ADAPTATION OF SPORTING ACTIVITY IN GENERALIZED JOINT HYPERMOBILITY SYNDROMES

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I. Introduction

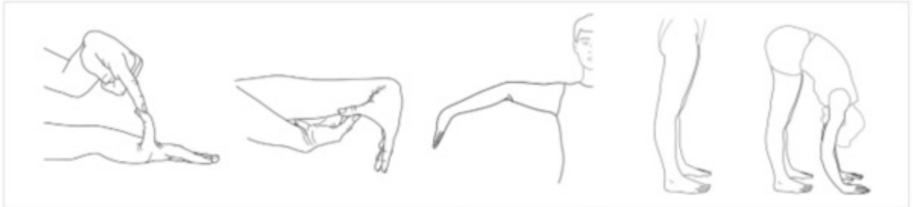
The terms joint hypermobility and hyperlaxity are often confused and used interchangeably in the literature. Hyperlaxity is defined as excessive movement of the joint in an abnormal plane of motion. Joint hypermobility is defined as increased range of motion in a normal plane of motion (1). Joint hypermobility is usually confined to a limited number of joints. Therefore, the etiology is generally localized to the joint and may be due to an abnormality within the joint itself or secondary to training (1). We will present below the etiologies associated with generalized joint hypermobility (GJH), i.e., involving all joints.

Syndromes of GJH may be associated with other manifestations, such as proprioceptive issues, joint instability, chronic pain, and involvement in other organs. Management is complex and requires the consideration of all said disturbances.

II. Generalized joint hypermobility

a. Diagnosis

The diagnosis of GJH is based on the Beighton score, which is modified by Horan (2). This score is based on a nine-point quotation system and tests the mobility of the metacarpo-phalangeal joints of the 5th ray, the elbows, the knees, the hips, the spine, the 1st ray of the hand, and the wrist.



Beighton score (Malfait et al. 2017)

According to the 2017 international consortium on the Ehlers-Danlos syndrome (3), the threshold for to diagnose GJH is set at 6 in pre-pubertal children, 5 in subjects younger than 50 years old, and 4 in subjects older than 50. If the modified Beighton score is lower than the set threshold by a single point, the 5QP questionnaire is then used. Two positive responses would suffice to diagnose GJH (3,4). Nevertheless, there is a large variety of definitions of GJH in the literature. The most frequently used one is with the Beighton score, but the threshold for diagnosis is also variable (5). A score of 4 is the most frequently used threshold regardless of the subject's age (1).

The threshold in children is set at 6 since a large number of children present with physiologic hypermobility that evolves with age (1).

b. Epidemiology

The exact prevalence of GJH has yet to be determined. There is a large variability in the prevalence of GJH in the general adult population with a lack of homogeneity both in the definition of joint hypermobility and in the characteristics of the studied populations in the different studies. This prevalence is higher in females compared to males and is around 4% to 23% with both sexes combined, 5.6% to 31.5% in females, and 2% to 14.7% in males (7-9).

In 2007, Jansson et al. published a prospective study on a national Swedish cohort of 1,845 children aged 9 to 15 years old. At 9 years old, 48% of girls and 38% of boys presented a Beighton score ≥4; 53% and 16% respectively at 15 years old (10).

A meta-analysis published in 2020 including 20 studies (15,097 boys and 6,48 girls) reported a prevalence of 34% in children and adolescents, including 32.5% in girls and 18% in boys (Beighton score ≥4) (11).

c. Pediatric considerations

Hypermobility evolves during growth. Within the same Swedish cohort, joint hypermobility in boys and girls plateaued at 9 years of age, followed by a progressive decrease until the age of 12. Between 12 and 15 years of age, boys did not have any further modification of their joint mobility, whereas joint hypermobility rebounded with a novel aggravation at the age of 15 (10).

		Beighton score					
Age (y)	Gender	≥4	≥5	≥6	≥7	≥8	9
9	Boys	37.6	20.2	16.1	5.6	**5.0**	0.3
	Girls	47.9	26.4	21.8	7.3	**5.7**	1.2
12	Boys	21.0	8.6	**6.2**	0.6	0.3	0.0
	Girls	37.8	19.9	14.9	**5.4**	3.0	0.9
15	Boys	15.5	7.9	**7.2**	2.8	1.7	0.3
	Girls	53.0	33.4	24.0	13.9	**7.4**	2.0

Table 1 - The distribution (%) of children with different cut-off points for general joint laxity estimated by the Beighton score – From A Jansson et al. 2007

III. Etiologies

Numerous etiologies have been suggested for GJH, all of which have connective tissue disease in common, which are secondary to abnormalities of certain proteins, such as collagen, fibrillin, elastin, or tenascin (12). Depending on the protein, different structures and organs may be affected. The capsuloligamentous structures, tendons, muscles, or other connective tissues, especially vascular, can be also affected.

