Hypermobility Spectrum Disorders

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Framework for Hypermobility Disorders Committee
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Conflicts of Interest

- None

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ARTICLE

A Framework for the Classification of Joint Hypermobility and Related Conditions

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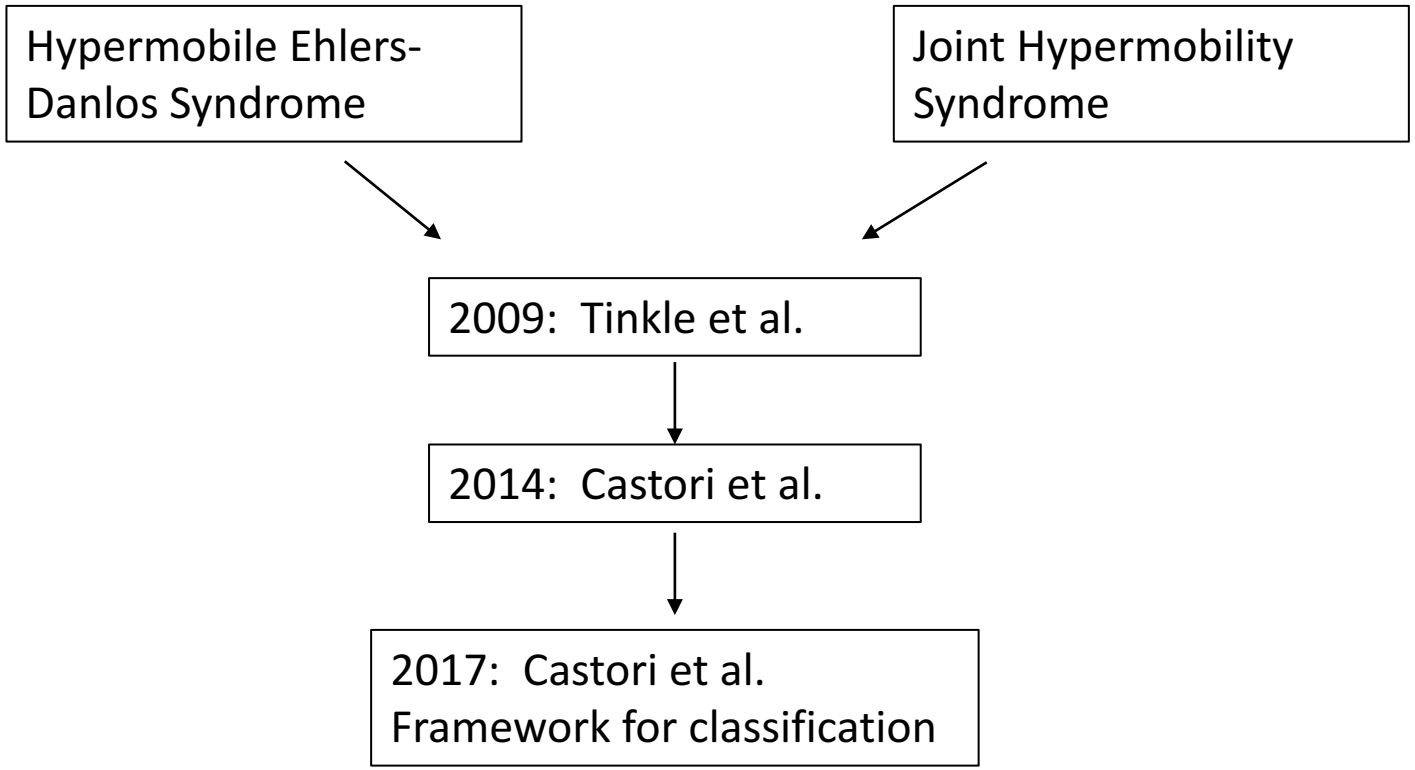
A Brief History of Joint Hypermobility and Hypermobile Ehlers-Danlos Syndrome

