a dentist on regular basis is recommended. Prescription medications such as Evoxac® and Salagen® may be helpful.

Esophagus (Food Pipe)

The esophagus transports food to the stomach by coordinated contractions of its muscular lining. This process is usually gradual and automatic and people are usually not aware of it, except when they swallow something too large, try to eat too quickly, or drink very hot or very cold liquids. They then feel the movement of the food or drink



down the esophagus into the stomach, which may be an uncomfortable sensation.

The esophagus is the area where most scleroderma patients have problems, and fortunately, it has been the area where the most advances have been made in therapy. The most common symptom is heartburn (sensation of burning behind the breast bone, also known as GERD [gastroesophageal reflux disease]), which is due to the irritation of esophagus by acid regurgitating (backing up or reflux) from the stomach. Other symptoms may include dry cough at night, recurrent chest pain behind the breast bone, persistent hoarse voice, asthma (wheezing and shortness of breath), regurgitation of food (expulsion of undigested food from the mouth), difficulty swallowing, mouth ulcers and acid taste in the mouth.

Reflux is caused by weakening of the gut muscle valve between the stomach and esophagus, allowing acid to “splash” back up into the esophagus. The acid, while tracking back into the food pipe, can some times go into the lungs. Some clinical studies have even suggested that the acid going into the lungs may cause lung inflammation in scleroderma. In addition, weakening of the esophageal muscles themselves results in less efficient “milking” of the food down the esophagus, and at times food can even get temporarily “stuck” in the esophagus and patients may need to vomit to clear the esophagus.

Diagnosis

Diagnosis is based on symptoms. Most physicians will first treat these symptoms with medications that can help decrease the acid production. If the symptoms continue, tests such as barium swallow, endoscopy and esophageal manometry can be performed. The barium swallow requires the person to swallow a liquid, which contains barium mixed in a drink, and then take an X-ray of their esophagus and stomach. Because these organs are normally not visible on X-rays, barium temporarily coats the lining of the esophagus, stomach and intestine, making the outline of these organs visible on the X-ray pictures. This process helps to look for the motility or gut muscle integrity and ulcers (breakdown in the

lining of the gut) in the esophagus and stomach. Esophageal manometry requires a small tube be put through the nose into the esophagus. The tube is built to sense pressure, so it can measure sequential muscle contractures (the “milking” motion), and evaluate the motility and function of the esophageal muscles and the esophagus stomach sphincter. Endoscopy requires a gastroenterologist to put a small camera at the end of a small tube (the endo scope) through your mouth into the esophagus and stomach to look for damage caused by the acid, such as ulcers and strictures (narrowing of the food pipe due to chronic acid damage).

Why do we need to treat reflux?

The first and foremost reason to treat reflux is to relieve symptoms and improve your quality of life.

As mentioned before, acid reflux can also lead to lung inflammation and even scarring of the lung tissue.

Continuous high acid production for a long period of time, when the esophagus stomach sphincter is weak, can cause inflammation and scarring of the esophagus (also known as stricture), which can lead to Barrett esophagus (a precancerous condition).

Periodic endoscopic examination s to look for early warning signs of cancer are generally recommended for people who have Barrett esophagus, an approach referred to as surveillance.

Therapy

The treatment of acid reflux requires both lifestyle changes and medications that can

1. Decrease acid production.
2. Increase the motility of the gut muscle.

Lifestyle Changes

Table 2 goes over the lifestyle changes that may help significantly improve reflux symptoms and also minimize the risk of aspiration.

Medications

Proton pump inhibitors (PPIs) The PPIs are medications that sup press acid production. The goal of the treatment is to completely stop the symptoms of heartburn because continuing symptoms, even if occasional, reflect ongoing

Table 2: Anti-Reflux Measures

- Keep head of the bed elevated, 6–8 inches (i.e. wedge pillow, blocks under head of bed, electric bed).
- Take your biggest meal of the day at noon, small meals otherwise.
- Avoid eating or drinking fluids two hours before bedtime.
- Take frequent small meals (5–6 per day).
- Do NOT use extra pillows. No tight garments around waist. (Both of them may increase pressure over your stomach when bending at the waist causing reflux symptoms.)
- Take anti-secretory and pro-motility agents (Table 2).
- Stop smoking (if currently smoking).
- Avoid or minimize acid producing foods (fats, chocolate, coffee).

