From: http://www.reumatologia-dr-bravo.cl/ “When to Suspect” document for patients(Dr. Bravo, Chile)

When to suspect the diagnosis of Ehlers-Danlos type III, also called Joint Hypermobility Syndrome (JHS). (In language for patients)

When there is: (one is enough to suspect JHS)

· **History of recurrent musculo-skeletal problems, such as**: tendinitis (tennis elbow, trigger finger, Aquiles tendinitis, etc.)¸bursitis (shoulder bursitis, trocantheric bursitis (hip) or recurrent sport injuries (ruptured tendons, ruptured ligaments or ruptured muscles). Frequent ankle sprains. “Growing pains” in children.

· **Joint pain (arthralgias), without inflammatory signs (redness, heat) for more than 3 months, without apparent cause**. There are no inflamed joint is JHS (synovitis). JHS is the most frequent cause of musculo-skeletal pain in any rheumatological clinic.

· **Frequent cracking noises of the joints.**

· **Soft skin (like velvet), lax, pale, transparent (permits to see the veins) with poor cicatrisation, at times queloides (bulging scars) or thins scars, like paper (papiraceous scars), which is seen in scars from vaccines**. Telangectasias (red lilaceous small veins). Livido reticularis (reddish reticular net). Striae without an apparent cause, in young people and specially in the lumbar area. “Droopy” (“tired”) eyes. At times dark skin on the dorsum of the elbows and interphalangeal joints (“dirty elbows”). Brown moles, the size of lentil peas (called lenticular moles) than can appear anywhere in the body, specially arms and face. Prominent veins on the dorsum of the hands. Skin alterations in JHS are frequent (94%). The skin characteristics can be so typical (soft, supple hand), that the diagnosis of JHS can be suspected just with a handshake.

· **Capillary fragility**: recurrent hematomas, with only a slight touch or without cause, a time looking like battered child or familiar battering. In children it can be confused with von Willebrand disease (vWD), since in both cases the coagulation studies are normal, except for the bleeding time, that is prolonged in both. The difference lies in that vWD has positive Factor VIII and JHS does not. Nosebleeds or gingival bleeding can be seen.

· **Hypermobility of one or more joints, with symptoms of pain, tendinitis, subluxations, etc**. Patients may be able to extend the fingers backward, touch the forearm within the thumb, hypermobility of the wrist and hyperextension of the elbows. Knees may go backwards (genu recurvatum). It is interesting to note that laxity may affect one or few joints and the patient may not be aware that she has hypermobility. Furthermore, someone can have no lax joints (Beighton score of 0/9) and still have JHS if she has alteration of tissues (**for this reason a better name is Ehlers-Danlos type III**),

like varicose veins, hernias, myopia, etc., and in this way having a positive **Brighton** criteria, that is diagnostic of JHS.

Hypermobility, at times, can be obvious just by looking at a person (affecting fingers, elbows, wrists, knees). The person can touch the floor with the palm of the hands, or could do those years before. As a child she could do "party tricks" with the fingers, or could contorsionate her body or suck her big toe.

· The patient can have one of the following signs, due to hypermobility:

- "**Flying bird hand sign**". Active extension of the fingers.
- "**Horizontal thumb sign**". Active flexion of the thumb over the palm.
- "**Hand holding the head sign**". As if tired.

New signs described by us:

- "**Elephant track sign**". The skin over the interphalangeal joint wrinkles in a circular form, simulating the foot imprint left by the elephant when walking.
- "**The hand of the lax scribe sign**". These patients hold the pencil with marked flexion of the fingers or they used 4 fingers instead of the usual 3. They also frequently turn a little the page when writing.
- "**Square shoulders sign**". Frequently in Marfanoid patients with SHA.

· **Articular subluxation** (the joint gets out of the usual position) this is usually seen in the base of the thumb, elbows, shoulders and knees (subluxation of the knee cap) and the temporomandibular joint, with bruxism and occasional locking of the mandible.

· **Back pain**: due to scoliosis (at times since early life), hiperlordosis
(deep lumbar area), due to lumbar disc problems or simply due to laxity of the spinal ligaments.

· **Alteration of the soft tissues**: hernias, umbilical or inguinal hernia, herniated nucleous pulposus, varicose veins in young people, hemorrhoids, varicocele (varicose vein of the testicles), vaginal or rectal prolapse (hanging tissues), Mitral valve prolapse, cysts of all types, including wrist Ganglion and Baker´s cyst (back of knees), reflux, constipation (even megacolon), irritable bowel syndrome, myopia and strabismus (cross-eyes).

