EHLERS–DANLOS SYNDROME

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EDS is a heritable collagen disorder

Heterogeneous group of diseases with:
- Multi-systemic involvement
- Phenotypic variability
- Monogenic inheritance

Mutations in

Fibrillar collagen genes

Genes for enzymes involved in collagen biosynthesis

Prevalence: 1:5000
General clinical manifestations of EDS

- **Skin hyperextensibility**: extends easily and snaps back after release (unlike cutis laxa). Skin is smooth and velvety to the touch.
- Skin is **fragile**: splits after minor trauma (pressure points and exposed areas).
- **Wound healing** is delayed with formation of widened atrophic scars.
- **Joint hypermobility** of large and/or small joints, dependent on age and assessed with Beighton score; is complicated by dis(sub)locations, sprains…
- **Muscle hypotonia**, delayed gross motor development.
- **Easy bruising and bleeding**: ecchymoses, hematomas after minor trauma.
- Manifestations of **tissue extensibility and fragility**: tears, prolapses, herniae…
General clinical manifestations of EDS

- Skin hyper-extensibility
- Atrophic scars
- Easy bruising
- Hernia
- Joint hypermobility

Consent from patients received.
## Villefranche Nosology (1997)

<table>
<thead>
<tr>
<th>Type</th>
<th>Gene</th>
<th>Protein</th>
<th>Transmission</th>
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<tbody>
<tr>
<td>Classical</td>
<td>COL5A1</td>
<td>Type V procollagen</td>
<td>AD</td>
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<tr>
<td></td>
<td>COL5A2</td>
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<tr>
<td>Hypermobility</td>
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<td>COL3A1</td>
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<td>PLOD1</td>
<td>Lysyl hydroxylase</td>
<td>AR</td>
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<td>Arthrochalasis</td>
<td>COL1A1</td>
<td>Type I collagen (N-propeptide-processing)</td>
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<td>ADAMTS2</td>
<td>Procollagen N proteinase</td>
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• Born at 37 weeks of gestation due to premature rupture of the membranes
• Age 7 months: corrective surgery for severe strabismus, repeated 4 times during childhood
• ‘Floppy infant’ and loose joints noted in the first months of life
• ‘Spontaneous’ ecchymoses and bleedings, splitting of skin following minor trauma became apparent at the time he started to walk independently
• Joint hyperlaxity involving large and small joints obvious in early childhood
• Age 5 yrs: suspicion of battered child syndrome because of confluent hematomas on the face (chin, forehead), upper and lower limbs → referred to clinical geneticist who established diagnosis of EDS, type V collagen mutation +
• Presently, at age 21 yrs, chronic pain in the back, shoulders and hands are the major subjective complaint and have lead to temporary inability to perform his job
Classic Ehlers–Danlos syndrome

- **Major diagnostic criteria:**
  - Skin hyperextensibility
  - Widened atrophic scars
  - Joint hypermobility

- **Minor diagnostic criteria:**
  - Smooth velvety skin
  - Molluscoid pseudotumours, subcutaneous spheroids
  - Complications of joint hypermobility
  - Muscle hypotonia, delayed gross motor development
  - Easy bruising
  - Manifestations of tissue extensibility and fragility
  - Surgical complications
  - Positive family history

Consent from patients received.
General features

Consent from patients received.
Skin

- Soft, velvety, doughy texture
- Skin splitting upon minor trauma
- Skin hyperextensibility
- Slow wound healing, cigarette paper scars
- Easy bruising
- Haemosiderotic plaques on shins
- Molluscoid pseudotumours
- Subcutaneous spheroids
- Other: Inguinal/umbilical hernia
Musculoskeletal system

- Generalised joint hypermobility
- Recurrent joint dislocations
- Muscle hypotonia and delayed gross motor development
- Congenital or progressive (kypho)scoliosis
- Broad and flat feet
- Club feet
- Congenital hip dislocation
- Broad hands, severe hyperlaxity of fingers with swan neck deformities
- Chronic joint pain