REMEMBER: Certain medications such as nifedipine (taken for Raynaud) can weaken esophagus-stomach sphincter causing reflux symptoms. As always a balance of treatment should be achieved.

acid production. To achieve this, higher than recommended doses of PPIs are sometimes used (Table 3). Another piece of advice for people with scleroderma and reflux is to NEVER leave home without the PPIs, as missing a couple of doses can cause an increase in acid production and rebound of severe symptoms. PPIs should be preferably taken 30 minutes before breakfast and dinner (if needed).

Recent studies have indicated an increased risk of diarrhea (may rarely cause *Clostridium difficile* infection), osteoporosis, dementia, and chronic kidney diseases with long term use of PPIs. Therefore, you should be aware of these and discuss with your physician. The benefits still outweigh risks in many people with scleroderma. Some people try certain over the counter medications, such as Zantac®, Pepcid® (known as H₂ blockers) which may provide temporary relief, but are usually not very effective in controlling the reflux symptoms and take PPIs as “on demand” therapy. Some physicians use combinations of the PPIs and H₂ blockers.

The prokinetic medications (those that improve motility of the gut muscles) can also be used if the symptoms of reflux continue even after reaching maximum doses of PPIs (Table 3). The prokinetic medication should be taken one hour

before the meal so the medication is “on board” when one eats.

Surgery

As mentioned before, the treatment of the stricture (which is the scarring of the esophagus due to repeated acid damage) may require dilatation of the narrowing of esophagus during an endoscopy procedure. Progressively longer tubes are gently passed through the narrowed areas to stretch it and open it up. This helps improve the downward motion of the food. This MUST be followed by good control of the reflux symptoms otherwise the damage to the esophagus will continue and the stricture will return. The stricture, in fact, may require repeated dilations to keep it open, but the need to redilate usually decreases over time. Surgery due to “non-functioning” esophagus should be the last resort as it often does not work very well. This should only be considered after a lengthy discussion with your rheumatologist. The procedure should be performed by surgeons who have experience in scleroderma.

Stomach

Stomach symptoms in scleroderma are due to slow emptying of the food (also known as gastroparesis) into the small intestine. The retention of food in the stomach leads to a sensation of nausea, vomiting, fullness, or bloating sensation and distention. In some people with scleroderma, the stomach can also have telangiectasias (dilated blood vessels) lining the walls of the stomach. This is also known as “watermelon stomach” due to its appearance on endoscopy. Slow and intermittent or rapid bleeding from these dilated blood vessels can cause anemia (low red blood cell count). The person may or may not have stomach symptoms and may only feel VERY tired and fatigued.

Diagnosis

Gastroparesis can be diagnosed using the barium study, as discussed in the esophagus section. Also, a gastric emptying study can be performed in which a person eats a meal (e.g. a sandwich or egg) which contains a very small amount of radiolabeled material (that is safe) followed by X-rays of their stomach. The doctors are trying to see how long it takes the food to empty into the small bowel. In scleroderma, the food and

Table 3: Medications

Some of the medications used to treat gut problems in scleroderma:

ACID-SUPPRESSING AGENTS

Proton-pump inhibitors

- Prilosec® (omeprazole) 20-40 mg 1-2 times/day
- Prevacid® (lansoprazole) 15-30 mg 1-2 times/day
- Aciphex® (rabeprazole) 20 mg 1-2 times/day
- Protonix® (pantoprazole) 40 mg 1-2 times/day
- Nexium® (esomeprazole) 20-40 mg 1-2 times/day
- Dexilant® (dexlansoprazole) 30-60 mg once/day

H-2 blocker (Over the counter)

- Pepcid®, Tagamet®, Zantac®, Axid® 1 tablet at night and as needed if on maximum doses of proton-pump inhibitors

PRO-MOTILITY AGENTS

- Reglan® (metaclopramide) 10 mg 3-4 times/day†
- E-Mycin® (erythromycin) 250-333 mg 3-4 times/day
- Domperidone®* 10-20 mg 3-4 times/day
- Sandostatin® (octreotide)** 50 mcg, 1-2 times/day