The most common diagnoses are asymptomatic GJH, generalized hypermobility spectrum disorders (G-HSD), and Ehlers-Danlos syndrome (EDS). These entities make up the spectrum of hypermobility disorders according to the 2017 international consortium (3). The limits between these different syndromes are somewhat blurred, where, in fact, they represent a pathological continuum (13).

HYPERMOBILITY SPECTRUM DISORDER			
	Phenotype	Beighton score	Musculo-skeletal disorder
Asymptomatic	Asymptomatic PJH	Generally negative	Absent
	Asymptomatic LJH	Negative	Absent
	Asymptomatic GJH	Positive	Absent
HSD	P-HSD	Generally negative	Present
	L-HSD	Negative	Present
	H-HSD	Negative	Present
	G-HSD	Positive	Present
EDS	HEDS	Positive	Possible

PJH: Peripheral joint hypermobility; LJH: Localized joint hypermobility; GJH: Generalized joint hypermobility
P-HSD: Peripheral hypermobility spectrum disorder; L-HSD: Localized hypermobility spectrum disoder; H-HSD: Historic hypermobility spectrum disorder; G-HSD: Generalized hypermobility spectrum disorder; HEDS: Hypermobile Ehlers-Danlos syndrome

Figure 1 – Hypermobility spectrum disorders – From sedinfrance.org

Other causes may also lead to hypermobility, such as genetic syndromes with more widespread and severe organ involvement, such as Marfan syndrome, Down syndrome, Osteogenesis

Imperfecta, and other rarer syndromes (Loyes-Dietz, Beals, Larsen, Desbuquois, Rapadilino, Dubowitz, Stickler, Kabuki, etc.) (3,12,14).

a. Ehlers-Danlos syndrome (EDS) and generalized hypermobility spectrum disorders (G-HSD)

Ehlers-Danlos syndrome and generalized hypermobility spectrum disorders are integrated pathologies and form in a clinically and genetically heterogeneous group of connective tissue disorders. They have in common certain clinical signs including generalized joint hypermobility, proprioception issues, cutaneous anomalies, chronic myalgia and arthralgia, abdominal pain, and asthenia and muscle fatiguability (3). G-HSD is diagnosed when patients do not present all the criteria for the diagnosis of EDS despite a similar clinical presentation. The divide between these two entities is arbitrary, but management is similar.

There are 13 subtypes of EDS that are classified according to the affected organs, their predominance in the clinical scenario (vascular, cutaneous, spine, etc.), and the identified genetic mutations. Hypermobile HEDS is the only subtype that has as of yet no clearly identified mutation (3,15). Vascular EDS is usually left out in studies on EDS and sports since the risk of severe vascular complications drastically modifies their management (16).

b. Confusion between GJH, HSD and HEDS

Patients are considered as having GJH if there is absence of pain or trauma accompanying the hypermobility and when there is an absence of other systemic manifestations.

Practically speaking, properly differentiating between GJH, G-HSD, and HEDS is difficult and rarely achieved (13). As such, it is agreed that, in many studies on patients with joint hypermobility, the study populations present with GJH, G-HSD, and HEDS in unknown proportions.

IV. RISK FACTORS FOR GJH

Multiple risk factors for generalized joint hypermobility have been identified, independently of the etiological diagnosis of JGH, G-HSD, or EDS.

Sex is considered as a risk factor for GJH. The effects of female hormones on joint mobility remains to be fully understood. Studies present contradictory results; while some find an increase in joint mobility during certain phases of the menstrual cycle (17,18), others have not found any associations between these two parameters (19,20). It is also admitted that females are at higher risk of GJH, with identical thresholds used for both sexes.

Ethnicity is considered by some authors as a risk factor for GJH (1). In fact, some studies in India and Nigeria have reported a much higher prevalence of hypermobility (21).

Nevertheless, data analysis should be undergone with caution. Firstly, the homogeneity of the samples used for calculating the true prevalence remains controversial. Moreover, the absence

of distinction between localized hypermobility and GJH in some papers could represent a significant bias. In fact, other authors showed differences in mobility in some joints between the two ethnicities, but did not show, or did not search for, differences in GJH prevalence (22,23). These differences would more likely be due to lifestyle than a systemic pathology.

Apart from the diagnoses of EDS linked to known mutations, there are also genetic factors at play in the transmission of GJH and HSD (24).

