COLLAGEN-
GINGIVAL COLLAGEN

Department Of Periodontology

Karpaga Vinayaga Institute Of Dental Sciences

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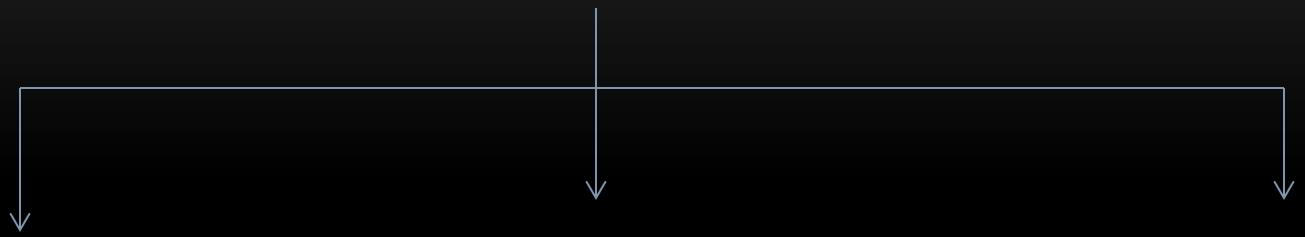
INTRODUCTION

- Collagen is protein structures distributed throughout in mammals.
- Collagen constitutes about one third of the total protein in the body (25 - 30%).
- The word collagen is derived from Greek *'kola'* meaning 'glue'
- French word *'collagene' designates glue producing constituents because collagenous tissues were used as sources of glue and gelatin.*

EXTRA CELLULAR MATRIX



PROTEOGLYCANS

- MATRIX

NON COLLAGENOUS PROTEINS

(stick cells to matrix)

- FIBRONECTINS
- LAMININ

STRUCTURAL PROTEINS

(strength / flexibility)

- COLLAGEN
- ELASTIN

COLLAGEN

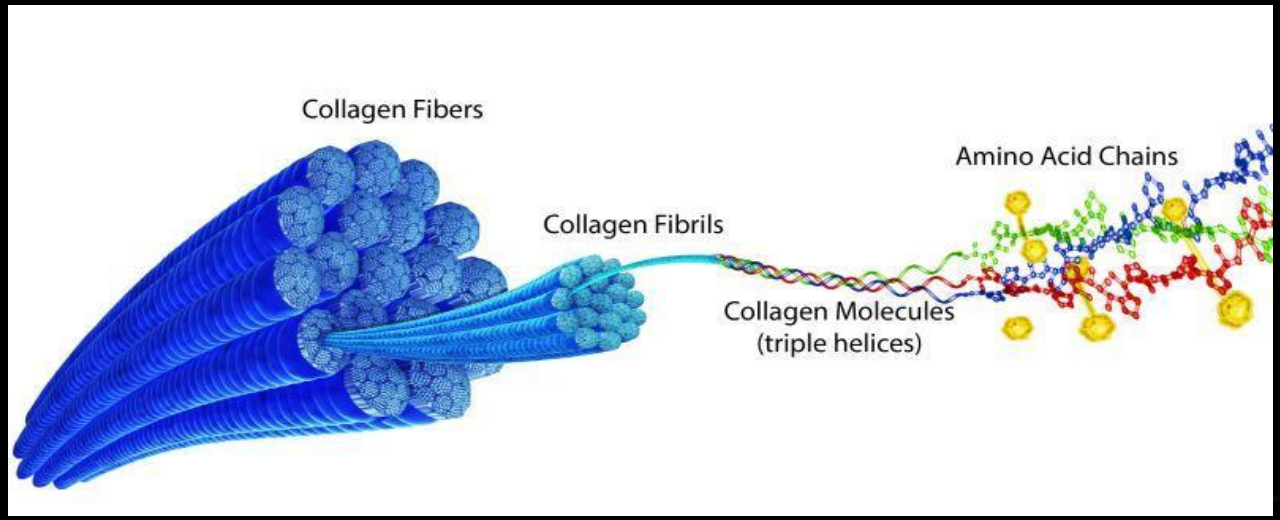
- The collagen molecule is a rigid, rod like structure that resists stretching,
- fibers made up of collagen have high tensile strength.
- Collagen forms the major structural component it also alters the cell shape, differentiation and the activities of extracellular matrix forming an important group of multifunctional connective tissue protein.