BACTERIA SUPPRESSING ANTIBIOTICS

- Amoxil®, Trimox® (amoxicillin) 500 mg 3 times/day
- Augmentin® (amoxicillin/ clavulanate) 500/125 or 875/125 mg 2 times/day
- Cipro® (ciprofloxacin) 500 mg 3 times/day
- Flagyl® (metronidazole) 500 mg 3 times/day
- Doxy-100® (doxycycline) 100 mg 2 times/day
- Bactrim® Double Strength 1 tablet 2 times/day (trimethoprim-sulfamethoxazole)
- Xifaxan® (rifaximin) 400 mg up to 3 times/day
- Neomycin 500 mg 2-4 times/day

LAXATIVES@

- Colace® (Docusate sodium) 100 mg 1-2 times/day
- Lactulose 15-30 ml 1-2 times/day
- Milk of magnesia 30-60 ml once/day
- Senna® (sennosides) 1 capsule 1-2 times/day
- Amitizia® (Lubiprostone) 8-24 ug 2 times/day

† has a black box warning. Rare cases of tardive dyskinesia, a rare movement disorder with prolonged use.

radiolabeled material remain in the stomach longer than normal (sometimes hours) before emptying completely. In a person with normal stomach function, approximately 50 percent of food is remaining in the stomach after 90 minutes. Other radiographic test includes a wireless motility capsule which is a single use, orally ingested, non-digestible, capsule with data recorder. This can assess the gastric emptying time but also help with monitoring small and large bowel motility as discussed below.

Diagnosis of “watermelon stomach,” with its characteristic appearance, can be made by an experienced gastroenterologist using endoscopy (Figure 2).

Treatment

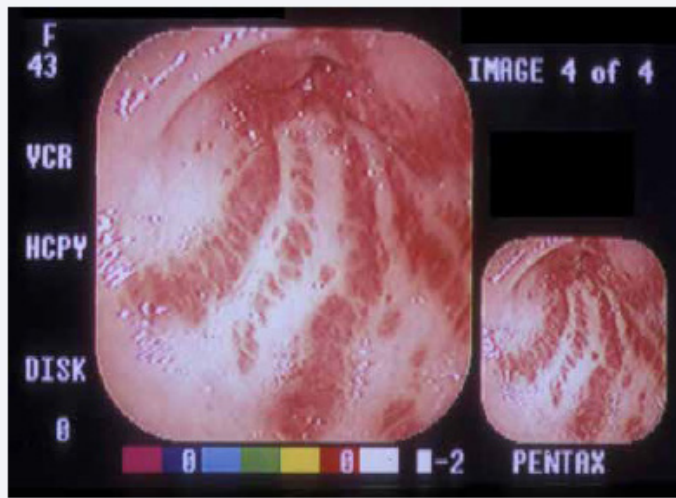
The treatment of gastroparesis requires similar measures as mentioned in Table 2, and use of prokinetic medications mentioned in Table 3. For “watermelon stomach,” use of an argon laser to coagulate or burn the bleeding vessels can lead to improvement in the anemia and symptoms. Patients may require multiple laser treatments (every two to four weeks) before the bleeding stops completely.

Small Intestine (Small Bowel)

The small bowel is the place where we gain most of the nutrition from our food. The food is pushed from the stomach into the small bowel by the rhythmic motions of the gut. Once in the small bowel, the nutrients and vitamins are extracted from the food and the waste is propelled into the large bowel and excreted as stool. The symptoms of bowel involvement are due to lack of muscle tone, leading to stagnation of food in the small and large bowel.

Three common causes of weight loss or inability to gain weight are: gastroparesis, small bowel bacterial overgrowth and untreated depression.

In the small bowel, the symptoms are similar to gastroparesis (bloating sensation and distention, nausea and vomiting), but abdominal pain may also occur. In addition, due to stagnation of food, the bacteria, which normally reside in small quantities in the small bowel, can multiply in the food causing “bacterial overgrowth syndrome.” These bacteria compete with nutrients and vitamins causing vitamin deficiencies, weight loss, and inability to gain weight. There may also be symptoms of diarrhea with foul smelling stools, which may be oily or hard to flush.

