Medical Care of Patients with Ehlers Danlos Syndromes

This article is intended for medical generalists caring for patients with an Ehlers Danlos Syndrome. I encourage patients with EDS to read it too, so as to better collaborate with their physicians. It's based on much input from national and international experts in the field, plus my own clinical experience of working with EDS patients for the last 13 years.

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INTRODUCTION

This document aims to help doctors provide good medical care to people with Ehlers Danlos Syndromes. Family doctors, internists and pediatricians can do this, and no one else will. Since most of the tools for helping people with EDS are already familiar to doctors in relation to other illnesses, this is not hard. Most patients with EDS are young, intelligent, and highly motivated to overcome their illness. Helping these young people through their challenges to find a fulfilling life can be both satisfying, and inspiring, for the generalist physician. (Note that I will refer to EDS patients as "she" in this article in view of the pronounced female predominance of this condition; but its contents refer equally to male patients.)

Why primary care practitioners should treat people with EDS

Ehlers Danlos Syndrome is not rare. My estimates suggest a prevalence of at least one in five hundred: so most high schools include one, or several, adolescents struggling with EDS. But most of these will never see a doctor who is familiar with their condition. In the USA, the only medical specialty that "owns" EDS is that of genetics. Geneticists *diagnose* EDS, but they do not *treat* it. Referrals to rheumatologists, orthopedists and other specialists are often fruitless, or positively harmful. But since EDS affects several body systems, the doctor best equipped to manage EDS patients is the primary care generalist. ***A family doctor, general internist or pediatrician can provide much, or all, the medical care needed by most people with EDS.*** This article, together with others on my website (AlanSpanosMD.com), summarizes what the primary care practitioner needs to know, based on the consensus of national and international experts.

The Ehlers Danlos Syndromes

The term "Ehlers Danlos Syndrome" (EDS) denotes a group of inherited conditions in which connective tissue is mechanically faulty, so that ligaments and some other tissues are lax and fragile. Patients with EDS also have various medical problems that can not be easily ascribed to loose connective tissue, such as low stamina, hypersomnia, orthostatic intolerance, gastrointestinal disorders, anxiety and panic attacks. Several types of EDS are distinguished, based on clinical and genetic differences. These are "spectrum conditions" which vary greatly in severity: they may be subclinical, or cause symptoms severe enough to be disabling, or even life-threatening. But with proper medical care, most people with EDS can live full and fulfilled lives.

Patients are usually right if they think they have EDS

People with EDS commonly make the diagnosis themselves, based on searching on the internet. My clinic experience is that those who "find themselves," in online descriptions of EDS, nearly always do indeed have it. Hence my website at AlanSpanosMD.com has an article, *I Think I May Have EDS.* Some have been told they have "Joint Hypermobility Syndrome (JHS)" but not EDS. However, the expert consensus is now that there is no distinction between the two, and the term Joint Hypermobility Syndrome is being abandoned. By the time they approach a doctor about EDS, many patients have learned more about it than most of their doctors know. So it's unwise to brush off such patients' opinions. **Rather, the PCP can often learn from the research done by the patient herself, in a collaboration that serves both patient and doctor.**

Nearly all EDS is the "hypermobile type"

Categorization of the Ehlers Danlos Syndromes into distinct types is an ongoing scientific challenge with no end in sight. However, there is general agreement that ***the vast majority of EDS patients have the "hypermobile type",*** previously known as Type 3. This is defined by relatively severe trouble with loose joints, but less trouble with fragile skin, blood vessels or viscera, which characterise other EDS types. The hypermobile type has been denoted by several confusng abbreviations, but H-EDS or HEDS is increasingly used. Most doctors will see a number of H-EDS patients in their career, but will probably never see a single case of the rarer types.

There is no lab test for H-EDS, though geneticists have tests for some of the other types. Patients with EDS should be assumed to have H-EDS and treated for this, while awaiting a diagnostic consultation with a geneticist, which can take over a year. ***Treatment of H-EDS is, in fact, the basic treatment for each of the other types.*** If the patient turns out to have one of the other types, then specific treatment for that type will add to, rather than change, this basic treatment.

