hEDS

hEDS – HYPERMOBILE EDS (1,10,11)

- Most common of the Ehlers Danlos Syndromes
- No genetic basis yet identified therefore diagnosis is phenotypic
- See hEDS Diagnostic Checklist for details and how to apply criteria – includes a downloadable pdf (10)
  - **Criterion 1 - Main feature (must be present)**
    - Generalised Joint Hypermobility (Beighton Score ≥ 4/9 over age 50; ≥ 5/9 in young adults; ≥ 6/9 in children and adolescents) (12)
  - **Criterion 2 (at least 2 features)**
    - Feature A – Generalised connective tissue disorder (at least 5/12 present)
      - Soft, velvety skin
      - Mild skin hyperextensibility (not as much as cEDS)
      - Unexplained striae
      - Piezogenic papules (nodules on side of feet)
      - Recurrent/multiple hernias
      - Atrophic scarring
      - Arachnodactyly
      - Arm span-Height ratio: ≥ 1.05
      - Pelvic floor prolapse
      - Dental crowding
      - Mitral valve prolapse
      - Aortic root dilatation
    - Feature B
      - Family history (vertical transmission down generations but some individuals can be non-penetrant)
    - Feature C (at least 1) - see details in checklist
      - Musculoskeletal pain
      - Chronic widespread pain ≥ 3 months
      - Recurrent joint dislocations/instability in absence of significant trauma (may also occur with trauma)
  - **Criterion 3 – All must be present**
    - No skin fragility
    - Reasonable exclusion of other connective tissue disorders e.g. Marfan syndrome
    - Exclusion of other disorders that could cause GJH

To diagnose hEDS all 3 criteria must be satisfied.

- Other features that can occur (not an exhaustive list)
  - Sleep disturbance, chronic fatigue, Postural orthostatic tachycardia syndrome (POTS), functional GIT disorders, unusual hernias, internal hernias, dysautonomia, Raynaud's, MCAS, some cardiac features, osteoarthritis secondary to joint instability, headaches, TMJ dysfunction, increased gynaecological presentations, pelvic floor dysfunction, anxiety, depression. Multiple other features that affect quality of life may be part of the spectrum.
- Overall effect on life may range from severe (bed-ridden) to relatively minor

vEDS

vEDS – VASCULAR EDS (1,4)

- Rare and dangerous

Major criteria	Minor criteria
• Family history proven vEDS • Arterial rupture at young age • Spontaneous colon perforation in absence of other disease • Uterine rupture without predisposing cause • Carotid-cavernous sinus fistula without trauma	• Bruising not related to trauma or in unusual sites • Thin, translucent skin with easily visible veins • Characteristic facial appearance • Spontaneous pneumothorax • Acrogeria • Talipes equinovarus • Congenital hip dislocation • Hypermobility of small joints • Tendon and muscle rupture • Keratoconus • Gingival recession and fragility • Early onset varicose veins

To diagnose need a family history with arterial rupture or dissection younger than 40 or any of the other major features.

Genetic testing is important to corroborate a clinical diagnosis.