V. Sports and hypermobility spectrum disorders

a. Epidemiology

Multiple studies have shown a higher prevalence of GJH in athletes compared to the general population. Akodu et al. reported a prevalence of GJH as high as 50% in 102 cricket players (25). Soper et al. reported a prevalence of GJH of 63% in 27 professional netball players (26). Multiple studies have found similar results in other types of sports as well, such as figure skating, dancing, gymnastics, etc. (27,28).

However, some athletic groups, such as rugby and lacrosse players, have not shown a higher prevalence of GJH (29,30).

Finally, some sports such as football (soccer) have shown a varied prevalence depending on the studies, ranging from 8.8% to 33% (31,32).

This higher prevalence of GJH in certain athletes remains to be fully elucidated but may be explained by the advantages that hypermobility brings to certain types of sports requiring more agility (28,33-35). This hypothesis has yet to be proven, since this advantage in agility does not always compensate for the disadvantages, such as proprioceptive and musculoskeletal disorders (33).

b. Effect of hypermobility spectrum disorder on the physical and psychological abilities and the risk of injury

From an orthopedic point of view, patients with HEDS or a G-HSD present with varying degrees of proprioception issues, hyperlaxity, fatigability, alterations in muscular functioning, chronic atraumatic musculoskeletal pain, and dysautonomia with a postural syndromes or orthostatic tachycardia. All these issues may lead to troubles with stasis, joint deformities (e.g., pes planus), and increased risks of articular and extra-articular injuries (12,16,36). In children, acute joint pain is aggravated by physical activity in 81% of patients and appear within 24h of physical activity. These pains are primarily localized to the knees and the shoulders. These could be secondary to joint overuse during activity, although the pathophysiology is not well elucidated (37).

Patients suffering from G-HSD present with proprioception and equilibrium issues, and decreased quadriceps and the hamstrings muscle strength (37). Furthermore, some studies indicate

alterations in musculoskeletal control and coordination at the knee in patients with GJH (38,39). Nevertheless, these anomalies of knee function are controversial (40).

Dysautonomia and repetitive trauma may sometimes lead to kinesiophobia (12,41,42). Patients with GJH or HEDS present with more health-related subjective complaints, which is aggravated by ignorance of their symptoms and a sense of lack of control (37,43). 48% of these patients cannot participate in sports at school (37).

Patients with EDS or HSD are at increased risk of injury (44,45). However, this affirmation remains dependent on the type of practiced sport, the level of involvement, and the type of physical preparation. Contact sports are increase the risk of knee injury. In a 2010 meta-analysis, Pacey et al. found a positive association between knee injury and GJH with an odds ratio of 2.62, regardless of the type of sport. This increased to 4.7 in contact sports (44).

The risks are not identical between amateur and professional athletes. In a study on 816 students who occasionally participated in sporting activities, Reuter did not find higher rates of musculoskeletal injury in GJH (46).

The risk of osteoarthritis is also not increased in GJH (47,48) but could even decrease according to some authors (49,50).

c. Ability to recuperate and surgical risk

Patients with GJH have a slower recuperation after physical activity or after sustaining an injury (5,35,51). This could be due to the slower rate of scar formation in patients with HEDS (52,53). On the surgical level, some authors have reported an association between HEDS and G-HSD with a higher risk of intraoperative bleeding, and a longer period of wound healing. A few cases of resistance to local anesthetics have also been reported, but evidence confirming this hypothesis is lacking (54). Anesthesia should also be adapted. In some GJH syndromes, cervical instability during intubation has been described. Hemodynamic parameters may be altered in case of dysautonomia. Fragility of the dura mater increases the risk of cerebrospinal fluid leak and intracranial hypotension during spinal anesthesia (52,53).

VI. Specific joint injuries

a. Shoulder

The most frequent clinical manifestation in patients presenting with GJH is multidirectional shoulder instability (MDI) (6). In the literature, 40% to 70% of patients with an MDI have GJH (55). In a study on a cohort of 714 young military cadets with an average age of 18 years old, 88% of which were male, Cameron et al. found a relative risk of 2.5 of presenting an MDI if the Beighton score was ≥2 (56). Athletes with GJH are at increased risk of shoulder injury (45, 57). In case of acute structural injury to the shoulder, management is similar to those without GJH (58). Conservative management of chronic shoulder instability in GJH has shown satisfactory results

(58,59). Nevertheless, the results of G-HSD and HEDS are less satisfactory than the general population. In a case-control study including 250 individuals with MDI (110 HEDS and G-HSD vs 140 controls), Johannessen et al. showed that G-HSD and HEDS were poor prognostic factors for shoulder function, pain, and quality of life (60).

