

EDS Overview & Question on Cure
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What is Ehlers Danlos Syndrome or EDS?

EDS is a type of Heritable Connective Tissue Disorder, and there are 13 sub-types of EDS. Each of these sub-types is different. The most common sub-type is Hypermobile EDS, which affects people who are exceptionally flexible such as gymnasts, dancers, and contortionists (1-5, 8, 10-13, 17-19)

The connective tissue is the glue that holds the skin, tendons, ligaments, muscles, bones, organs, eyes, teeth, and blood vessels. EDS patients are born with defective connective tissues, and mutations in at least 19 genes have been linked to EDS. Some are associated with the body's production of collagen, which is the main component of connective tissues giving structure and strength to its connective tissues, such as tendons, ligaments, and cartilage. These disorders weaken the body's connective tissue, which means that most people with EDS have highly elastic joints that dislocate or subluxate/partial dislocation (1-5, 8, 10-13, 17-19, 23, 24)

Hypermobility, like other diseases, varies with a) females' hormones, estrogen and progesterone, there are more women than men with hEDS (6, 7); b) ethnicity, found most frequently in Asians, next in Africans, and the least in Europeans (8); and c) age, decreases as we get older (4, 17)

What are the current thoughts on prevalence?

According to the EDSociety website and Diana Jovin's recent book Disjointed (chapter 3), the number of people with hypermobile EDS/ Hypermobile Spectrum Disorder is not known. However, according to internationally recognized geneticists also EDSociety members Drs. Castori, Francomano, Hakim, and Malfait, and Disjointed book, about 1 in every 5,000 people around the world, thus Canada too, lives with some form of EDS (9, 13, 17).

How is hEDS diagnosed?

The EDSociety recommends their Diagnostic Criteria Checklist for doctors across all disciplines to be able to diagnose hEDS → For the link see References 18. For hEDS neurological manifestations (craniocervical & cervical instability, tethered cord, Chiari, CSF, Tarlov cyst) special neuroimaging required-Upright MRI, Rotational CTScan (3, 13, 17, 19) → Not available in Canada

What are the symptoms?

Because hEDS affects multiple organ systems and also has multiple co-existing conditions, the patients can present doctors with an unusual group of symptoms, such as:

- neurologic: pain, migraines, neuropathy caused by nerve injuries from dislocations, sensory loss, droopy eyelid, involuntary movements, fatigue, dizziness, imbalance, falls, sleep disorders
- musculoskeletal: pain, loose joints & ligaments, early-onset osteoarthritis caused by dislocations & subluxations, muscle atrophy, ruptured ligament, tendons, and muscles
- digestive: pain, IBS, GERD, hernias, diarrhea, constipation, nausea, difficulty swallowing,
- urogenital: pain, incontinence, neurogenic bladder, frequent UTI, prolapsed uterus & bladder,
- cardiovascular: pain, defective heart valves, enlarged aorta, extremities blood pooling, phlebitis,

- oral: pain, jaw dislocations, temporomandibular disorders, shifting teeth,
 - ocular: retinal tear, vitreous/middle of the eye detachment leading to early-onset macular degeneration, dry eyes, meibomian gland dysfunction, pain
 - autonomic nervous system: dysautonomia, postural orthostatic tachycardia, fainting/pre fainting, thus, falls, pain
 - immune system: mast cell activation causing reactions to foods, chemicals (in foods, air, drugs), and temperature, pain
 - dermatologic: pain, skin bruises easy, is stretchy, wounds heal slow
- ➔ As you see, pain is everywhere!

➔ All these multiple symptoms make it difficult to diagnose hEDS (1-5, 8, 10-13, 17-19, 31), thus, most times it is undiagnosed, underdiagnosed, misdiagnosed, and thus, it takes years or decades to receive the correct diagnostic.