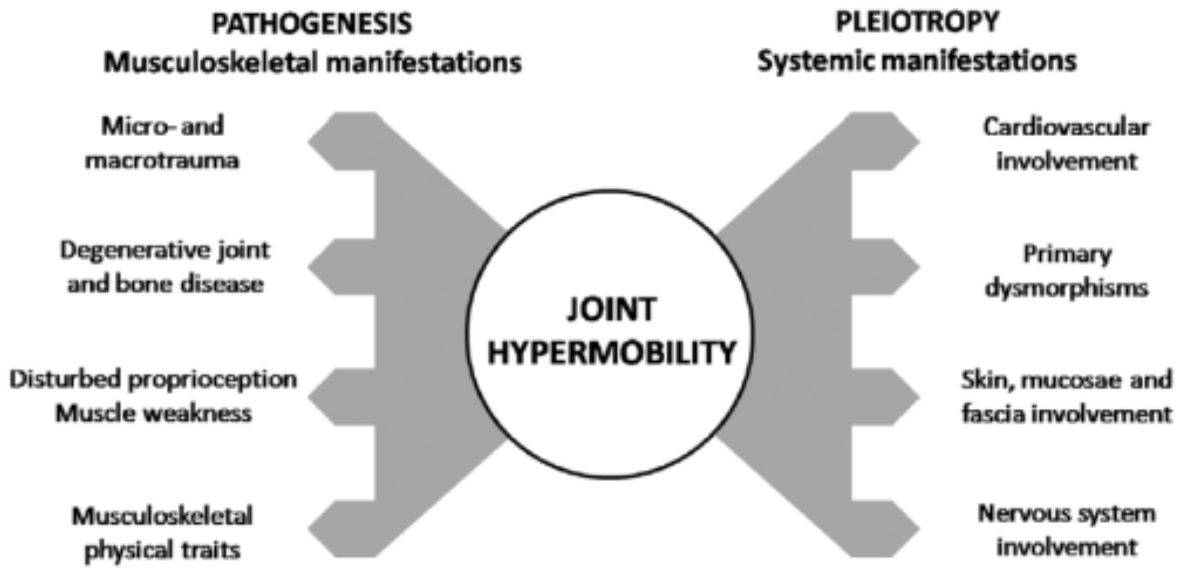


…the delineation of a single entity arising as the full-blown expression of the phenotype in common between EDS-HT and JHS leaves without an "identity" many individuals with symptomatic joint hypermobility (JH) and/or features of hEDS, who do not meet the stricter criteria incorporated in the new EDS nosology. The classification of such cases requires resolution.

Castori et al. 2017

Aims of the Framework Paper

- Summarize the terminology of Joint Hypermobility and related disorders
- Present the different types of Joint Hypermobility, secondary musculoskeletal manifestations and a simplified categorization of genetic syndromes associated with Joint Hypermobility
- Consider the spectrum of secondary musculoskeletal manifestations and range of pleiotropic manifestations of syndromes featuring Joint Hypermobility, noting that these are two separate domains that only partially overlap


PATHOGENESIS
Musculoskeletal manifestations
Micro- and macrotrauma
Degenerative joint and bone disease
Disturbed proprioception
Muscle weakness
Musculoskeletal physical traits
JOINT HYPERMOBILITY
PLEIOTROPY
Systemic manifestations
Cardiovascular involvement
Primary dysmorphisms
Skin, mucosae and fascia involvement
Nervous system involvement

Rationale for an Evolution in Thinking

- Nosology

  distinguishing pathogenesis and etiology is the background for a classification aimed at identifying more effective scientific, therapeutic, and healthcare strategies

- Management

  JH-related musculoskeletal manifestations likely require homogeneous rehabilitation/treatment issues shared by the different genetic conditions

- Research

  a clear separation of the JH secondary musculoskeletal manifestations from the primary pleiotropic manifestations of EDS may help indissecting the intra-familial and inter-individual variability of hEDS for studies aimed at deciphering its molecular basis

Defining Joint Hypermobility

- Joint hypermobility (JH) is the term universally accepted to define the capability that a joint (or a group of joints) has to move, passively and/or actively, beyond normal limits along physiological axes.
- Hence, JH is a descriptor rather than a diagnosis.
- JH may exist as an isolated diagnostic finding, but is often a feature of a larger syndromic diagnosis
- Synonyms: Joint laxity, hypermobility, hyperlaxity

Measuring Joint Hypermobility

- Use professional tools, such as the orthopedic goniometer
- Follow specific procedures (e.g., [Juul-Kristensen et al., 2007])
- Compare the measured range of motion (ROM) with normal parameters.