Rarer types of EDS

The two main rarer types are the Classic and Vascular types. The primary care physician may suspect them, based on the features below. If suspected, a geneticist can then make a firm diagnosis. Meanwhile, management can follow that for Hypermobility-Type EDS (H-EDS), which shares most of their features.

In the **Classic type, C-EDS**, skin is loose and "stretchy." It can easily be pulled up into large folds without subcutaneous fat also pulling up. Skin heals slowly and poorly, and the patient has multiple old scars which are wide, and very thin. Specific genetic markers are present in some of these patients.

In the **Vascular type, V-EDS**, skin is thin and translucent, so veins are easily seen through it, and there's a personal and/or family history of sudden death, catastrophic bleeding or rupture of an abdominal viscus. If this is suspected, a geneticist may agree to see the patient urgently, to validate the diagnosis, in view of the possibly-fatal complications that the patient needs to be aware of. Genetic markers are usually positive in this type of EDS.

There are several even rarer EDS types, with which the generalist need not be concerned.

CLINICAL PRESENTATION OF H-EDS

Main features of H-EDS are listed below. The patient may have any or all of them. Onset is in childhood, with symptoms often worsening in adolescence and early adulthood. Most patients are female. Some only come to medical attention when they are already parents, if a child is found to have EDS and it then becomes clear that the parent is also affected.

There is no established way to prioritize the items listed below. (An international panel is working on this and I will update this article accordingly, when they make their recommendations.) For the present, we can say that the more of these features the patient has, and the more severe are some of them, then the more appropriate it is to designate their condition as H-EDS. A history of a similar cluster of features in one or more family members adds confidence to the diagnosis.

Main features of Hypermobility-Type Ehlers Danlos Syndrome (H-EDS)	
Multiple hypermobile joints	Some of these subluxate or dislocate, and some are painful.
Widespread pain	Pain is not restricted to joints. It often has neuropathic features, i.e. is burning, jolting, or tingling, and may be associated with altered tactile sensation.
Orthostatic intolerance	On prolonged standing the patient is dizzy, mentally "foggy", or very soon just needs to sit or lie down. She may feel her heart rate is very rapid.
Gastrointestinal disorders	A wide variety of functional and structural GI conditions are common in EDS. An article on these is at AlanSpanosMD.com.
Reduced stamina	This may be due to hypersomnia, orthostatic intolerance, or it may resembles the profound prostration of post-viral fatigue syndromes, lasting for days or weeks after exertion.
Hypersomnia	Long sleep time, and often a need to nap during the day, are typical. Sleep may be light and restless, or unusually deep, so that the patient may sleep through alarms.
Anxiety +/- panic attacks	These symptoms may overlap with those of orthostatic intolerance, i.e. episodic faintness, tachycardia, sweating.
Easy bruising +/- bleeding	Clotting studies are generally normal except for bleeding time. The cause is probably fragile or permeable small blood vessels.
Slow healing of injuries	Sprains, fractures, lacerations and surgical incisions heal slowly and may be wide with depressed, thin skin in the scars.
Family history	One or more family members usually have at least some of the patient's problems.
Other features	Many features including facial structure, migraines, dysmenorrhea, and various neurologic syndromes are seen in H-EDS, but they are not currently used in its diagnosis.

TREATMENT FOR H-EDS: GENERAL PRINCIPLES

I suggest the following four general principles, for effective management of suspected or confirmed H-EDS in primary care.

1. Doctor-patient collaboration

People with H-EDS are used to dealing with doctors who know nothing about their condition. Typically, these patients have themselves learned a lot about H-EDS, mainly through online sites. These include videos of lectures by EDS experts, often at a level appropriate for doctors as well as patients. So EDS is a topic on which doctors should expect to be educated by their patients, and should encourage them in this. Information presented by the patient is generally credible, and relevant to her care. Taking this seriously is helpful in itself, and strengthens the therapeutic alliance with the patient.

