

Table Attachment
L-230

2017 International Criteria for Classical EDS

Minimal criteria suggestive for Classical EDS (cEDS):

- Major criterion 1, PLUS either:
 - Major criterion 2, and/or
 - At least three minor criteria.

Major criteria for cEDS	Minor criteria for cEDS
1. Skin hyperextensibility and atrophic scarring 2. Generalized joint hypermobility	1. Easy bruising 2. Soft, doughy skin 3. Skin fragility (or traumatic splitting) 4. Molluscoid pseudotumors 5. Subcutaneous spheroids 6. Hernia (or history thereof) 7. Epicanthal folds 8. Complications of joint hypermobility (e.g., sprains, luxation/subluxation, pain, flexible flatfoot) 9. Family history of a first-degree relative who meets clinical criteria

2017 International Criteria for Classical-like EDS

Minimal criteria suggestive for Classical-like EDS (clEDS):

- All three major criteria, AND
- A family history compatible with autosomal recessive transmission.

Major criteria for clEDS	Minor criteria for clEDS
1. Skin hyperextensibility, with velvety skin texture and absence of atrophic scarring 2. Generalized joint hypermobility with or without recurrent dislocations (most commonly shoulder and ankle) 3. Easy bruisable skin/spontaneous ecchymoses	1. Foot deformities: broad/plump forefoot, brachydactyly with excessive skin; pes planus; hallux valgus; piezogenic papules 2. Edema in the legs in absence of cardiac failure 3. Mild proximal and distal muscle weakness 4. Axonal polyneuropathy 5. Atrophy of muscles in hands and feet 6. Acrogeric hands, mallet finger(s), clinodactyly, brachydactyly 7. Vaginal/uterus/rectal prolapse

2017 International Criteria for Cardiac-Valvular EDS

Minimal criteria suggestive for Cardiac-Valvular EDS (cvEDS)

- Major criterion 1, AND
- A family history compatible with autosomal recessive inheritance, PLUS either:
 - One other major criterion, and/or
 - At least two minor criteria.

Major criteria for cvEDS	Minor criteria for cvEDS
<ol style="list-style-type: none"> 1. Severe progressive cardiac-valvular problems (aortic valve, mitral valve) 2. Skin involvement: skin hyperextensibility, atrophic scars, thin skin, easy bruising 3. Joint hypermobility (generalized or restricted to small joints) 	<ol style="list-style-type: none"> 1. Inguinal hernia 2. Pectus deformity (especially pectus excavatum) 3. Joint dislocations 4. Foot deformities: pes planus, pes planovalgus, hallux valgus

2017 International Criteria for Vascular EDS

Minimal criteria suggestive for Vascular EDS (vEDS):

- A family history of the disorder, and/or
- Arterial rupture or dissection in individuals less than 40 years of age, and/or
- Spontaneous pneumothorax in the presence of other features consistent with vEDS, and/or
- A combination of the other minor clinical features listed below.

Major criteria for vEDS	Minor criteria for vEDS
<ol style="list-style-type: none"> 1. Family history of vEDS with documented causative variant in COL3A1 2. Arterial rupture at a young age 3. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology 4. Uterine rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears 5. Carotid-cavernous sinus fistula (CCSF) formation in the absence of trauma 	<ol style="list-style-type: none"> 1. Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back 2. Thin, translucent skin with increased venous visibility 3. Characteristic facial appearance 4. Spontaneous pneumothorax 5. Acrogeria 6. Talipes equinovarus 7. Congenital hip dislocation 8. Hypermobility of small joints 9. Tendon and muscle rupture 10. Keratoconus 11. Gingival recession and gingival fragility 12. Early onset varicose veins (under 30 and nulliparous if female)

2017 International Criteria for Hypermobile EDS

Diagnosis of Hypermobile EDS (hEDS) requires the simultaneous presence of criteria 1 AND 2 AND 3:

- Criteria 1: Generalized joint hypermobility
- Criterion 2: Two or more among the features (A-C) listed in the table below must be present (for example: A and B; A and C; B and C; A and B and C).
- Criterion 3: All of the following prerequisites must be met:
 - Absence of unusual skin fragility, and
 - Exclusion of other heritable and acquired connective tissue disorders, including autoimmune rheumatologic conditions, and
 - Exclusion of alternative diagnoses that may also include joint hypermobility by means of hypotonia and/or connective tissue laxity.