- collagen is an important component of tissues like periodontal ligament and tendon where mechanical forces need to be transmitted without loss.

STRUCTURE OF COLLAGEN

- There are 25 different genes coding for 14 different collagen molecules.

- 6 different collagen types detected in Periodontium



MICROSCOPIC APPEARANCE

- unstained collagen fibers of connective tissue are usually less than 10 µm in diameter and are colorless

- Hematoxylin and eosin → Long, wavy, pink fibers bundles

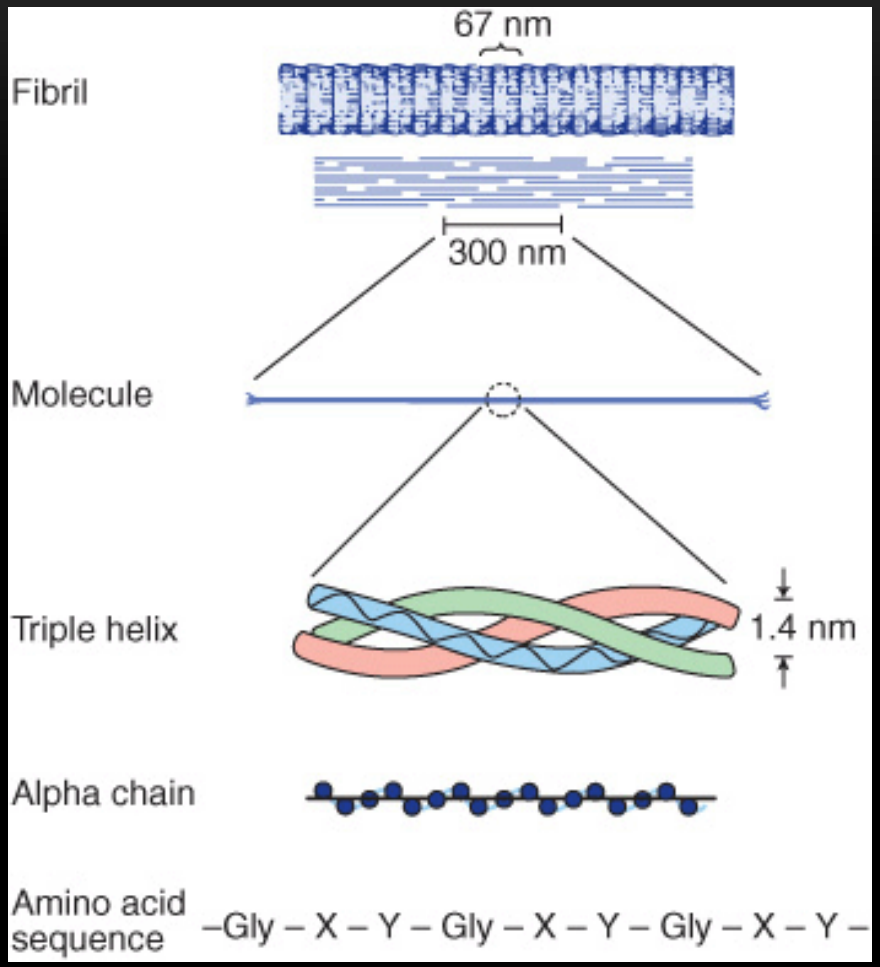
- Electron micrographs → heavy metals → crossbanding at regular intervals of 67nm.