The 2017 international classification of the Ehlers–Danlos syndromes

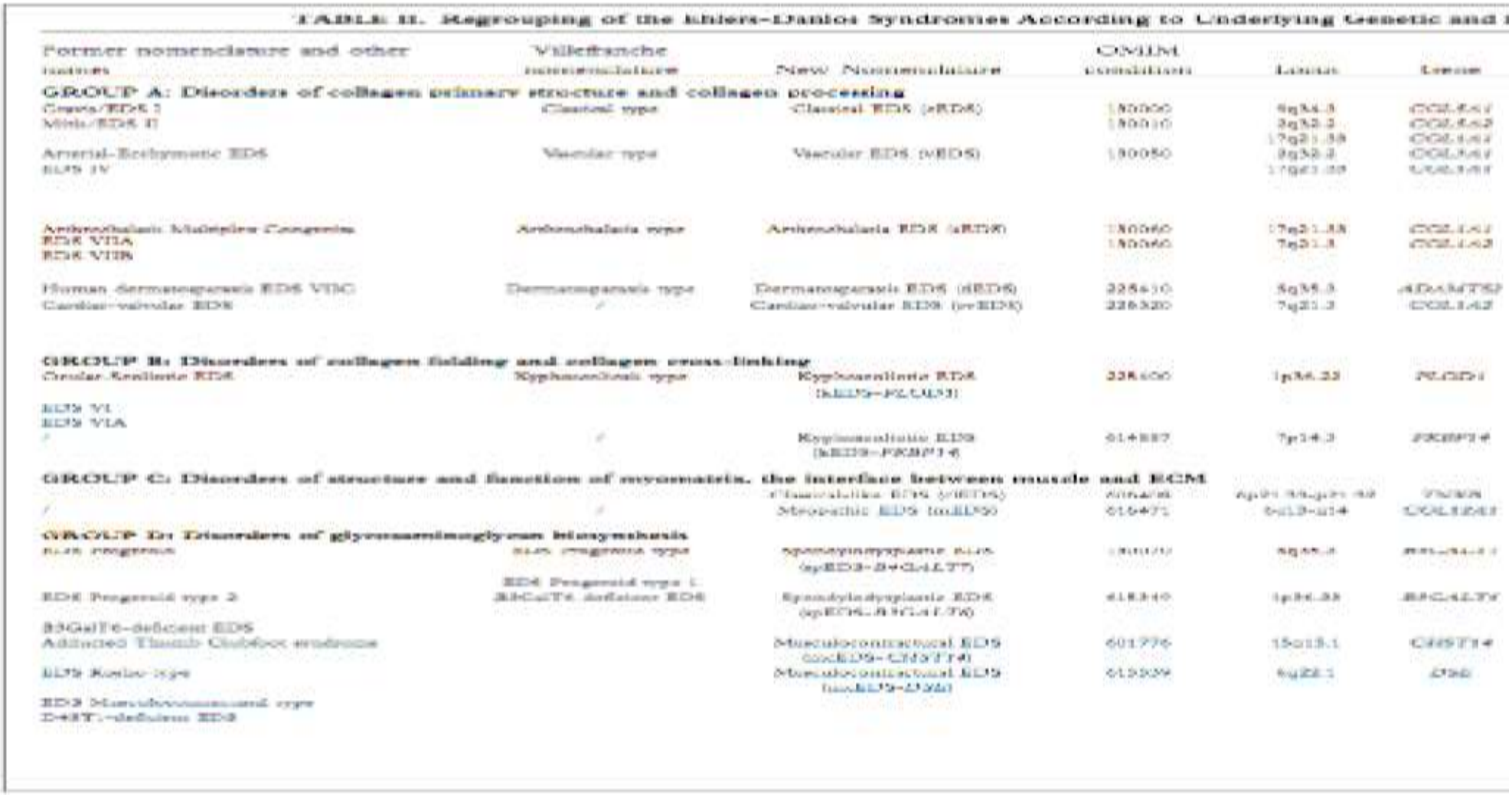
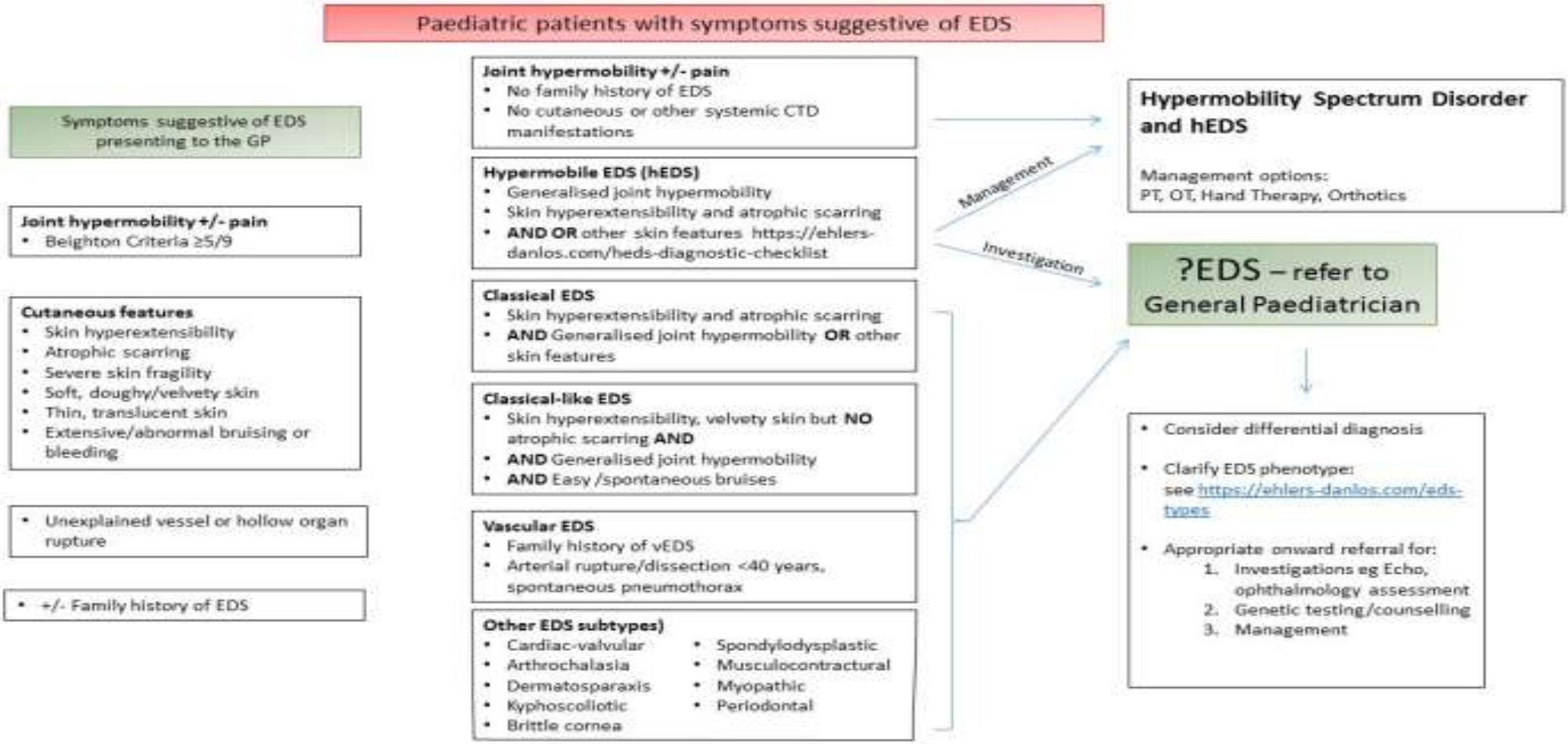