Figure 2: Watermelon Stomach

Another small bowel symptom that occurs in scleroderma is pseudo (false) -obstruction. In this condition, the bowel is not physically blocked as in true bowel obstruction but has just “had enough” and stops working. This is caused by weakening of the gut muscle. The patient complains of belly pain, distention, vomiting, and inability to “pass gas.”

Diagnosis

Bacterial overgrowth is usually diagnosed based on symptoms and treated accordingly. If the symptoms persist after treatment, a breath test can be performed. In this, a person ingests sugar (lactose), which is broken down by the bacteria in the small bowel and the byproduct, hydrogen, is detected in the breath. The physician should also evaluate vitamin deficiencies such as Vitamin B12, D and folic acid. Diagnosis of pseudoobstruction requires a plain X-ray and a CT scan of the abdomen. The CT scan detects whether the symptoms are due to a tired “gut,” one that needs rest, or there is something obstructing the small bowel.

Treatment

Bacterial overgrowth is treated using antibiotics to reduce the overgrowth of bacteria in the small bowel. This is achieved by using antibiotics for 10 to 14 days at a time (Table 3), although some people may require longer courses. Any antibiotic may be tried based on previous response, side effects and coverage by the insurance. Rifaximin and neomycin are oral antibiotics that have minimal systemic absorption. Usually a person notices

improvement in the symptoms after a course of treatment and may notice a slow weight gain. Very often, the treatment has to be repeated every month or so to keep the bacteria level low. Occasionally treatment must be continuous and some physicians use different antibiotics every month to prevent the bacteria from becoming resistant. Pro motility agents (Table 3) can also help. Patients may also obtain symptomatic relief in the bacterial overgrowth syndrome by regular use of yogurt containing bowel-friendly bacteria. Probiotics are bacteria that have a beneficial effect in the prevention and treatment of gut problems when they are ingested. Florastor™, Culturelle™, and Align™ are three standardized choices (one or two doses daily) that can be used. Care should be taken not to use probiotics if you are taking immunosuppressive therapies as probiotics can rarely cause blood infection from live bacteria. Also, there is lack of high quality published data to support their efficacy.

Sandostatin® (octereotide) has been successfully used during attacks of pseudoobstruction, and if attacks are frequent, can some times be used on a regular basis to prevent any further attacks. Once treated, a person should take prescribed multivitamins to prevent or treat vitamin deficiencies.

Pseudo-obstruction usually requires hospitalization and complete rest of the small bowel. The person is given nutrients through the veins along with pro-motility agents.

Venting is also performed when needed.

“Venting” means to put a small surgical tube into the jejunum (small intestine) to aspirate out the air. This keeps the patient from becoming severely distended while in treatment. Total parenteral nutrition (TPN) [high energy liquid diet through the veins] may be prescribed by your physician to give your bowel a prolonged rest and help provide you with essential nutrition and energy. In many patients, the bowel slowly recovers after two to three months, and people can go back to eating regular food.

Large Intestine (Colon)

The main function of the large bowel is to reabsorb water and salts that have been secreted by the rest of the gut. This helps the formation of stools and helps to move the waste

along. In scleroderma, there is, as is the case with the rest of the gut, weakening of the gut muscles and impaired motility. This can lead to constipation. Constipation means different things to different people. For many people, it simply means infrequent stools. Medically speaking, constipation usually is defined as fewer than three bowel movements per week. Severe constipation is defined as less than one bowel movement per week. This is usually associated with pain and a feeling of incomplete emptying of the bowel.

Also, one may get wide-mouthed diverticula (large pouches) in the colon. These do not ordinarily cause any symptoms. However, on rare occasions, the stool can get impacted in them causing inflammation of the diverticula, called diverticulitis (this is similar to, but not exactly the same as the common diverticulosis that you often hear about).

Diverticulitis usually presents with belly pain and fever. People can also get diarrhea due to impacted stool.

Diagnosis

Diagnosis usually starts with symptoms related to the colon. A barium study can help look at the large bowel. Other radiographic tests include radiopaque markers and motility capsule.