- Collagen consist of triple helical structure formed by three polypeptide chain called α chains.
- The α chains are left handed helices which wrap around each other into a right handed ⟶ ropelike triple helical rod.
- Depending on type of collagen ⟶ molecule made up of 3 identical α chains , or 2 or 3 different α chains.

- The triple helix may be a continuous stretch or it may be interrupted by noncollagenous segments.
- Glycine occupies every third position in the repeating amino acid sequence in the triple helical domain.
- Proline frequently occupies the X & Y position.
- Hydroxyproline (Hyp) & Hydroxylysine (Hyl) are unique amino acids in collagen.

sequence follows Gly-ProX or Gly-X-Hyp.

- The collagen molecule is stabilized by a number of lysine derived intra and inter molecular cross links.


67 nm
Fibril
300 nm
Molecule
Triple helix
1.4 nm
Alpha chain
Amino acid sequence
–Gly – X – Y – Gly – X – Y – Gly – X – Y –

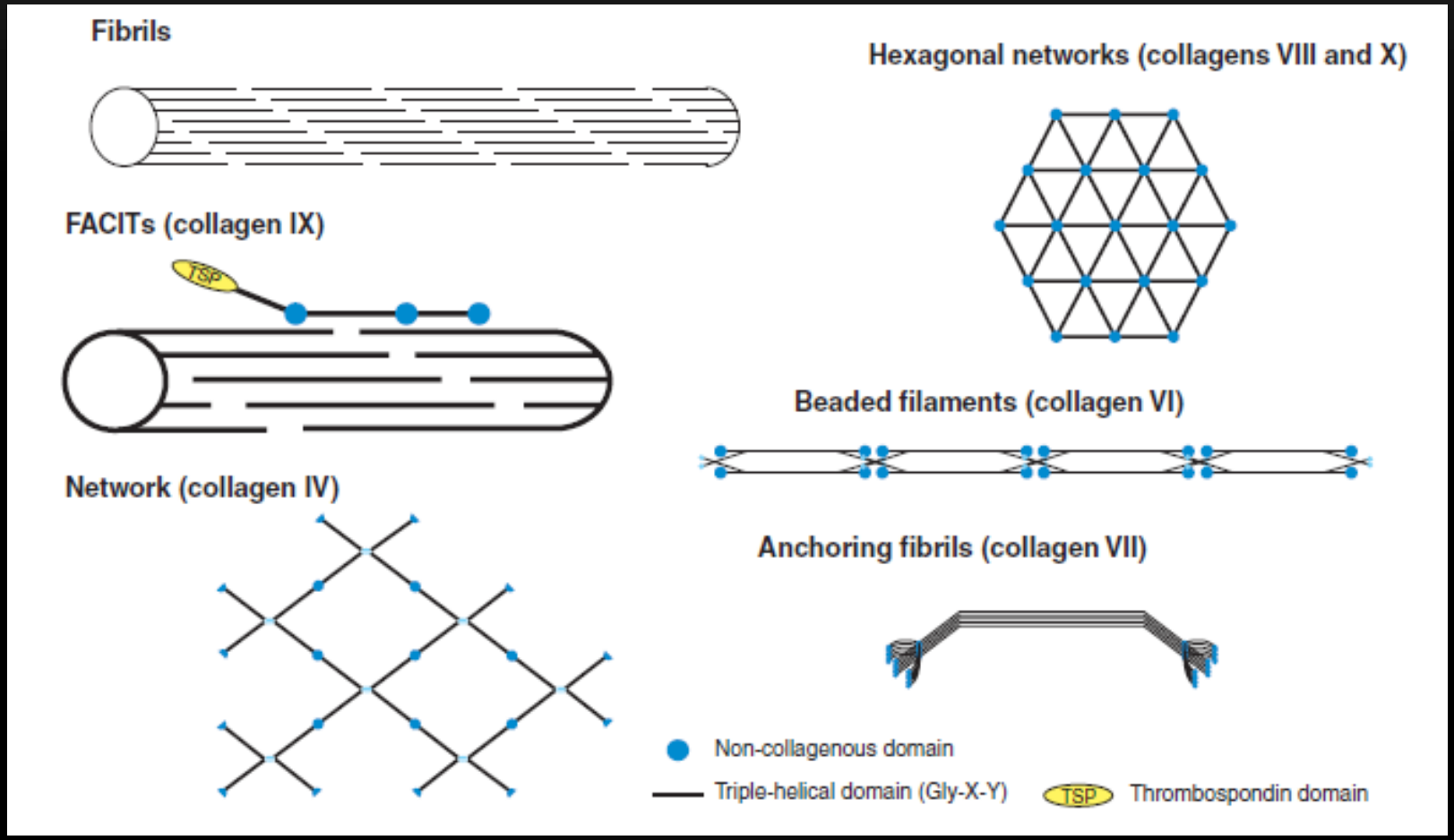
TYPES OF COLLAGENS, FUNCTIONS AND TISSUE DISTRIBUTION

Type	*Gene*	*Tissue distribution*	*Major function*
Fibrillar collagens			
I	COL1A1 COL1A2	Abundant in skin, bone, dentin, cementum, tendons, ligaments and most connective tissue	Provides strength to connective tissue
II	COL2A1	Cartilage, vitreous humor, and intervertebral disk	Provides strength to connective tissue
III	COL3A1	Embryonic connective tissue, pulp, skin, blood vessels, and lymphoid tissue (reticular fibers)	Provides strength to connective tissue
V	COL5A1 COL5A2 COL5A3	Basement membrane, blood vessels, ligaments, skin, dentine, and periodontal tissues	Forms core of type I fibrils; provides tensile strength