· **Spontaneous rupture of the lungs (spontaneous pneumothorax).** This frightening complication is more frequently seen in **Marfan syndrome**, but also can be seen in JHS and in the Vascular Ehlers-Danlos. It is more frequent in males. The lung tissue may rupture with minimal or no trauma. The patient experiences sudden chest pain and severe difficulty breathing and requires emergency treatment, but is not fatal.

· **Neurological and psychological problems**. It is known that depression; anxiety, panic crisis and phobias can be inherited together with JHS, as described by Bulbena. Patients can have nervousness,

headaches, migraines, and poor memory, lack of concentration and lack of energy. At times cramps, nervous legs and poor response to inyectable analgesics, like by the dentist.

· **Marfanoid habitus (MH). Tall, thin adolescents with long extremities, long fingers and big feet**. At times with flat, sunken or prominent chest and /or prominent ribs (lower ribs are prominent in anterior chest). Young girls have the figure of models, because of slender bodies and long neck, square shoulders and long fingers. MH is a minor sign of the Brighton criteria that is diagnostic of JHS. The name MH comes from the fact that these patients resemble patients with Marfan syndrome, that is a more serious disease, since it can have arterial ruptures. Marfanoid patients, males and females can have square shoulders.

· **Blue sclerae**. Normal sclerae (**the white of the eye**) is white like marble, but in JHS, especially in females, it is slightly blue. The reason being that because of lack of collagen, the membrane (sclerae) is transparent to the bluish color of the veins. Blue sclerae is seen in about 90% of JHS females, but is rare in males. Blue sclerae is normal in children up to 2 years of age.

· **Typical JHS faces** (described by us in 2006). Is characterized by (other link):

- Triangular face (pointed chin).
- Blue sclerae.
- Atypical ears: Prominent ("Dumbo").
  - Pointed ears ("Mr. Spock" ears).
  - Kidney shape (prominent middle part).
  - Question mark ears.
  - Soft cartilage.
  - Small, round ears.
  - Flat superior border of the ears.
  - Lobule attached to the face.
  - Absence of the ear lobule.
  - Operated ears.
- Atypical nose: Asymmetry (deviated nasal septum).
  - Bony nodule at the union of the bone and cartilage.
  - Soft tip of the nose (soft cartilage).
  - Operated nose.
- "Droopy" eyelids.
- Antimongolic slant of the eyes (opposite to the Chinese eyes).

In women the blue sclerae are useful and in men looking at the ears is more useful, since they seldom have blue sclerae, but frequently they have atypical ears. Both have triangular face, a feature that is helpful in suspecting the diagnosis. With experience, it is very easy to detect the "typical JHS facies", as easy as to recognize a person with Down syndrome.

· **Alteration of the involuntary nervous system (simpatico-vagal) producing:**

A.- **Dysautonomia (Dys).** A very frequent yet usually undiagnosed problem that we see and treat daily, with good results. In our study of 1226 JHS patients, Dys was seen, in patients younger than 30 years, in 72% of females and 40% of males. This condition is seen frequently in young females, usually adolescents, presenting with chronic fatigue, sleepyness, with no energy to attend social events. Usually they are labeled as lazy, depressed or unsociable, because they have no energy to alternate with other people. Frequently they have cold intolerance and low blood pressure (unfortunately most physicians do not know that low blood pressure is not normal).

Characteristics of Dys:

- **Chronic fatigue and somnolence**. It appears when standing for too long or when walking slowly. Also when stopping or finishing a job and starting to relax. More than tiredness, it is a lack of energy, like "running out of batteries". It is interesting to note that this fatigue, somnolence and lack of energy, does not happen when the person is working or playing a sport, but after finishing it or at midday or evenings, when relaxing. Many patient tells us, that they arrive home just ready to go to bed. Usually Dys is mistaken as chronic fatigue due to anemia or other chronic diseases, hypoglycemia (low sugar), hypothyroidism or depression.

- **Low blood pressure**. This is many times unknown to the patient. At times, instead of low blood pressure, Dys manifest itself with tachycardia (this is called POTS). The body tries to compensate the decrease of oxygen to the brain with tachycardia (rapid pulse). As time goes by, the blood pressure starts to increase and in older patients Dys may happen even if they are known to have hypertension. In these people the problem is that all of a sudden they have a drop in blood pressure and they get Dys symptoms.

- **Dizziness**. The patient gets dizzy when standing up suddenly or getting out of bed in a hurry. True syncope is rare, but is frequent that these patients have pre-syncopal episodes.