The outcomes of surgical treatment remain scarce in patients with GJH. A few studies with small sample sizes have shown encouraging results with capsular shift surgery (54, 61,62). In a series of 50 adolescents with MDI who were treated with arthroscopic capsular shift, Mitchell et al. did not find a relationship between the 6-year postoperative outcome and the presence of GJH (63). In a cohort of 81 patients who were operated for shoulder instability with a Bankart repair, Joon-Ryul Lim et al. reported a higher incidence of Hill-Sachs lesions in patients with GJH, which were deeper than in the general population, but found no differences in functional outcomes after 2 years of follow-up (64).

Patients with a G-HSD or HEDS are also at increased risk of presenting a thoracic outlet syndrome. Its management is primarily based on rehabilitation. Botox injections at the level of the anterior scalene muscles and the pectoralis minor may also be effective. Surgery is usually reserved for patients who have failed conservative management (54).

b. Elbow

Elbow pathologies associated with GJH have been scarcely studied.

Patients with G-HSD or HEDS are at increased risk of medial and lateral epicondylitis and radial tunnel syndrome. Treatment with rehabilitation and platelet-rich plasma may also be effective. Surgical treatment may be considered in case of failure of conservative treatment, although data regarding its effectiveness are lacking.

Some authors have suggested that an association between GJH, G-HSD, and HEDS may exist, leading to posterolateral rotatory instability of the elbow (6,65,66).

c. Wrist and hand

The association between wrist hypermobility and ligamentous injuries of the carpal bones has yet to be made. Gracia et al. showed a correlation between wrist hypermobility and ulnar variance, thereby leading to a theoretical increase in the tensions at the level of the TFCC, and thereby an increased risk of injury (67). They also found that wrist hypermobility increased tensions on the pre-scaphoid ligaments with a theoretical increased risk of injury (68). However, clinical studies have not shown an increase in the prevalence of wrist injury in patients with GJH, even in athletes relying markedly on repeated wrist movements (25-30). For Ericson and Wolman, chronic wrist pain is secondary to trauma from repetitive falls on the hand. Rehabilitation and physical exercises would aggravate the symptoms. Surgical treatments aimed at stabilizing the wrist have not been thoroughly studied but might prove effective (54).

Some authors have reported that hypermobility of the carpo-metacarpal joint of the 1st ray could be a risk factor for osteoarthritis (69). However, many studies have not shown this association with GJH; they have even shown that GJH might be a protective factor against osteoarthritis of the hand (49,50). In both the recommendations of the Ehlers-Danlos Society and the 2017 consortium, non-arthritic carpo-metacarpal injuries of the 1st ray of the hand are described and, based on the scant data found in the literature, surgical strategies, such as arthrodesis and stabilizing surgeries, were found to be effective (54).

Long finger subluxations are also frequent, and their treatment includes figure-of-8 splinting (54).

Cases of chronic sesamoiditis have also been described and are usually treated by sesamoidectomy (54).

d. Hip

Studies on dancers have shown that individuals presenting with hip hypermobility were at increased risk of hip instability, extra-articular injuries, femoro-acetabular impingement, and osteocartilagenous and capsuloligamentous injuries (28). Studies on the hip have mostly concentrated on dancers and gymnasts who, due to their training regimens, are at increased risk of developing focal hypermobility. The influence of generalized hypermobility on the occurrence of such events has not been studied, but several authors consider it to be a risk factor (28,34). In a study on 100 hips evaluated by arthroscopy, Devitt et al. found that patients with GJH presented with a finer joint capsule, which could inherently lead to instability (70).

In EDS, the arthrochalasia subtype is characterized by bilateral congenital dislocations of the hips (71). Furthermore, an association between hip dysplasia and GJH has been hypothesized (72,73).

Iliotibial band syndrome due to impingement on the greater trochanter is frequent in this population. First line of treatment is rehabilitation and steroid injections. In case of failure, surgical treatment may be suggested (54).

Patients with HSD or HEDS could also have pain due to sacro-iliac instability. Recommended treatment is primarily rehabilitation and temporary splinting, with arthrodesis as a last resort (54).

Piriformis syndrome is also frequent in this population, with an ill-defined prevalence. The recommended treatment is rehabilitation and chiropractic treatment (54).

e. Knee

Patients with GJH can also present with hypermobility during knee extension and anterior cruciate ligament (ACL) laxity during the pivot shift test (74). They can become symptomatic in adulthood, with an alteration of knee function and activities (38,75). Numerous studies have shown that GJH is a risk factor for sports-related knee injury (46). In a meta-analysis of 4 studies

including 1167 athletes, Pacey et al. found a global incidence of knee injury of 8.65%, with an odds-ratio of 4 in patients with GJH regardless of the type of sport, and of 4.7 in contact sports (44).