XI	COL11A1 COL11A2	Cartilage and vitreous humor	Forms core of type I fibrils; provides tensile strength
Basement membrane collagens			
IV	COL4A1 COL4A2 COL4A3 COL4A4 COL4A5 COL4A6	Basement membranes (basal lamina)	Structural network of basement membranes

Fibril associated collagens with interrupted triple helices (FACIT)			
IX	COL9A1 COL9A2 COL9A3	Cartilage and vitreous humor	Attaches functional groups to surface of type II fibrils
XII	COL12A1	Widespread in many connective tissues	Modulated fibril interactions
XIV	COL14A1	Widespread in many connective tissues	Modulated fibril interactions
Meshwork-forming collagens			
VIII	COL8A1 COL8A2	Cornea (Descemet's membrane) and endothelium	Tissue support and porous meshwork
X	COL10A1	Hypertrophic zone of cartilage growth plate	Calcium binding
Anchoring-fibril collagen			
VII	COL7A1	Epithelium (skin and mucosa)	Strengthens epithelial – connective junction

Microfibril-forming collagens			
VI	COL6A1 COL6A2 COL6A3	Ligaments, skin and cartilage	Bridging between cells and matrix
Transmembrane collagens			
XIII	COL13A1	Cell surfaces, focal adhesions, and intercalated disks	Cell matrix and cell-cell adhesion
XVII	COL17A1	Hemidesmosomes	Cell attachment to matrix
Endostatin-forming collagens			
XV	COL15A1	Endothelial basement membranes	Proteolytic release of antiangiogenic factor
XVIII	COL18A1	Endothelial basement membranes	Proteolytic release of antiangiogenic factor
Other collagens			
XVI	COL16A1	Endothelial, perineural, muscle, and some	Unknown
		endothelial basement membranes	
XIX	COL19A1	Endothelial, perineural, muscle, and some endothelial basement membranes	Unknown