2. Dealing with one problem at a time

Most H-EDS problems can be managed separately, allocating a visit to each. This greatly reduces the feeling of overload every doctor experiences when confronting a patient with a complex disorder affecting several organ systems. A problem list also helps define which items the PCP will be managing, and which deferred to another specialist.

2. Precautions for surgery and anesthesia

When unconscious, the EDS patient can easily suffer ligament and joint injuries while being moved before, during and after surgery. Also, as all connective tissues are more fragile, and heal more slowly, in EDS, surgical technique should be refined to take account of this. And post-operatively, allowance should be made for the prolonged healing time expected. These concerns apply also to procedures like endoscopy if they require anesthesia. These issues are spelled out in a one-page handout for the surgeon and/or anesthesiologist, available on my website at *AlanSpanosMD.com* under the Articles menu. I advise that patients themselves have a copy and follow its guidance on how get better, safer treatment during surgery or anesthesia.

4. PCP-specialist collaboration

When the PCP refers an H-EDS patient to a specialist, it's most helpful if a referral letter is sent, with a copy for the patient to take to the appointment. This should let the specialist know the patient has H-EDS and that this should be considered in the specialist's assessment and treatment. The patient should be encouraged to take to the appointment any printed materials she can find on these items. Handouts at *AlanSpanosMD.com* may be a useful starting point. Relevant pages from *Joint Hypermobility Handbook,* by Brad Tinkle MD, are also helpful, and I encourage all EDS patients to get a copy of this book.

TREATMENT FOR H-EDS: SPECIFIC SYMPTOMS

PAIN

Pains in H-EDS have multifactorial causes. Some joints hurt when they dislocate, though many do not. Also, people with H-EDS often have pain and tenderness in areas without joints: for instance, in the hands at around the midpoints of the metacarpal bones. Sometimes these pains are referred from distant joints, but sometimes no joint can be incriminated. Pains commonly have the burning, tingling or shock-like features of neuropathic pain. It's thought that these may be due to deformation of nerves around subluxing joints. Pains often respond to work with a physical therapist, whether the mechanism is clear or not. Given these uncertainties, the following suggestions seem prudent, and are supported by clinical practice and expert consensus.

Pain medications that commonly help in EDS are listed in the table on the next page. Note that for **Migraines** (which are common in EDS), the usual abortive and preventive medications may be tried. There's no evidence on whether EDS alters the success rate with any of these. However, their side effects may affect other EDS symptoms. Propranolol may prevent migraine and also help orthostatic hypotension and anxiety; nortriptyline may reduce migraines and also help sleep and pain.

Physical therapy is invaluable for people with an EDS, but a therapist should be sought who meets three criteria:

1. They must have training and experience in one or other technique of manual therapy.
2. They must work one-on-one with clients for the full duration of each treatment session because these patients are complex and treatment protocols need to be adjusted repeatedly in the light of unpredictable responses, both good and bad.
3. The PT must be prepared to do some study of methods useful in EDS. A handout on my website at AlanSpanosMD.com provides **downloadable materials and references on this, for physical therapists.**

Swimming is often uniquely helpful for people with EDS, if a convenient, and suitably warm, pool is available. A PT can give directions on helpful workout routines, but many EDS patients also benefit from just getting in the water and moving around in it, doing whatever feels good.

Braces can be very helpful, especially for knees, ankles, elbows, wrists and fingers. **The physical therapist should be in charge of recommending and fitting them.** Most commonly-used brands don't work well for people with EDS. The best range is by Bauerfeind. For fingers, Silver Ring Splints are excellent, and can be fitted at home via an online Skype interview with one of the company's orthotists.

