* denatured → reversible. easier to break down than degradation → irreversible break to peptide bond.

* Synthesis of collagen : ① Transcription of mRNA. genes for synthesis α-peptide.

② pre-pro-peptide formation. mRNA (nucleus → cytoplasm). ↓ ribosome for translation

↳ Signal seq. (N terminal) recognition center → EPR ↳ for post translation process

③ α-peptide to procollagen. 3 Modifications:

A. N.terminal dissolved ⇒ propeptide (XX procollagen).

B. Hydroxylation (OH) of lys + pro [prolyl hydroxylase / lysyl hydroxylase] ⇒ Cross linking of the α-peptides [U.C collector]

* lack of (OH) of pro, lys insecure ⇒ looser triple helix.

C. Glycosylation (glcare, galactose) onto (OH) in (lysines) not prolines. * ↳ each (OH, g) peptide twists towards left very tightly ⇒ procollagen.

twisted portion 2 loose ends "center"

④ Golgi Apparatus modification.

* the last modification on post translation ⇒ + Oligosch. not mono → put in secretory vesicle destined for extracellular spaces.

packaged into transfer vesicle destined for golgi apparatus

⑤ Formation of tropocollagen.

In extracellular space. * outside the cell. "collagen peptidase" remove "loose end" ⇓ Tropocollagen.

⑥ Formation of the collagen Fibril.

act on

* lysyl oxidase, EC enzyme" final step. lys + hydroxylysines ⇒ aldehyde groups → covalent bond (↓ the tropocollagen ⇒ collagen fibril.

Some of the lysine side chains are oxidized to aldehyde derivatives, which react with another lysine or another oxidized lysine via the action of lysyl oxidase

* Aldehyde + Aldehyde → Aldol cross-link.

Collagen	Genes
I	COL1A1, 2
II	COL2A1
III	COL3A1
IV	COL4A1, 2, 3, 4, 5, 6
V	COL5 A1, 2, 3
VI	COL6 A 1, 2, 3

Most forms of the condition are inherited in an autosomal dominant pattern

Inheritance	Characteristics	Type
Autosomal dominant	Joint hypermobility, skin hyperextensibility, and fragility	Classical type
Autosomal dominant	Joint hypermobility, frequent dislocations	Hypermobility type
Primarily autosomal dominant, recessive described	Spontaneous rupture of arteries and bowel, can lead to death	Vascular type
Autosomal recessive	Fragile eyes, significant skin and joint laxity, severe scoliosis	Kyphoscoliosis type
Autosomal dominant and recessive	Short height, severe joint laxity and dislocations, variable skin involvement	Arthrochalasia type
Autosomal recessive	Severely fragile skin, soft and doughy with sagging and folding	Dermatosparaxis type
Autosomal recessive	Joint hypermobility, hyperelastic skin, and fragile tissue	Tenascin-X deficient type

Ehlers Danlos syndrom (EDS)

⇒ group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen (Type I or III). The collagen in connective tissue helps tissues resist deformation.
abnormal collagen leads to increased elasticity

Mutations can cause EDS:

Fibrous p
- COL1A1 / COL1A2
- COL3A1
- COL5A1 / COL5A2
- TNXB

Enzymes
ADAMTS2
PLOD1
B4GALT7

Abnormalities in tenascin protein also → play role in regulation the normal distribution of collagen.

Description	Symptoms/Risk Factors	Causes	Condition
Affects connective tissue, caused by defects in type II or XI collagen.	Abnormal bone development, short stature, enlarged joints, etc.	Mutations in COL11A1, COL11A2, COL2A1	**Collagenopathy (Type II & XI)**
Results from defects in the COL2A1 gene affecting connective tissues.	Abnormal bone development, short stature, premature arthritis, etc.	Defects in the COL2A1 gene	**Collagenopathy, Type 2 Alpha 1**
Genetic disorder characterized by end stage kidney disease, hearing loss.	End-stage kidney disease in male relatives, hearing loss before age 30	Mutations in COL4A3, COL4A4, COL4A5	**Alport Syndrome**
Affects skeletal muscles, severe muscle weakness from birth.	Severe muscle weakness, inability to walk unassisted.	Mutations in COL6A1, COL6A2, COL6A3	**Ullrich Congenital Muscular Dystrophy**