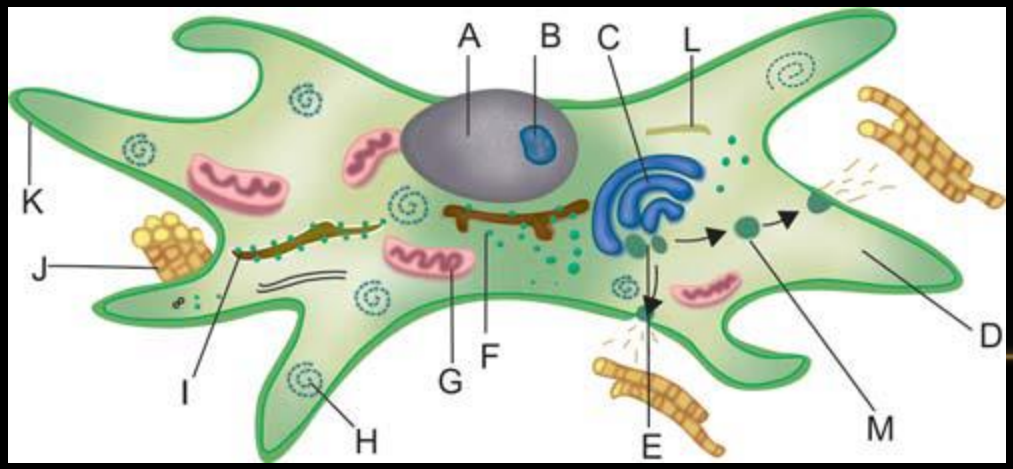
Class	*Type*
Fibril forming	I, II, III, V and XI
Network like	IV, VIII, X
FACITs*	IX, XII, XIV, XVI, XIX
Beaded filaments	VI
Anchoring fibrils	VII
Transmembrane domain	XIII, XVII
Others	XV, XVIII


Fibrils
Hexagonal networks (collagens VIII and X)
FACITs (collagen IX)
TSP
Beaded filaments (collagen VI)
Network (collagen IV)
Anchoring fibrils (collagen VII)
Non-collagenous domain
Triple-helical domain (Gly-X-Y)
TSP
Thrombospondin domain

BIOSYNTHESIS OF COLLAGEN

Sites For The Synthesis of Collagen :
1.Mesenchymal Cells & Their Derivatives
FIBROBLASTS (major cells)
Chondrocytes
Osteoblasts
Odon oblasts
Cementoblasts
2.Other Cells : Epithelial cells. Endothelial cells. Muscle cells. Schwann cells.

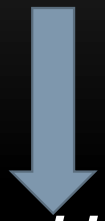
- Fibroblast is the most common cell of connective tissue that produces and maintains the extracellular matrix.
- Fibroblasts provide a structural framework for many tissues and play an imperative role in wound healing.
- The key function of fibroblasts is to maintain the structural integrity of connective tissues by continuously secreting precursors of the extracellular matrix, primarily the ground substance and a variety of fibers.
- They are recognized by their association with collagen fibers bundles.



- **The entire process of collagen synthesis can be best understood under the following stages …**

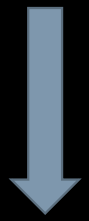
Gene Expression

nucleus



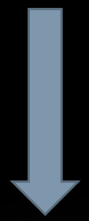
Translational and post translational events or intracellular steps in collagen synthesis procollagen formation

