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Genetic basis of Ehlers-Danlos syndrome (Rubber syndrome)

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Abstract
In this report, we will discuss the genetic and biochemical data, the current Villefranche classification subdivides EDS into six major subtypes, , which are caused by mutations in genes encoding fibrillar collagens or enzymes involved in collagen biosynthesis. Mutations in type V and type III collagen cause classic and vascular EDS, respectively, whereas mutations affecting the processing of type I collagen lead to the kyphoscoliotic, arthrochalasic and dermatosparactic EDS types.

Introduction
EDSs are due to a mutation in one of more than a dozen different genes. The specific gene affected determines the specific EDS. Some cases result from a new mutation occurring during early development while others are inherited in an autosomal dominant or recessive manner.

Discussion:
First study:
Ehlers-Danlos syndrome is a group of disorders that affect connective tissues supporting the skin, bones, blood vessels, and many other organs and tissues. Defects in connective tissues cause the signs and symptoms of these conditions, which range from mildly loose joints to life-threatening complications. The various forms of Ehlers-Danlos syndrome have been classified in several different ways. Originally, 11 forms of Ehlers-Danlos syndrome were named using Roman numerals to indicate the types (type I, type II, and so on). In 1997, researchers proposed a simpler classification (the Villefranche nomenclature) that reduced the number of types to six and gave them descriptive names based on their major features. In 2017, the classification was updated to include rare forms of Ehlers-Danlos syndrome that were discovered more recently. The 2017 classification describes 13 types of Ehlers-Danlos syndrome. Other types of Ehlers-Danlos syndrome have additional signs and symptoms. The cardiac-valvular type causes severe problems with the valves that control the movement of blood through the heart. People with the kyphoscoliotic type experience severe curvature of the spine that worsens over time and can interfere with breathing by restricting lung expansion. A type of Ehlers-Danlos syndrome called brittle cornea syndrome is characterized by thinness of the clear covering of the eye (the cornea) and other eye abnormalities. are among the characteristic signs of the musculocontractural and myopathic forms of Ehlers-Danlos syndrome. The periodontal type causes abnormalities of the teeth and gums[(1)] .

Second study:
Ehlers-Danlos syndrome (EDS) consists of a group of inherited heterogeneous disorders that share a common decrease in the tensile strength and integrity of the skin, joints, and other connective tissues. This group of connective-tissue disorders is characterized by abnormal collagen synthesis causing hyperextensibility of the skin,

hypermobility of the joints, and tissue fragility, as is seen by easy bruising and delayed wound healing with atrophic scarring.
People with lax joints and multiple scars were first described in the medical writings of Hippocrates, dating back to 400 BCE. In 1892, Dr. A. Tschernogobow, a Russian dermatologist, presented 2 case studies of patients to the Moscow Venereology and Dermatology Society who had marked loose fragile skin, and hypermobile large joints. His work reports the first detailed clinical description of EDS The syndrome derives its name from additional clinical case reports presented by 2 physicians: Edvard Ehlers, a Danish dermatologist, in 1901, and Henri-Alexandre Danlos, a French physician with expertise in chemistry of skin disorders, in 1908. Both physicians combined the pertinent features of the syndrome and accurately delineated the phenotypic features of this group of inherited disorders. The name, Ehlers-Danlos syndrome, was coined in 1936. Some patients with EDS can demonstrate amazing, almost unnatural, contortions, often arousing the curiosity of onlookers. Niccolo Paganini (1782-1840) the famous Italian violinist, who was capable of miraculous feats in his playing owing to his hypermobile and loose joints, had phenotypic traits of EDS. In the late 19th century, historians described performers with traits of EDS who displayed their hyperextensible maneuvers publicly in circuses and travelling shows. Some achieved celebrity status, acquiring titles such as "The India Rubber Man," Patients displaying clinical capabilities ."The Elastic Lady," and "The Human Pretzel such as these raise suspicion of the diagnosis when identified on physical examination. Unfortunately, patients with EDS are often not diagnosed for many years [(2)] .

Third study :
Only some Ehlers–Danlos syndromes can be positively identified as tied to specific genetic variation.

Mutations in the following genes can cause Ehlers–Danlos syndromes :

- Fibrous proteins: COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, and TNXB .
- Enzymes: ADAMTS2, PLOD1, B4GALT7, DSE, and D4ST1/CHST14 .

Mutations in these genes usually alter the structure, production, or processing of collagen or proteins that interact with collagen. Collagen provides structure and strength to connective tissue. A defect in collagen can weaken connective tissue in the skin, bones, blood vessels, and organs, resulting in the features of the disorder Inheritance patterns depend on the specific Ehlers–Danlos syndrome. Most forms of Ehlers–Danlos syndromes are inherited in an autosomal dominant pattern, which means only one of the two copies of the gene in question must be altered to cause a disorder. The minority are inherited in an autosomal recessive pattern, which means both copies of the gene must be altered for a person to be affected by a disorder. It can also be an individual (de novo or "sporadic") mutation. Refer to the summary for each Ehlers–Danlos syndrome for a discussion of its inheritance pattern[(3)] .

Conclusion :

EDSs are due to a mutation in one of more than a dozen different genes. The specific gene affected determines the specific EDS .

References :

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