Another symptom is anxiety and according to Dr Pocinki a member of EDSociety, the anxiety in EDS patients is caused mainly by physical triggers such as pain (neuro-musculo-skeletal-visceral), fatigue, dehydration, drop in the blood sugar and blood pressure (4). My question is: Who would not be anxious if they dislocate/subluxate during regular daily activities & night sleep, especially the craniocervical joint where the brainstem is located ➔ the headquarter of autonomic functions such as walking, talking, swallowing, opening eyes, urination, defecation, heart and lungs functions?

Symptoms vary from mildly loose joints to life-threatening complications related to brainstem and spinal cord injuries caused by craniocervical and cervical instability, Chiari malformation, tethered cord syndrome, cerebrospinal fluid leaks, Tarlov cyst (1-5, 8, 10-13, 17-19), which require neurosurgeries ➔ Not available in Canada. Thus, many EDS patients had neurosurgeries in Maryland, such as craniocervical & cervical fusions, and tethered cord release surgery.

What are the treatments? ➔ For details, see all articles in References 13, 17

The treatment needs to be adapted to the EDS sub-type and individual. For those with hEDS, the most common form of the disorder, exercise is key to its management because stronger muscles stabilize weaker joints, thus preventing dislocations, subluxation, and falls. Patients with EDS, especially those with hypermobility, need to practice posture control during daily activities and night sleep; and avoid high impact sports and spinal manipulation (1-5, 8, 10-17, 19-22, 31).

Medication, such as medicinal CBD, is also helpful for pain, neuropathy, migraine, inflammation, IBS, sleep, anxiety, involuntary movements (13 - chapter 19, 25-43). Dr. Arash Taghvai, Manager of Clinical Affairs at the Apollo Cannabis Clinics will present an overview of medicinal cannabis.

Answer to Advance Webinar Question: Other than pain management is there any upcoming cure?

a.-We can cure/fix co-existing EDS conditions, such as surgery (craniocervical and/or cervical instability, dislocating joint, ruptured ligament or tendon, inguinal hernias), and lifestyle changes provided by PT who help patients restore physical function, OT who focus on how that function affects the ability to do the things that are important, and physiatrist a medical doctor who

focuses on diagnosing, preventing, and treating all types of disabilities related to brain, nerve, bones, and muscles.

b.- But we cannot cure/fix the EDS itself that affects the entire body being a genetic disease with mutations in at least 19 genes. Gene therapy is used to correct defective genes in order to cure a disease or help your body better fight it, such as Replacing mutated genes or Fixing mutated genes turn on/off.

=> Yes gene therapy is promising, but also has risks: unwanted immune system reaction, targeting the wrong cell, infection caused by the virus, possibility of causing a tumor → see **Reference 23, Gene Therapy Mayo Clinic**

Answers to questions about the process on gene therapy in Canada → see **Reference 24, From Research to Reality, The Expert Panel on the Approval and Use of Somatic Gene Therapies in Canada, 2020**

EDSociety early 2019 started recruiting 1000 patients for an international genetic study HEDGE = Hypermobile Ehlers-Danlos Genetic Evaluation. Mid 2021, thus, 2 ½ years later started collecting blood samples. As we can see, it takes many years to find a treatment/cure, drugs or gene therapy. For example:

- recruit 1000 EDS participants willing to participate (many do not want to have their blood analyzed due to privacy concerns) and must meet the strict selection criteria,
- collect the data, blood samples, from 1000 EDS patients worldwide
- analyze the data, the genes with mutations and how can be tricked to find a cure
- write a report (several authors from different medical fields and different countries
- publish it (peer reviewed) => all the above over 5 years,
- clinical trial tests in Canada & USA are done in 3 phases and write report after each one => about 10-15 years
- if not successful, find new treatment and test again this new treatment => 15 years = this is the case now with Alzheimer treatment after 20 years the new drug is very controversial
- finally receive approval for treatment from federally regulated medical bodies in Canada, USA, UK, etc => up to 5 years

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