Types of Joint Hypermobility

- Localized: Involving a limited number of joints (<5)
- Peripheral: Involving primarily the small joints of the hands and feet with absence of large and axial joint involvement
- General: Joint hypermobility at >5 sites, including large and axial joints
- Historical: A history of Joint Hypermobility which is no longer present on examination

Joint Hypermobility ≠ Joint Instability

- Hypermobile joints may be unstable, but joint instability is not a mandatory consequence of joint hypermobility
- Not all unstable joints are hypermobile

Secondary Manifestations of Joint Hypermobility

- Joint hypermobility may be asymptomatic
- There are a series of musculoskeletal symptoms and complications that may be interpreted as secondary manifestations of joint hypermobility
  - Trauma
  - Chronic pain
  - Disturbances of proprioception

“Occasional and recurrent musculoskeletal pain is a quite common immediate manifestation of JH as the natural consequence of predisposition to trauma. The development of chronic pain is sometimes a long-term complication of JH. Preliminary studies suggest the existence of hyperalgesia as a possible form of pain sensitization in patients with EDS and chronic pain.”

Other Musculoskeletal Traits Associated with Joint Hypermobility

- Pes planus (flexible type)
- Valgus deformity of hindfeet, halluces and elbows
- Mild to moderate scoliosis (>7 degrees)
- Accentuated dorsal kyphosis and lumbar lordosis
- Deformational plagiocephaly
- Reduction in bone mass (may be a pleiotropic genetic effect)

Definition of a Syndrome

“a pattern of anomalies, at least one of which is morphologic, known or thought to be causally (etiologically) related.”

Hennekam et al, 2013

The presence of JH in combination with secondary musculoskeletal anomalies does not suffice for the delineation of a genetic syndrome. The appellation “syndrome with JH” should be restricted to genetic conditions featuring JH together with the primary involvement of at least a second tissue/structure (e.g., skin involvement in classical EDS and hEDS)

Castori et al., 2017

Genetic Syndromes with Joint Hypermobility

- The Ehlers-Danlos Syndromes
- Many skeletal dysplasias
- Marfan Syndrome
- Loeys-Dietz Syndrome
- Hereditary myopathies
- Down Syndrome and other chromosomal aneupleudies
- And many others

Classifying Joint Hypermobility

- Asymptomatic persons with Localized, Peripheral or Generalized JH
  - LJH
  - PJH
  - GJH
- Persons with a well-defined syndrome associated with JH
- Persons with symptomatic JH who do not meet diagnostic criteria for any other known hereditary syndrome associated with JH
  - The Hypermobility Spectrum Disorders

The Hypermobility Spectrum Disorders (HSD)

- Joint Hypermobility plus one or more secondary musculoskeletal manifestations of joint hypermobility
- Overall clinical picture does not meet the diagnostic criteria for any of the syndromes associated with joint hypermobility
- Intended as alternative labels for individuals with symptomatic joint hypermobility who do not have any of the rare types of EDS and do not meet the diagnostic criteria for hypermobile EDS.
- Also intended to identify discrete subtypes filling the full gap between asymptomatic JH and hEDS.

The Hypermobility Spectrum Disorders

- Generalized Hypermobility Spectrum Disorder – G-HSD
- Localized Hypermobility Spectrum Disorder – L-HSD
- Peripheral Hypermobility Spectrum Disorder - P-HSD
- Historical Hypermobility Spectrum Disorder – H-HSD

Extra-Articular Disorders Associated with Generalized Joint Hypermobility

- Orthostatic tachycardia (POTS)
- Functional gastrointestinal disturbances
- Pelvic and bladder dysfunction
- Anxiety

Any of these may be seen in persons with the hypermobility spectrum disorders and should be recognized and treated promptly

What do we call these associated disorders?

- The committee felt that we do not yet have sufficient evidence to call these extra-articular manifestations true pleiotropic features of generalized joint hypermobility
- The recommendation is that they be considered “Joint Hypermobility associated co-morbidities”
- Chronic pain - a late consequence of JH or a JH-related co-morbidity?