Feature A	Feature B	Feature C
<p>A total of 5 must be present:</p> <ol style="list-style-type: none"> 1. Unusually soft or velvety skin 2. Mild skin hyperextensibility 3. Unexplained striae 4. Bilateral piezogenic papules of the heel 5. Recurrent or multiple abdominal hernia(s) 6. Atrophic scarring involving at least two sites 7. Pelvic floor, rectal, and/or uterine prolapses in children, men or nulliparous women without a history of morbid obesity or other known predisposing medical condition 8. Dental crowding and high or narrow palate 9. Arachnodactyly 10. Arm span-to-height \geq 1.05 11. Mitral valve prolapse (MVP) 12. Aortic root dilatation with Z-score $>$ +2 	<p>Positive family history, with one or more first degree relatives independently meeting the current diagnostic criteria for hEDS.</p>	<p>Must have at least one</p> <ol style="list-style-type: none"> 1. Musculoskeletal pain in two or more limbs, recurring daily for at least 3 months. 2. Chronic, widespread pain for \geq 3 months 3. Recurrent joint dislocations or frank joint instability, in the absence of trauma: <ol style="list-style-type: none"> a. Three or more atraumatic dislocations in the same joint or two or more atraumatic dislocations in two different joints occurring at different times, or b. Medical confirmation of joint instability at two or more sites not related to trauma

2017 International Criteria for Arthrochalasia EDS

Minimal criteria suggestive for Arthrochalasia EDS (aEDS):

- Major criterion 1, PLUS either:
 - Major criterion 3, and/or
 - Major criterion 2 and at least two other minor criteria.

Major criteria for aEDS	Minor criteria for aEDS
1. Congenital hip dislocation	1. Muscle hypotonia
2. Severe generalized joint hypermobility, with multiple dislocations/subluxations	2. Kyphoscoliosis
3. Skin hyperextensibility	3. Radiologically mild osteopenia
	4. Tissue fragility, including atrophic scars
	5. Easy bruisable skin

2017 International Criteria for Dermatosparaxis EDS

Minimal criteria suggestive for Dermatosparaxis EDS (dEDS):

- Major criterion 1, AND
- Major criterion 2, PLUS either:
 - One other major criterion, and/or
 - Three minor criteria.

Major criteria for dEDS	Minor criteria for dEDS
1. Extreme skin fragility with congenital or postnatal skin tears	1. Soft and doughy skin texture
2. Characteristic craniofacial features, which are evident at birth or early infancy, or evolve later in childhood	2. Skin hyperextensibility
3. Redundant, almost lax skin, with excessive skin folds at the wrist and ankles	3. Atrophic scars
4. Increased palmar wrinkling	4. Generalized joint hypermobility
5. Severe bruisability with a risk of subcutaneous hematomas and hemorrhage	5. Complications of visceral fragility (e.g., bladder rupture, diaphragmatic rupture, rectal prolapse)
6. Umbilical hernia	6. Delayed motor development
7. Postnatal growth retardation	7. Osteopenia
8. Short limbs, hands and feet	8. Hirsutism
9. Perinatal complications due to connective tissue fragility	9. Tooth abnormalities
	10. Refractive errors (myopia, astigmatism)
	11. Strabismus

2017 International Criteria for Kyphoscoliotic EDS

Minimal criteria suggestive for Kyphoscoliotic EDS (kEDS):

- Major criterion 1, AND
- Major criterion 2, PLUS either:
 - Major criterion 3, and/or
 - Three minor criteria (either general or gene-specific criteria).

Major criteria for kEDS	Minor criteria for kEDS	Gene-specific minor criteria for kEDS
1. Congenital muscle hypotonia 2. Congenital or early onset kyphoscoliosis (progressive or non-progressive) 3. Generalized joint hypermobility with dislocations/subluxations (shoulders, hips, and knees in particular)	1. Skin hyperextensibility 2. Easy bruisable skin 3. Rupture/aneurysm of a medium-sized artery 4. Osteopenia/osteoporosis 5. Blue sclerae 6. Hernia (umbilical or inguinal) 7. Pectus deformity 8. Marfanoid habitus 9. Talipes equinovarus 10. Refractive errors (myopia, hypermetropia)	PLOD1 1. Skin fragility 2. Scleral and ocular fragility/rupture 3. Microcornea 4. Facial dysmorphism
		FKBP14 1. Congenital hearing impairment (any type) 2. Follicular hyperkeratosis 3. Muscle atrophy 4. Bladder diverticula

2017 International Criteria for Brittle Cornea Syndrome

Minimal criteria suggestive for Brittle Cornea Syndrome (BCS):

- Major criterion 1, PLUS either:
 - At least one other major criterion, and/or
 - Three minor criteria.