Surgery is often considered, to stabilize painful joints in H-EDS. However, the operations often fail. Indeed, a common way that people with H- EDS get diagnosed is when several joint stabilizations have been done, and none have succeeded. The patient herself should be made aware of this. She should deal with only those orthopedists who are prepared to modify their surgical techniques, and their recommendations, when the patient has H-EDS. Decisions surrounding **spinal surgery** present especially formidable dilemmas, which are beyond the scope of this article.

Main useful pain medications for H-EDS patients over age 18*

This table reflects experience in one EDS clinic. There are no comparative studies, or placebo-controlled trials, of any analgesics for EDS pain. Since EDS symptoms shift unpredictably, **all medications should be reviewed every few months**. Each medication should be trialled **one at a time, at an adequate dose, for the minimum time needed to establish benefit and adverse effects.** The commonest error in prescribing for EDS is to leave the patient on a drug for months or years without every having established what it is, and isn't, doing for them.

* The usual cautions apply when considering these medications for children under 18; experience with several of them is limited in this age group, and lower starting doses may be appropriate. Similar cautions apply to the elderly.

Medication	Typical starting regimen	Comments
NSAIDS	Specific for each agent	Some help for some patients, but GI side effects often limit use. Renal dysfunction is a special concern if patient has orthostatic intolerance.
NORTRIPTYLINE 10mg	1 QHS an hour before bedtime. Increase by 1 every 5 days, but not over 5 QHS (50mg). Titrate to maximum benefit vs adverse effects.	For use daily, not episodically. Helps sleep as well as pain. For most patients the only side effects are dry mouth and mild constipation, and these often subside with use. But may worsen tachycardia in patients with orthostatic intolerance.
GABAPENTIN 300mg	1 QHS x 5 days, increase by 1 QHS every 5 days, up to 4 QHS. Titrate against benefit vs adverse effects. Also consider 1 QAM for 5 days then BID for 5 days, then double those doses if tolerated.	For use daily, not episodically.Helps sleep as well as pain. Unsteadiness and morning sedation are main initial adverse effects. Once optimum day and night regimens are established, further adjustment of any of the doses may be tried.
TRAMADOL 50mg	1 QD for 3 days 1 BID for 3 days (at least 4 hours apart) 1 TID for 3 days 1 QID. Rare patients may tolerate 2 TID or QID.	May help pain but not sleep. A wide range of adverse effects and interactions limit its value. But has the advantages of episodic or daily use, and avoidance of the issues surrounding Schedule 2 opioids.
TIZANIDINE 4mg	1 QHS for sleep disruption due to pain. Can be titrated up, e.g. 2 QHS, and 1-2 up to TID PRN if daytime analgesia also needed.	Common adverse effects are chest pain, dysuria, agitation, drowsiness, exhaustion, feverishness. Main advantage is brief action, so if taken at night should not cause morning sedation. It can be used routinely or episodically.
OTHER MUSCLE RELAXANTS	See above for tizanidine. Other muscle-relaxants seem only rarely helpful for EDS, and are dosed as for other conditions.	Some patients get more subluxations after taking muscle relaxants at night: they may impair reflex holding patterns so that hypermobile joints sublux more than usual, during sleep.
OPIOIDS	Use standard dose titrations as for other conditions.	Usual adverse effects and risks apply. Despite them, some patients insist that "I can only move" because of a daily opioid regimen. Be alert for unusual allergic or inflammatory effects due to mast cell activation. Beware serious skin damage risk from transdermal preparations.
BENZODIAZEPINES	Use standard dose titrations as for other conditions.	Some patients report improved neuropathic pain, not just better sleep and reduced anxiety. This may reflect their effect as mast cell stabilizers.

HYPERSOMNIA

This can be a major handicap, since several productive hours may be lost every day to the unusually long sleep times many EDS sufferers exhibit, and also due to a need for daytime naps. Sleep studies are hardly ever helpful unless there's clear evidence of sleep apnea or narcolepsy. Often, treatment of pain reduces total sleep requirement and improves daytime alertness and energy. A single low dose of an amphetamine may help, preventing sleepiness during a segment of the day when the patient needs to be fully alert, for instance a student who needs not to nap during an afternoon class, or a mother who needs to be alert so as to drive and go shopping. This simple measure can add a worthwhile amount to the useful time the patient has during the day.