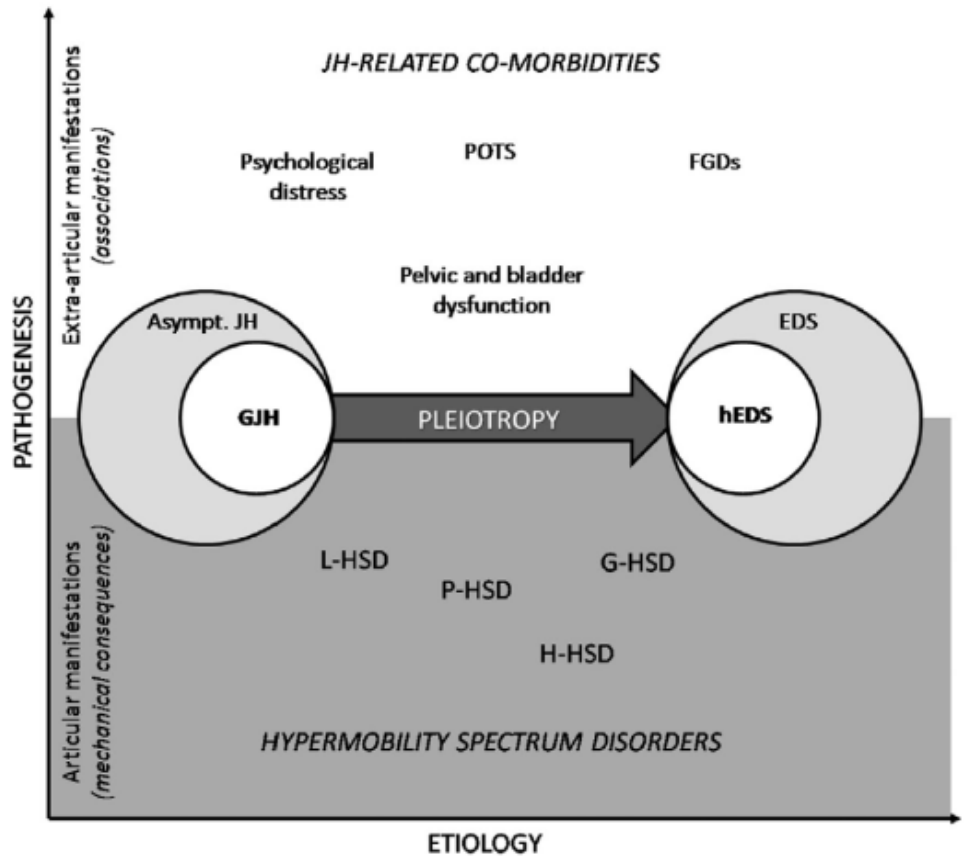
This is still a matter of debate and further research is needed to clarify

Genetic Basis of JH, HSDs and hEDS remains unknown

- Should be a high priority target for future research endeavors
- Will help validate and refine the existing diagnostic criteria
- Should guide more rationale approaches to management and therapy

TABLE I. Phenotypes Belonging to "the spectrum"

Phenotype	Beighton score	Musculoskeletal involvement	Notes
Asymptomatic GJH	Positive	Absent	–
Asymptomatic PJH	Usually negative[a]	Absent	–
Asymptomatic LJH	Negative[b]	Absent	–
G-HSD	Positive	Present	–
P-HSD	Usually negative[a]	Present	–
L-HSD	Negative[b]	Present	–
H-HSD	Negative	Present	Historical presence of joint hypermobility (e.g., positive 5-point questionnaire)
hEDS	Positive[c]	Possible	Plus positive family history (first-degree relatives) and/or specific systemic manifestations (see new criteria)


JH-RELATED CO-MORBIDITIES
Extra-articular manifestations (associations)
Psychological distress
POTS
FGDs
Pelvic and bladder dysfunction
Asympt. JH
GJH
PLEIOTROPY
EDS
hEDS
PATHOGENESIS
L-HSD
G-HSD
P-HSD
H-HSD
Articular manifestations (mechanical consequences)
HYPERMOBILITY SPECTRUM DISORDERS
ETIOLOGY

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