Major criteria for BCS	Minor criteria for BCS
1. Thin cornea, with or without rupture (central corneal thickness often <400 μm)	1. Enucleation or corneal scarring as a result of previous rupture 2. Progressive loss of corneal stromal

(Continued below)

Major criteria for BCS	Minor criteria for BCS
2. Early onset progressive keratoconus	depth
3. Early onset progressive keratoglobus	3. High myopia, with normal or moderately increased axial length
4. Blue sclerae	4. Retinal detachment
	5. Deafness (often mixed)
	6. Hypercompliant tympanic membranes
	7. Developmental dysplasia of the hip
	8. Hypotonia in infancy, usually mild if present
	9. Scoliosis
	10. Arachnodactyly
	11. Hypermobility of distal joints
	12. Pes planus, hallux valgus
	13. Mild contractures of fingers (especially fifth)
	14. Soft, velvety skin, translucent skin

2017 International Criteria for Spondylodysplastic EDS

Minimal criteria suggestive for Spondylodysplastic EDS (sEDS):

- Major criterion 1, AND
- Major criterion 2, PLUS
- Characteristic radiographic findings and at least 3 other minor criteria (general or type-specific).

(Continued below)

Major criteria for sEDS	Minor criteria for sEDS	Gene-specific minor criteria for sEDS
<ol style="list-style-type: none"> 1. Short stature 2. Muscle hypotonia 3. Bowing of limbs 	<ol style="list-style-type: none"> 1. Skin hyperextensibility, soft, doughy skin, thin translucent skin 2. Pes planus 3. Delayed motor development 4. Osteopenia 5. Delayed cognitive development 	<p>B4GALT7</p> <ol style="list-style-type: none"> 1. Radioulnar synostosis 2. Bilateral elbow contractures or limited elbow movement 3. Generalized joint hypermobility 4. Single transverse palmar curve 5. Characteristic craniofacial features 6. Characteristic radiographic findings 7. Severe hypermetropia 8. Clouded cornea <p>SLC39A13</p> <ol style="list-style-type: none"> 1. Protuberant eyes with bluish sclerae 2. Hands with finely wrinkled palms 3. Atrophy of the thenar muscles, tapering fingers 4. Hypermobility of distal joints 5. Characteristic radiologic findings <p>B3GALT6</p> <ol style="list-style-type: none"> 1. Kyphoscoliosis (congenital or early onset) 2. Joint hypermobility

Major criteria for sEDS	Minor criteria for sEDS	Gene-specific minor criteria for sEDS
		<ol style="list-style-type: none"> 3. Joint contractures 4. Peculiar fingers 5. Talipes equinovarus 6. Characteristic craniofacial features 7. Tooth discoloration, dysplastic teeth 8. Characteristic radiographic findings 9. Osteoporosis with multiple spontaneous fractures Ascending aortic aneurysm 10. Lung hypoplasia, restrictive lung disease

2017 International Criteria for Musculocontractural EDS

Minimal criteria suggestive for Musculocontractural EDS (mcEDS):

- At birth or in early childhood:
 - Major criterion 1, AND
 - Major criterion 2
- In adolescence and in adulthood:
 - Major criterion 1, AND
 - Major criterion 3.

Major criteria for mcEDS	Minor criteria for mcEDS
<ol style="list-style-type: none"> 1. Congenital multiple contractures and/or talipes equinovarus (clubfoot) 2. Characteristic craniofacial features, which are evident at birth or in early infancy 3. Characteristic cutaneous features including skin hyperextensibility, easy bruisability, skin fragility with atrophic 	<ol style="list-style-type: none"> 1. Recurrent/chronic dislocations 2. Pectus deformities (flat, excavated) 3. Spinal deformities (scoliosis, kyphoscoliosis) 4. Peculiar fingers (tapering, slender, cylindrical) 5. Progressive talipes deformities

Major criteria for mcEDS	Minor criteria for mcEDS
scars, increased palmar wrinkling	<ol style="list-style-type: none"> 6. Large subcutaneous hematomas 7. Chronic constipation 8. Colonic diverticula 9. Pneumothorax/pneumohemothorax 10. Nephrolithiasis/cystolithiasis 11. Cryptorchidism in males 12. Strabismus 13. Refractive errors (myopia, astigmatism) 14. Glaucoma/elevated intraocular pressure

2017 International Criteria for Periodontal EDS

Minimal criteria suggestive for Periodontal EDS (pEDS):

- Major criterion 1, OR major criterion 2, PLUS
 - At least two other major criteria and one minor criterion.

Major criteria for pEDS	Minor criteria for pEDS
<ol style="list-style-type: none"> 1. Severe and intractable periodontitis of early onset (childhood or adolescence) 2. Lack of attached gingiva 3. Pretibial plaques 4. Family history of a first-degree relative who meets clinical criteria 	<ol style="list-style-type: none"> 1. Easy bruising 2. Joint hypermobility, mostly distal joints 3. Skin hyperextensibility and fragility, abnormal scarring (wide or atrophic) 4. Increased rate of infections 5. Hernias 6. Marfanoid facial features 7. Acrogeria 8. Prominent vasculature