GJH has been shown to be a risk factor for traumatic ACL rupture, even in the absence of knee hypermobility (76). This risk is also increased in patients with genu recurvatum (77,78). ACL ligamentoplasty is an effective technique in this population, but with an increased risk of failure. According to a study by Magnussen et al. on 2,333 patients with a 2-year follow-up, ACL ligamentoplasty (regardless of technique) in patients with GJH showed good results, comparable to those of the general population, but with a higher risk of revision surgery (79). In a literature review, Krebs et al. found a risk of failure of around 6% to 30% in case of GJH, compared to 0% to 12% in the rest of the population (80). In a cohort of 72 patients with a 2-year follow-up, Kim et al. found that double-bundle quadriceps tendon grafts had better clinical results in this population, compared to quadruple-bundle semitendinosus-gracilis or patellar tendon grafts (81). The same team showed in 2008 that a patellar tendon graft was superior to a quadruple-tendon semitendinosus-gracilis graft (82). Krebs et al. were also veering in the same direction (80). Repair by quadriceps tendon showed a lower postoperative anterior translation when the repair was undergone with 2 bundles, although a clinical difference was not seen (83). The different ligamentoplasty techniques and postoperative physiotherapy programs might explain the discrepancies found between the different authors in terms of functional outcomes in patients with GJH (84,85).

Furthermore, GJH has been shown to be a risk factor of recurrent subluxations of the patella. Nevertheless, localized patellar instability (with or without GJH) remains the primary risk factor (86). Between 40 and 57% of patients with HEDS present with patellar instability (87). To our knowledge, no study has evaluated a relationship between the incidence of patellofemoral primo-dislocation and GJH. Today, the techniques of patellar stabilization are essentially medial patellofemoral ligamentoplasty (MPFL). This technique is effective in the treatment of this type of instability in patients with GJH (88,89). When comparing the functional outcomes after MPFL reconstruction in patients with and without GJH, Howells et al. found lower functional outcomes in patients with GJH (88), while Hiemstra et al. did not find any differences (89). This could be explained by different surgical techniques between the two studies.

In addition, GJH seems to be a risk factor for meniscal injury, although evidence is still scarce (90,91). Nevertheless, GJH does not appear to increase the risk of early osteoarthritis. In a systematic review of 3 studies and 1,937 patients, Shiue et al. did not find an increased risk of post-traumatic osteoarthritis in patients with GJH when controlling for knee injury as a confounding factor (47). Chen et al. had similar conclusions, even suggesting that GJH could be a factor protecting against osteoarthritis (49).

f. Ankle

It is uncertain whether GJH is a risk factor for ankle injury. Data in the literature are contradictory. Multiple studies have shown an increased risk of injury during physical activity (92,93). In a

literature review of 6 studies and 1,361 patients, Pacey et al. did not find an increased incidence of ankle injury in patients with GJH (44). This risk is probably due to the etiology of GJH, the type of sport, the level of sporting activity, and the type of training.

Lateral ankle instability is the most frequently described chronic injury in hypermobile patients. However, its incidence remains unknown, and no studies have assessed GJH as a risk factor for this pathology. Some studies have suggested that treatment of this instability be undergone with the Broström technique. Failure rates are markedly increased in patients with GJH (94,95). Park et al. found a failure rate of 45% in patients with GJH, compared to 11% in the absence of hypermobility, with the risk of failure peaking around the 20th month (94). Nonetheless, Dong Yeo et al. operated their patients with arthroscopic Broström reconstruction and found similar results between patients with and without GJH (96). As such, adaptation of the surgical technique could be the solution. Regardless of the chosen technique, patients with GJH improved both radiographically and clinically (objective and subjective) postoperatively (94-96). In 2017, the international consortium on Ehlers-Danlos syndrome and G-HSD recommended avoiding these types of surgeries and preferred rehabilitation with flexible orthoses and in-soles (54).

g. Foot

The impact of hypermobility on injuries of the foot have scarcely been studied. Recent studies have shown that GJH was associated with an altered loading and gait patterns, with a higher prevalence of flat feet (97-102). In terms of managing symptomatic flat feet in these patients, orthopedic insoles may be effective, but evidence is lacking. Surgical treatment in this population has yet to be studied. Subtalar arthroereisis could be an interesting option based on its encouraging outcomes (54,103).

Golightly et al. found that knee hypermobility was associated with talonavicular osteoarthritis and foot and ankle pain, without any direct relationship with GJH (104).

