EDS for the Gastroenterologist

Gastrointestinal problems are routine in patients with any of the Ehlers-Danlos Syndromes (EDS), a loose term for a number of inherited conditions. These notes are brief reminders to gastroenterologists of items to keep in mind when dealing with people with an EDS.

The medical literature contains numerous papers over several decades, documenting the high incidence of joint hypermobility syndromes among patients with a wide variety of gastroenterologic problems, presenting at specialist GI clinics. However, there seems to be no research on whether the diagnosis or treatment of such problems presents special features in these patients. The remarks below are therefore based on a clinical consensus of international experts, as presented at two international meetings in 2016.[1]

The Ehlers-Danlos Syndromes

The great majority of people with an EDS have the "Classic Type" or the "Hypermobility Type". In both these, there is marked looseness or hypermobility of joints. In the Classic Type the skin is very elastic (stretchy). In the Hypermobility Type, skin is often normal or nearly so. A rarer type is the Vascular Type, in which joint hypermobility may be minor, but there are frequent, very dangerous complications due to rupture of hollow organs, including arterial aneurysms and abdominal viscera. See below for more on this.

The underlying lesion is different in different kinds of EDS. Mechanical defects in the microscopic structure of collagen are nearly always present, and in the Classic and Vascular Types can be attributed to specific gene mutations. However, in the Hypermobility Type no such genetic fault has been identified. Moreover, many of the *extra-articular* features of EDS can not be plausibly explained on the basis of mechanically faulty collagen. A popular current hypothesis is that in the Hypermobility Type, the ligaments are loose not because of an alteration in their chemistry, but in the manner of their *assembly*,

It has been known for decades that various problems in the gastrointestinal tract occur frequently in patients with EDS. These were formerly assumed to be due to mechanical defects in connective tissue. However, it is now believed that such conditions are much more complex than can be attributed simply to "loose tissues". Disordered functioning of (at least) the nervous system, cellular processing of nutrients, and immune processes are now thought to be involved, as very briefly described below.

Diagnosis of GI problems in EDS

The most important priority for the gastroenterologist seeing a patient with EDS is to bear in mind **the wide range of GI conditions that can be present, often at the same time,** in this group of conditions. For most of these, the treatment can be similar to that in patients without EDS, with one general caveat. This is, that EDS patients commonly present with GI syndromes in which the usual tests that confirm those syndromes are negative. In EDS, this predicament often leads to diagnosis of a psychiatric rather than an organic condition. This is a serious error. ***When EDS patients have symptoms referrable to the digestive tract, they nearly always have an organic cause for those symptoms.***

Vascular EDS, Visceral Rupture and The Acute Abdomen

In the Vascular Type of EDS, potentially-fatal ruptures of abdominal viscera can occur without warning at any age, as can dissection or rupture of aortic aneurysms. ***If a patient with Vascular EDS (VEDS or EDS-V) has new-onset, severe abdominal pain, then they should be assumed to have one of these life-threatening catastrophes and should be assessed at once in an emergency room.*** Immediate institution of two wide-bore IV lines and emergency imaging after a rapid clinical evaluation, will usually make the diagnosis. Detailed handouts are available from the Ehlers Danlos Society at http://ehlers-danlos.com/resource-guides. The main one is:
http://ehlers-danlos.com/wp-content/uploads/MRGVascularTypeS.pdf.

Treatment of non-emergency GI problems in EDS

There are no controlled studies that attempt to define whether, or how, EDS patients should be treated any differently than other patients with similar GI conditions. It follows that a general gastroenterologist is capable of delivering good care to such patients, so long as he or she has a high degree of suspicion for the presence of one, or more likely several, of the conditions mentioned below.

A general principle in how to approach EDS patients with GI symptoms is, however, possible, base on expert consensus. This is that **many such symptoms are best seen as resulting from one, or both, of two underlying pathophysiologies**. The first is mechanical weakness of connective tissue, similar to that affecting joint ligaments. The possible contribution of this to conditions like gastroparesis or colonic dilataion is obvious. Another manifestation may be excessive permeability to large molecules, especially in the wall of the small intestine, hence leaky gut syndrome. The fragility and stretchiness of connective tissue mandates special precautions for patients with all types of EDS who are to have surgery, or anesthesia. **This includes GI procedures such as endoscopies.** A separate article on this website deals with these.[2]

The second major pathophysiologic process in EDS seems to by disordered functioning of the autonomic nervous system. This dysautonomia is demonstrable in several body systems including the gut, in EDS. It may include any combination of hyper- or hypo-function. **Thus, trials of cholinergic or adrenergic stimulants or suppressants should be considered, based on symptoms, in EDS-associated GI disorders.**

Pyridostigmine should probably be considered more often in EDS-related GI conditions, than in the absence of EDS. Its cholinergic effects may also improve cardiovascular dysautonomia manifesting as orthostatic intolerance.