TABLE II. Regrouping of the Ehlers–Danlos Syndromes According to Underlying Genetic and

Former nomenclature and other names	Villefranche nomenclature	New Nomenclature	OMIM condition	Locus	Gene
GROUP A: Disorders of collagen primary structure and collagen processing					
Gravs/EDS I	Classical type	Classical EDS (cEDS)	130000	9q34.3	COL5A1/
Mitis/EDS II			130010	2q32.2	COL5A2
				17q21.33	COL1A1/
Arterial-Ecchymotic EDS	Vascular type	Vascular EDS (vEDS)	130050	2q32.2	COL3A1/
EDS IV				17q21.33	COL3A1/
Arthrochalasic Multiplex Congenita	Arthrochalasia type	Arthrochalasia EDS (aEDS)	130060	17q21.33	COL1A1/
EDS VIIA			130060	7q22.1	COL1A2
EDS VIIB					
Human Dermatosparaxis EDS VIIC	Dermatosparaxis type	Dermatosparaxis EDS (dEDS)	225410	5q35.3	ADAMTS2
Cardiac-valvular EDS	/	Cardiac-valvular EDS (cvEDS)	226320	7q21.3	COL1A2
GROUP B: Disorders of collagen folding and collagen cross-linking					
Ocular-Scoliotic EDS	Kyphoscoliotic type	Kyphoscoliotic EDS (kEDS-PLOD1)	225400	1p36.22	PLOD1
EDS VI					
EDS VIA					
/	/	Kyphoscoliotic EDS (kEDS-FKBP14)	614557	7p14.3	FKBP14
GROUP C: Disorders of structure and function of myomatrix, the interface between muscle and ECM					
/	/	Myopathic EDS (mEDS)	616471	6q13-q14	CCDC41
GROUP D: Disorders of glycosaminoglycan biosynthesis					
EDS progeroid	EDS progeroid type	Spondylodysplastic EDS (spEDS-B4GALT7)	130070	5q35.3	B4GALT7
EDS Progeroid type 2	EDS Progeroid type 1 B4GalT6-deficient EDS	Spondylodysplastic EDS (spEDS-B3GALT6)	615349	1p36.33	B3GALT6
Adducted Thumb-Clubfoot syndrome		Musculocontractural EDS (mcEDS-CHST14)	601776	15q15.1	CHST14
EDS Kosho type		Musculocontractural EDS (mcEDS-DSE)	615539	6q22.1	DSE
EDS Musculocontractural type					
D4ST1-deficient EDS					

Of the three most common forms of EDS, only vEDS and cEDS have an established genetic basis. Determining the exact molecular basis for these conditions can be useful for diagnosis, management and reproductive decision-making. It is, however, not mandatory that every person with a clinical diagnosis of EDS undergoes molecular analysis. For those who meet the minimal clinical requirements for an EDS subtype—but who have no access to molecular confirmation; or whose genetic testing shows one (or more) gene variants of uncertain significance in the genes identified for one of the EDS subtypes; or in whom no causative variants are identified in any of the EDS-subtype-specific genes—a "provisional clinical diagnosis" of an EDS subtype can be made.



New Zealand Hypermobility and Ehlers-Danlos Syndromes Guideline 2019

Further Investigation

- ECHO - showed mild aortic root dilatation - for 12-18 month follow up.
- Normal platelet function and von Willebrand screening

PROGRESS

- Saw genetic
- Diagnosed Ehlers Danlos Syndrome – No genetics

Management issues

ACUTE EMERGENCIES

- Vascular rupture – appropriate vascular surgery or interventional radiology referral
- Dislocations – appropriate orthopaedic referral
- Acute pain – usual principles
- Bleeding - DDAVP (Desmopressin) intra-nasally is recommended for acute haemorrhage to help stop bleeding

PAIN – INITIAL (ACUTE)

INJURIES – INSTABILITY, SUBLUXATIONS, DISLOCATIONS, TENDON & LIGAMENT

JOINT INSTABILITY AND PAIN – LONG TERM STRATEGIES TO STABILISE

SURGERY AND ANAESTHESIA (5,23,24)

Clinicians planning surgery or anaesthesia in a patient with EDS: Wiesmann et al:
Recommendations for anaesthesia and perioperative management in patients with Ehlers-Danlos Syndrome(s) [26]

- Surgical complications may be increased due to slow healing and potential for bleeding. Appropriate strategies should be planned and discussed in EDS context
- DDAVP (Desmopressin) intra-nasally pre-operatively will reduce the risk of a life-threatening haemorrhage
- Recurrence of prolapse, hernias, etc. after surgery may occur because of the inherently abnormal ligaments
- Some issues with anaesthesia:
    - Unstable neck may be an issue with positioning
    - Slow and suboptimal response to local anaesthetic including epidurals
    - Tourniquet can cause bruising and compartment syndrome
    - Positioning can cause unexpected subluxations including temporomandibular joint during anaesthesia

Reference

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- Pediatric joint hypermobility: a diagnostic framework and narrative review Tofts et al. Orphanet Journal of Rare Diseases (2023) 18:104
- Hypermobility and EDS – New Zealand Guideline 2019. https://ehlers-danlos.org.nz/wp-content/uploads/2023/01/NZ-EDS-Guideline-V1-2019-1.pdf