Some authors described cases of metatarsalgia in patients with G-HSD in whom treatment with insoles was shown to be effective (54).

h. Spine

Multiple spinal pathologies have been linked to HEDS, such as C1-C2 instability, C0-C1 instability, and segmental kyphosis with instability. These pathologies could lead to spinal cord and surrounding tissue microtrauma, especially vascular, and thereby lead to multiple symptoms, such as headache, neurovegetative symptoms, back pain, and radiculo-myelopathy (105). Studies concerning the complications of GJH are contradictory. According to some, GJH unrelated to HEDS or any other systemic syndrome, could be associated with an increased risk of low-back pain (106-107), neck pain (108), degenerative cervical discopathy (108), and lumbar disk hernias (109). However, these associations remain controversial (108,110-112). Some authors have suggested that GJH could be, in fact, a protective factor against lumbar arthritis (110,112).

To our knowledge, no studies have evaluated the relationship between sports-related traumatic spinal injury and GJH.

According to the 2017 consortium, spondylolysis is frequently found in this population, and its management is similar to that of the general population (54).

VII. Recommandations during sporting activity

Screening of G-HSD and EDS seems necessary in athletes due to the high prevalence of these pathologies in this population (5).

Physical exercise in patients with EDS or HSD present several advantages, such as decreased joint pains, fatigue, and improved proprioception and quality of life (12,112).

Patients with G-HSD or EDS should be managed based on their needs. In fact, the multiple disorders secondary to the G-HSD and EDS require a specialized multidisciplinary approach. The Ehlers Danlos society published in 2017 recommendations on the management of these patients (37,113). In France, the French rare diseases Healthcare Network: bone, cartilage and calcium diseases (OSCAR) published in 2020 its recommendations on the management of non-vascular EDS (36). The Study and Research Group for Ehlers-Danlos Syndrome (GERSED), based on its literature review along with the experience of the specialists managing EDS, established numerous detailed and easy to access recommendations that are useful in the management of these patients (114).

Patients presenting a G-HSD and EDS should be informed of the risks related to their pathology and be guided during the adjustment of their lifestyle and physical training. Some authors suggest adjusting physical activity based on the following moto “star low, go slow” (114). Many patients could potentially experiment with cycles known as “boom and bust”, where training takes the form of a phase of hyperactivity for a day, followed by a phase of hypoactivity for a week, based on the pain experienced and global fatigability. Patients should learn to avoid this phenomenon of cycles by regulating their activities; we speak of “pacing” (114).

In the pediatric population, the factors favoring adherence to suggested management strategy should be strived for and include explaining the objectives of the management strategy and of their foundations to the children, maximizing parental support, and partaking in activities as a family (37).

Rehabilitation is essential for pain management, increase of physical strength, and improvement of proprioception both in children and adults. There is still insufficient evidence to devise the optimal rehabilitation protocol for these patients (37). Nevertheless, some authors have suggested focalizing physiotherapy on proprioceptive training and working on postural and progressive isometric and eccentric exercises with complete use of the patient’s range of motion (54, 114-117).

Soft stretching exercises have shown to be beneficial on both the patient's mental state and arthralgia, as long as they avoid extreme positions that may lead to joint subluxation (114,118).

Certain devices may improve proprioception and thereby reduce the risk of injury. The physiology of this effect in being increasingly illuminated, but clinical studies are to this day limited. Among these devices, we cite thoraco-lumbar braces and plantar, wrist orthoses, knee, and cervical spine orthoses. Shoulder and muscle reinforcement orthoses, as well as compressive clothing seem to be ineffective (114).

Contact sports place the patient at increased risk of lower limb injury and must be avoided (44). In case of spinal instability, despite the lack of data in the literature, the potential for spinal cord injury should contraindicate high-risk sports (119).

In case of import dysautonomia or cardiovascular involvement, management becomes more complex and requires a multidisciplinary approach at a rare-diseases specialized center (12,37,114).

Fatigue may be aggravated by EDS, and G-HSD leads to a decrease in proprioception and might increase the risk of injury. As such, these entities should be treated, and their consequences not be underestimated (114).

The GERSED published recommendations for the management of dislocations and subluxations of patients with EDS that could be useful during sporting activity. Reduction maneuvers under sedation or general anesthesia usually fail due to the muscular contractions that often lead to an immediate relapse. This may be reduced by injecting Lidocaine at the level of the insertions of the muscles that cause this recurrent dislocation, although data in the literature are lacking. The management strategy is primarily on muscle relaxation associated with painkillers. Dislocations and subluxations may require multiple days to be reduced, but without increased risk of joint injury. In most cases, they do not lead to neurovascular compression (114).

There is a lack of recommendations for participation in sports in patients with asymptomatic GJH.

Practically, clinicians should be able to adapt to each patient since clinical presentations and etiologies are greatly variable.

VIII. Other syndromes and hypermobility disorders

a. Cardiovascular Ehlers-Danlos syndrome (CvEDS) and Marfan syndrome

Cardiovascular Ehlers-Danlos and Marfan syndromes have a significant increased risk of vascular complications, thus guiding management.