Gastroenterologic Problems in EDS by Region

Mouth, teeth, face[3]

- Gingival hyperplasia and/or inflammation.
- Early-onset periodontitis.
- Crowded, malformed, translucent teeth.
- Pulp stones and abnormal dental roots.
- Slow healing after trauma or dental surgery.
- TMJ subluxation, dislocation, or pain.
- Resistance to local anesthesia: large volumes and multiple doses are typically required. This is surmised to be due to rapid diffusion of injected drugs away from the injection site due to increased permeability of the intercellular matrix. **If the patient says the local anesthetic isn't working, then believe her!**

Esophagus

- **Dysmotility**, usually hypokinetic rather than hyperkinetic.
- **"Globus hystericus"** may be due to spasm of the pharyngeal constrictor muscle, itself secondary to excessive motion between midcervical vertebrae: an organic, not a psychiatric, condition.
- **Gastroesophageal reflux**.

Stomach

Gastroparesis is common, and greatly underdiagnosed in EDS. It can be severe enough to require a gastric or jejunal feeding tube. It is doubtful that this is a mechanical problem of loose tissues. It is more likely due to failure of nervous control of peristalsis, and perhaps other factors.

Dumping Syndrome can involve either too slow, or too rapid, emptying of the stomach in EDS.

Hepatobiliary system

Gallbladder disease, typically without stones, is common and may occur as early as the mid-teens. Imaging studies usually show some combination of poor galbladder filling or emptying, or a distended gallbladder. Such patients often have cholecystectomies, which sometimes help and sometimes don't (in the absence of gallstones).

Sphincter of Oddi dysfunction can mimic various abdominal conditions and is not rare in EDS. The difficulties in its diagnosis and treatment are similar to those in other patients.

Small Intestine

Small bowel overgrowth may be due to poor efficiency of peristalsis, itself due either to mechanical abnormalities in the bowel wall, or to abnormal neural control.

Leaky gut syndrome is presumed due to increased permeability of the bowel wall due to defects in the microstructure of collagen in its intercellular matrix.

Gluten intolerance may be of either the celiac or the non-celiac type. There is a strong clinical impression that both are quite common in EDS.

Multiple food intolerances are common. It is hypothesized that this is due to permeability of the bowel wall due to a mechanically defective collagen matrix. Food-related episodic arthritis may occur and complicate the presentation of joint pain due to abnormal ligaments in EDS.

Micronutrient deficiencies may occur, which can be surprisingly difficult to correct with oral supplements.

Colon & Rectum

Constipation may be severe, and a few EDS patients require weekly enemas to evacuate. Defective peristalsis rather than connective tissue laxity seems to be the usual cause.

Irritable bowel syndrome is common and without distinctive features.

Hemorrhoids are very common. **Rectocele** and **intussusception** may occur, presumably because of mechanical laxity of the bowel wall.

Crohn's disease and ulcerative colitis seem to be closely associated with EDS, at least based on specialist clinic populations.

Possible Role of Mast Cell Activation Syndrome (MCAS)

MCAS is thought to be common in EDS patients and may perhaps be a final common pathway for many of its manifestations. The cardinal gastrointestinal feature is multiple food intolerance, causing GI symptoms and often others, for instance skin rashes, arthralgia, asthma, edema, cognitive dysfunction or circulatory instability. It may closely mimic carcinoid syndrome in symptoms and signs. It may be associated with leaky gutIf suspected, referral to an allergist is warranted since treatment for MCAS is rapidly evolving.

Alan Spanos MD
Clinical Associate, UNC School of Medicine, Chapel Hill, NC
200A Franklin Square
1829 East Franklin Street Email
Chapel Hill, NC 27607

Ph (919)-967-2927
Fax (919)-928-5541
Email: Alan.Spanos@yahoo.com
Website: AlanSpanosMD.com

---

[1]At the EDS International Symposium New York in May 2016, experts from many countries set out to agree on criteria for defining each type of EDS, and on treatments for them. Participants are still working on this project and aim to publish their conclusions in March 2017. Meanwhile, however, at a Global Learning Conference in Baltimore in July 2016, a progress report was given by members of the symposium. I have summarized the consensus to date on gastroenterologic aspects of EDS, as expressed by speakers at that event, especially by Qasim Aziz, MBBS, FRCP, PhD, and Alan Hakim, MA, FRCP, both widely published researchers and clinicians in this field.
[2] See article *Surgical Precautions in H-EDS* at *AlanSpanosMD.com.*
[3] See the handout on dental issues in EDS at the website of the Ehlers Danlos Society: http://ehlers-danlos.com/wp-content/uploads/MRGDentistryS.pdf.