Treatment

Treatment for constipation requires liberal use of water and laxatives that stimulate the nerve endings in the gut wall, which make the muscles in the intestine contract with more force. A high fiber diet without a laxative is not helpful as it just adds to the amount of waste the bowel is struggling with. The person can take a laxative every other day to maintain a healthy bowel regimen. Other laxatives are included in Table 3.

Rectum

Stool incontinence (symptom of accidentally soiling the underwear before being able to get to a bathroom) occurs in up to a third of people with scleroderma. This is due to the weakening of the rectal muscle and poor control over the rectal sphincter. Anorectal manometry can assess function of this sphincter.

Biofeedback therapy may be helpful by improving voluntary squeezing of the rectal

Table 4: GI Questionnaire

- High Reflux scale score > anti-reflux, PPIs, and promotility (if needed)
- High Distention/Bloating scale score > Consider delayed gastric emptying or bacterial overgrowth
 - PLUS Diarrhea > trial of antibiotics
 - No Diarrhea > trial of promotility agents
- High Constipation scale score > stimulant laxatives, good bowel regimen
- Fecal soilage > appointment with a colorectal surgeon

muscle. Major scleroderma centers offer classes to teach people this technique. Surgery by an experienced surgeon might also be helpful. Preliminary studies have shown promise of sacral nerve stimulation (nerves that control rectal tone using a device [Interstim®] in decreasing episodes of rectal incontinence.

Liver

The liver plays an important role in the detoxification of drugs in our body. About 10 percent of scleroderma patients may have liver involvement, known as primary biliary cirrhosis. If this uncommon complication occurs, it usually occurs 10 to 15 years after the onset of scleroderma. Some patients may develop biliary cirrhosis before a diagnosis of scleroderma. Symptoms usually consist of itchy skin and fatigue. The diagnosis can be made by blood tests for anti-mitochondrial and anti-smooth muscle antibody and the treatment consists of doses of ursodeoxycholic acid.

Diet and Scleroderma

Eating Well with Scleroderma (www.scleroderma.org/eatingwell) provides important information regarding diet that may help or worsen gastrointestinal symptoms.

How to Measure Gut Involvement and Severity in Day-to-Day Care

Researchers have developed a 34-item questionnaire that can assess gut involvement and severity. The questionnaire is called the University of California- Scleroderma Clinical Trial Consortium Gastrointestinal Instrument. It has seven scales: five scales assess symptoms - reflux, distention/bloating, diarrhea, fecal soilage

Figure 3: GI Questionnaire
The UCLA SCTC GIT 2.0 Questionnaire



improvement or change in his/ her symptoms by completing the questionnaire at regular intervals. A red bar should also alert the person to notify their physician of worsening symptoms.

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<http://bit.ly/UMSclerodermaResearch>

<https://www.selfmanagescleroderma.com>

For an interactive version of the questionnaire please visit <http://bit.ly/sctcgit>

(or rectal incontinence), and constipation, and two scales assess the impact of gut symptoms on the emotional well-being and social functioning. All scales are scored from 0 (no symptoms or impact on quality of life) to 3 (severe symptoms or poor quality of life) except diarrhea and constipation scales that ranges from 0-2 and 0- 2.5, respectively. The questionnaire takes approximately 5-7 minutes to complete and is available free online at <http://bit.ly/sctcgit>.

The log-in takes less than a minute and asks optional questions regarding your name and e-mail address. These questions are asked so you may receive future e-mails on new developments regarding this questionnaire and invitations for future studies. In addition, the log- in screen asks for your age, gender, and if you have scleroderma. The questionnaire is available in 34 languages. The questionnaire can be used by a person to assess their GI health and monitor their response to treatment. Each scale is presented as a green bar (none-to-mild symptoms), a yellow bar (moderate symptoms), or red bar (severe-to- very severe symptoms).

Table 4 provides an example of an approach in using the scale scores for treatment purposes. As an example, the patient in Figure 3 has severe reflux symptoms, moderate diarrhea, mild distention/ bloating, with no fecal soilage and constipation.

These GI symptoms are leading to severe emotional and social distress. Treatment should include anti-reflux measures, PPIs and promotility agents. The person can assess