For CvEDS, there is a lack of recommendations for the proper rehabilitation strategy and the preferred type of sport that the child may safely engage in (120).

In case of Marfan syndrome, contact sports (rugby, boxing), weightlifting (which involves the Valsalva maneuver), activities with high G forces (including thrill rides), and submarine diving (due to the risk of pneumothorax and high tensions on the vascular system and the retina) are contraindicated (121).

Nevertheless, physical activity remains beneficial for these patients. A pilot study is actually being conducted in order to determine the most adapted type of training, the preliminary results of which have already shown improvements in quality of life, muscle strength, and cardio-respiratory capacities (122).

b. Down syndrome

According to Wetz et al., children with Down syndrome often have inferior levels of physical activity compared to typically developing children and are confronted with difficulties during physically activity (123).

Patients with Down Syndrome are submitted to higher oxidative stress (124), thus leading to early aging, dementia, and immunodeficiency (125). Rosety-Rodriguez et al. showed that physical activity allowed combatted against this oxidative stress (126). Others have shown that physical activity in these patients increased global survival, memory, and cognition (127,128).

Physiotherapy programs must be adapted and centered on the child's needs, while concentrating on their preferred activities (123). Some studies have shown the effectiveness of video games in the rehabilitation of patients with Down syndrome with a strong adherence and improved physical capacities (129). Familial accompaniment has also shown its importance in the management of these patients (130).

Atlantoaxial instability (AAI) is frequent and at risk of progression in these patients. In a cohort of 192 patients, Bauer et al. showed a global prevalence of AAI of 4.4% with a progression rate toward instability over 4 years of 1.6%. Considering this risk of instability of 1 over 23, the authors recommend an initial radiograph for children older than 3 years old with Down syndrome. The presence of an os odontoideum was a risk factor for progression toward AAI. For asymptomatic cases, repeated surveillance should be done in children with an os odontoideum. No age limit has been defined beyond which the risk of progression decreases, and thus after which follow-up may cease (131). In case of AAI, all contact sports and sports with a risk of fall are contraindicated.

c. Osteogenesis imperfecta (OI)

The 13th international conference on osteogenesis imperfecta published in 2018 a state-of-the-art paper concerning physical rehabilitation of patients younger than 18 who are affected by this pathology (132). This chapter will be based on this publication.

Osteogenesis imperfecta is due to mutations in the COL1A1/A2 genes coding for collagen. There is great phenotypical variability, ranging from an asymptomatic patient to intrauterine death. Patients present with a clinical scenario that is very identical to HEDS, with bony fragility that may be significant.

The development of bisphosphonates has considerably altered the management of these patients by significantly reducing the risk of fracture.

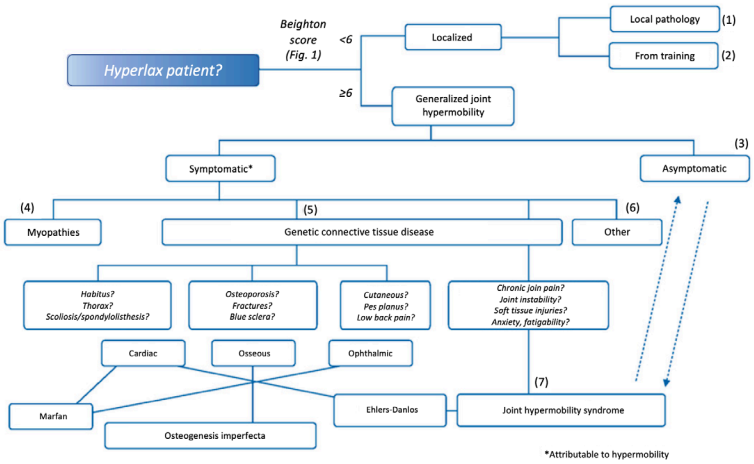
In addition to the beneficial effects of physical activity for EDS that were already described, maintaining joint mobility in patients with OI would limit the severity of bony deformities.