- **Cold intolerance**. This symptom is usually quite pronounced. Even though these patients usually prefer warmer weather, the heat occasionally causes them to suffocate, what we call "broken thermostat".

B.- Sweating especially of the hands. These patients usually complain of cold hands and feet and that if they have a nap without covering themselves with a blanket, they get a cold.

C.- Acrocianosis (red-lilaceous color of the hands). This phenomenon happens not only with cold weather, but also with dependency and with inactivity of the hands (is due to poor circulation).

· **Problems with altitude**, due to lack of oxygen to the brain. Patients may also have problems ridding the "Russian Mountain" at the amusement park.

· **Intolerance to prolonged hot baths or saunas**, seen in JHS patients with Dysautonomia.

· **Early Osteoarthritis (OA**). OA causes wear and tear of joints. Due to the alteration of collagen the cartilages of patients with JHS are weaker than normal and will wear out earlier. For this reason, we see OA in young JHS patients and in them, the cartilage destruction is more rapid.

· **Varicose veins and or Hallux Valgus in young people.** The presence of these in young people is suggestive of JHS.

· **Myopia (difficulty to see something close**). This eye problem appears to be usually associated to **astigmatism** and its presence may suggest JHS. Another eye problem that suggests JHS is strabismus (cross- eyes).

· **Extreme mobility of the tongue**. The tongue can be long, reaching the nose; mobile, able to make a tube; turn around or even make a rosette. The absence of lingual frenulum in children may herald hypermobility.

· **Low bone mineral density or osteoporosis in young males and females, without an apparent cause**. In our study of 972 JHS patients, osteoporosis was present in 19% of males and 19% of females younger than 30 years old. We have treated osteoporosis in adolescents with good result. These young patients with osteoporosis do not experience fractures with the frequency that older patients with other types of osteoporosis do.

· **Fibromyalgia (FM).** Many patients diagnosed as having Fibromyalgia really have JHS, since many symptoms are very similar, with recurrent pain, "trigger points", chronic fatigue and with normal laboratory tests. **It is my opinion that FM is part of the JHS disease, since all patients with FM that I see fulfill the Brighton criteria that is diagnostic for JHS. Wed call these pains "fibromyalgic pains of JHS".**

· **Associated congenital malformations**. JHS patients frequently have associated malformations, such as:

- Scoliosis, in infancy.
- Hip dysplasia.
- Malformations of the feet:
    - Flat feet.
    - Anterior or longitudinal lax foot.
    - Cavus foot (the opposite of flat feet).
    - Egyptian foot (second toe is longer than the first.
    - Hallux Valgus in young people.
    - Partial syndactily (toes glued together).
- Rotated knees.
- Spina bifida occulta (seen on x-rays of the lumbar spine).
- Spondylolisthesis (one vertebra sliding over the next, as seen on x-rays of the lumbar spine).

· Patients with some of the above signs or symptoms already described, that have seen many physicians, undergone multiple tests, with negative results and the **cause of their problem remain unknown.**

· **Relatives of JHS patients**, presenting signs or symptoms suggestive of JHS or that already carry the diagnosis of JHS.

· **Suggestive signs in children**. Hip dysplasia. Scoliosis in infancy. Delayed motor development (late walkers). Hypotonic muscles (soft). Recurrent sprains or subluxations. Lack of concentration. Alleged dyslexia. Growing pains. Frequent hematomas (alleged battered child). Children that perform "party tricks" with their hands. Parents with JHS. Presence of Hypermobility.

Note: Any of these signs or symptoms may start at any age. It is necessary to remember that children are more lax than adults and females more than males.

It is important to know that Joint Hypermobility without symptoms is a good quality to have, **but when it produces pain and symptoms, then we are dealing with a disease, Joint Hypermobility Syndrome (Ehlers-Danlos Syndrome type III).**

Name change:

We are in a campaign to convince physicians, public and patients that a better name for this disease should be Ehlers-Danlos Syndrome type III (EDS-III), instead of Joint Hypermobility Syndrome (JHS). The reason being is that at least 50% of the patients with EDS-III (61% negative Beighton Score) don't have hypermobility, thus we cannot catalog all of them as hypermobile. Furthermore, and very important, when we speak of Joint Hypermobility Syndrome we do not give the subject the importance it deserves, since, at a glance, it implies a good condition to have, rather than a disease with frequent complications. This has brought us to conclude that the name that we have been using, diverts the awareness of this disease, and is the reason for the lack of interest by physicians and poor understanding of this disease by patients and public in general.

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