EXHAUSTION

Exhaustion, i.e. poor stamina limiting normal activities, should be distinguished from daytime sleepiness. When not due to poor sleep, this may be due to circulatory instability (see below). Whether this is so or not, it may improve markedly with **low doses of amphetamines** (5-10mg of dextroamphetamine, mixed amphetamine salts (Adderall) or methylphenidate (Ritalin) QAM, repeated if necessary a few hours later. **Armodafanil** (Nuvigil) may also help, but is extraordinarily expensive and is usually not covered by insurance for this indication. However, the patient may get coupons online for at least a trial course to establish if it helps.

CIRCULATORY INSTABILITY

Most EDS patients have some degree of circulatory instability, typically manifesting as orthostatic intolerance (OI), i.e. dizziness or faintness on staying upright, or simply reduced stamina with physical tasks. Typically the patient gets cold, pale or blue hands and feet on staying upright, and may have marked tachycardia, which by definition would warrant a diagnosis of POTS (postural orthostatic tachycardia syndrome). This field is confused and confusing. Different categories continue to be proposed and argued over, including POTS, neurally mediated hypotension (NMH) and others. To date there is not a single prospective, randomized controlled trial of any treatment of these conditions. So treatment protocols mainly reflect the habits and biases of individual providers or institutions. These are essentially trial-and-error, and involve pharmacologic and also nonpharmacologic interventions. The interested generalist can often do at least as well as a cardiologist in this area, and perhaps better, since the cardiologist may be focused on titrating treatment against *measurements* (pulse and blood pressure changes) rather than patients' *symptoms*, and these are often discordant. Also, cardiologists' follow-up of these patients tends to be at long intervals, thus preventing them from doing the closely-monitored, symptom-based, brief treatment trials that seem to be most helpful.

GI SYMPTOMS

Many, perhaps most, EDS patients have GI symptoms.. These may be caused by relatively rare conditions such as gastroparesis, or malabsorption syndromes, as well as any of the common gastrointestinal conditions. Clinical clues to the diagnosis may be scanty, so a wide differential diagnosis should be considered. If a clinical diagnosis and symptomatic treatment are not helpful, then early workup is warranted. My website includes an article for the gastroenterologist on these conditions.

BLEEDING AND BRUISING

Multiple bruises, which may be spontaneous, are commonplace among people with EDS. The phenomenon itself rarely needs specific treatment. Claims have been made that Vitamin C supplementation may reduce this, but without supporting evidence. Clotting factors are normal, so the bruising is assumed to be due to fragility, or leakiness, of small blood vessels. **Prolonged bleeding** is common, perhaps due to failure of blood vessels to contract adequately after injury. This is relevant for the surgeon. **Menorrhagia** should be specifically enquired about, and treated in the usual ways, in EDS patients. Note that life-threatening **catastrophic bleeding**, especially in pregnancy or delivery, should prompt reconsideration of whether the patient has Vascular EDS (V-EDS), rather than the much more common Hypermobility type (H-EDS). A geneticist can make this determination.

ANXIETY AND PANIC ATTACKS

Assessment and treatment are the same in EDS as in its absence, with one important exception. This is, that instability of autonomic function may cause symptoms of anxiety and panic attacks in H-EDS patients. Thus, episodes of panic with tachycardia may respond better to low-dose propranolol (10-20mg) than to anxiolytics.

SURGERY AND ANESTHESIA

See page 4, above.

OTHER SYMPTOMS

Various other symptoms may be associated with EDS. In general, if any chronic symptoms in the EDS patient have unusual features, or fail to respond to their usual treatments, an online search should quickly reveal whether there's a relevant connection with EDS. Patients themselves can access such information, thereby helping the doctor and further strengthening the collaborative doctor-patient relationship that is a key to success with these patients.