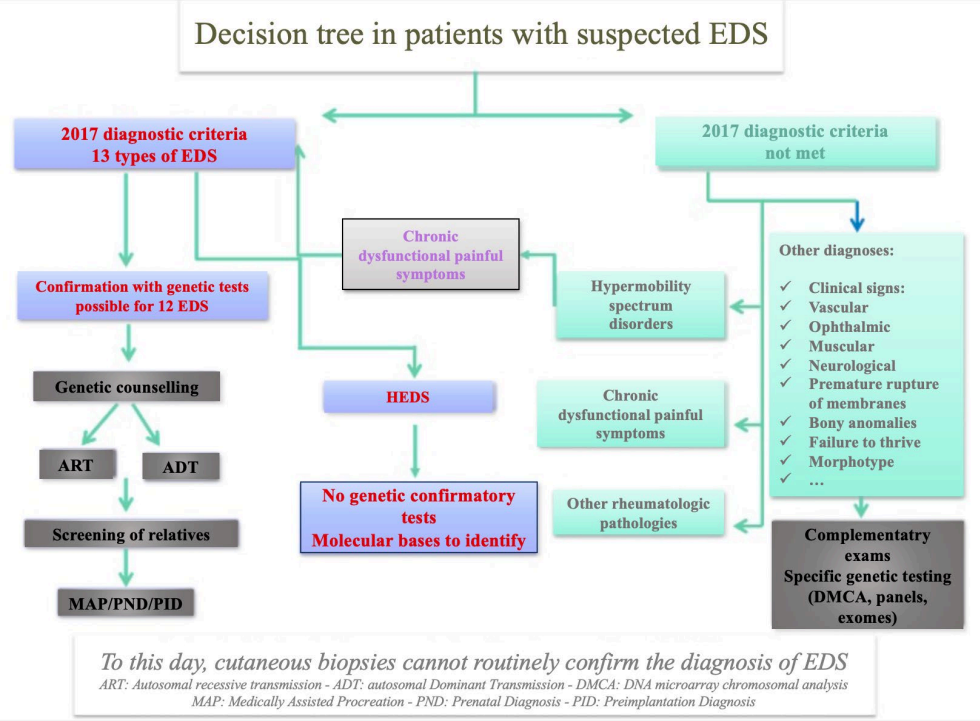
Although management is similar to that of patients with EDS, patients with OI must adjust to the risk of fracture (avoiding movements with torsion, limiting weights lifted, and reevaluating the patient after each fracture episode). 12-week training programs have showed improvements in strength, in fatigability, and in respiratory capacity in patients with both type I and IV OI. Physical activity must also be adjusted to the risk of fracture and to the physical abilities of the patient. Sports with a high risk of spinal trauma or high velocity trauma should be contraindicated in these patients if there is severe fragility of the bones.

d. Stickler syndrome

The presentation of GJH in Stickler syndrome is quite similar to that of EDS, with involvement of all of the joints, the presence of chronic pain, pes planovalgus, etc. It is distinguished by the presence of morphological epiphyseal anomalies and by an increased risk of osteoarthritis.

The literature is scarce concerning the management of sporting activities and contraindications to certain types of sports in these patients. Snead et al. suggest maintaining regular physical activity, due to its benefits on the quality of life of these patients. Sports with a low risk of impact, such as swimming and cycling, should be privileged. In severe cases, management should be adjusted to the morphological anomalies of the patient (133).





IX. Conclusion

Each patient presenting with GJH requires a specialized evaluation for a proper etiological assessment (genetic testing, other complementary tests) (figure 3). This assessment should not be neglected in patients with GJH, since patients with EDS may have a delayed diagnosis up to 12 years with significant psychosocial consequences (13).

When faced with GJH, a complete assessment of the joints, including imaging studies, if necessary, should be undergone, especially in search of signs of spinal instability. Based on patient's symptoms and the most severely affected joints, and in collaboration with a rehabilitation physician and physiotherapist, the physical conditioning of the patient could be adjusted. In case of GJH, contact sports contraindicated, especially in case of knee hypermobility. In case of spinal instability, sports with high risk of spinal trauma and those requiring extreme positions (rugby, horseback riding, certain types of gymnastics, etc.) are contraindicated. Patients with syndromes including vascular involvement (CvEDS or Marfan syndrome), bone fragility (OI), or behavioral issues (Down syndrome), should systematically benefit from a supervised management program in a specialized center.

In patients with EDS and HSD, the GERSED and the Reference centre for constitutional bone diseases (MOC), under the guidance of OSCAR, are the references for the management of these patients in France. Patient organizations, such as the SEDinFrance, may be a wonderful support system, rendering scientific information more accessible and comprehensible to patients. They

could also support these patients with the administrative proceedings, especially when filing for a long-term illness exemption (ALD).

The orthopedic surgeon's role is primordial in the management of these patients with GJH. In most cases, the treatment of instability should preferentially be conservative. The surgeon must be capable of recognizing these pathologies and properly guiding them toward reference centers. In cases of surgical treatment, the specificities of these patients must be kept in mind in order to adapt the surgical technique and indication, as well as the postoperative care. Ideally, these patients should be addressed to surgeons who are affiliated with these reference centers.

X. Annexes

Figure 2 – Diagnostic decision tree in children presenting with joint hypermobility – From Chotel et al. 2010

Figure 3 – Decision tree in patients with suspected EDS – From Bénistan 2018

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