Ehlers-Danlos syndrome classic type (types I and II)

Genetics

-COL5A1 (75%-78%), COL5A2 (14%), COL1A1 (<1%)

-AD; 50% inherited, 50% de novo

Clinical findings/Dysmorphic features

-Skin hyperextensibility; atrophic scarring; generalized joint hypermobility; hypotonia; chronic pain; easy bruising; hernia (part of an internal organ bulges through a weak area of muscle)

-Aortic root dilation (more common in young individuals and rarely progressive)

Etiology

-1:20,000

Pathogenesis

-40%-50% of COL5A1 are haploinsufficiency --> half amount of normal type V collagen

-Small proportion COL5A1 variants affect the structural integrity of type V collagen --> production of functionally defective type V collagen (dominant-negative variant)

Genetic testing/diagnosis

-Diagnosis of cEDS is established in a proband with the minimal clinical diagnostic criteria:

--> skin hyperextensibility and atrophic scarring and either GJH or ≥3 minor clinical criteria and

--> identification of a heterozygous pathogenic variant in COL5A1, COL5A2, or COL1A1

-COL5A1 null allele test on cDNA from a skin biopsy

Others

-Beighton Criteria for GJH

-No genotype/phenotype correlations known