cytoplasm

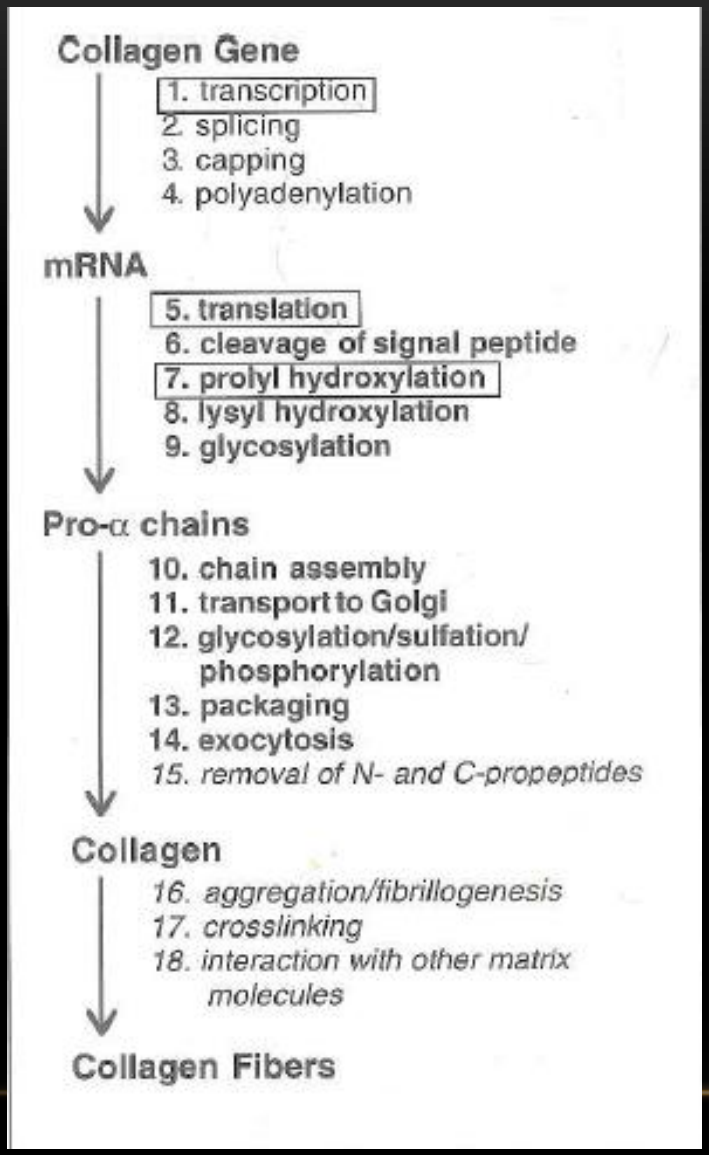


Extracellular collagen biosynthetic events

extracellular



Regulation of synthesis


Collagen Gene
1. transcription
2. splicing
3. capping
4. polyadenylation
mRNA
5. translation
6. cleavage of signal peptide
7. prolyl hydroxylation
8. lysyl hydroxylation
9. glycosylation
Pro-α chains
10. chain assembly
11. transport to Golgi
12. glycosylation/sulfation/ phosphorylation
13. packaging
14. exocytosis
15. removal of N- and C-propeptides
Collagen
16. aggregation/fibrillogenesis
17. crosslinking
18. interaction with other matrix molecules
Collagen Fibers

INTRA NUCLEAR STEPS

The 3 polypeptide chains of collagen molecule are formed separately under the direction of their respective genes. The initial RNA transcript is processed to mRNA.

After Nuclear steps the mRNA translocates to cytoplasm where it binds to ribosome to get translated & codes for PreProCollagen.

CYTOPLASMIC STEPS

Pre Pro collagen Cleavage of Signal Peptide PROCOLLAGEN α CHAIN

Hydroxylation

Glycosylation Association C terminal Peptides Disulphide Bond Formation ***PROCOLAGEN MOLECULE***

Passes in to golgoi complex combines with Secretory Vacuoles to move outside cell .

EXTRACELLULAR MATRIX:

- ***REMOVAL OF TERMINAL PRO PEPTIDES:***

  Cleavage of C & N Pro peptides by C & N Proteinase .

- ***ASSEMBLY OF COLLAGEN***

  The collagen molecules then align themselves laterally to each other , having a quarter over-lap such that there is typical 64nm banded appearance. These fibrils are immature and lack strength

- ***CROSS LINK OF FIBRILS TO FORM FIBRES***

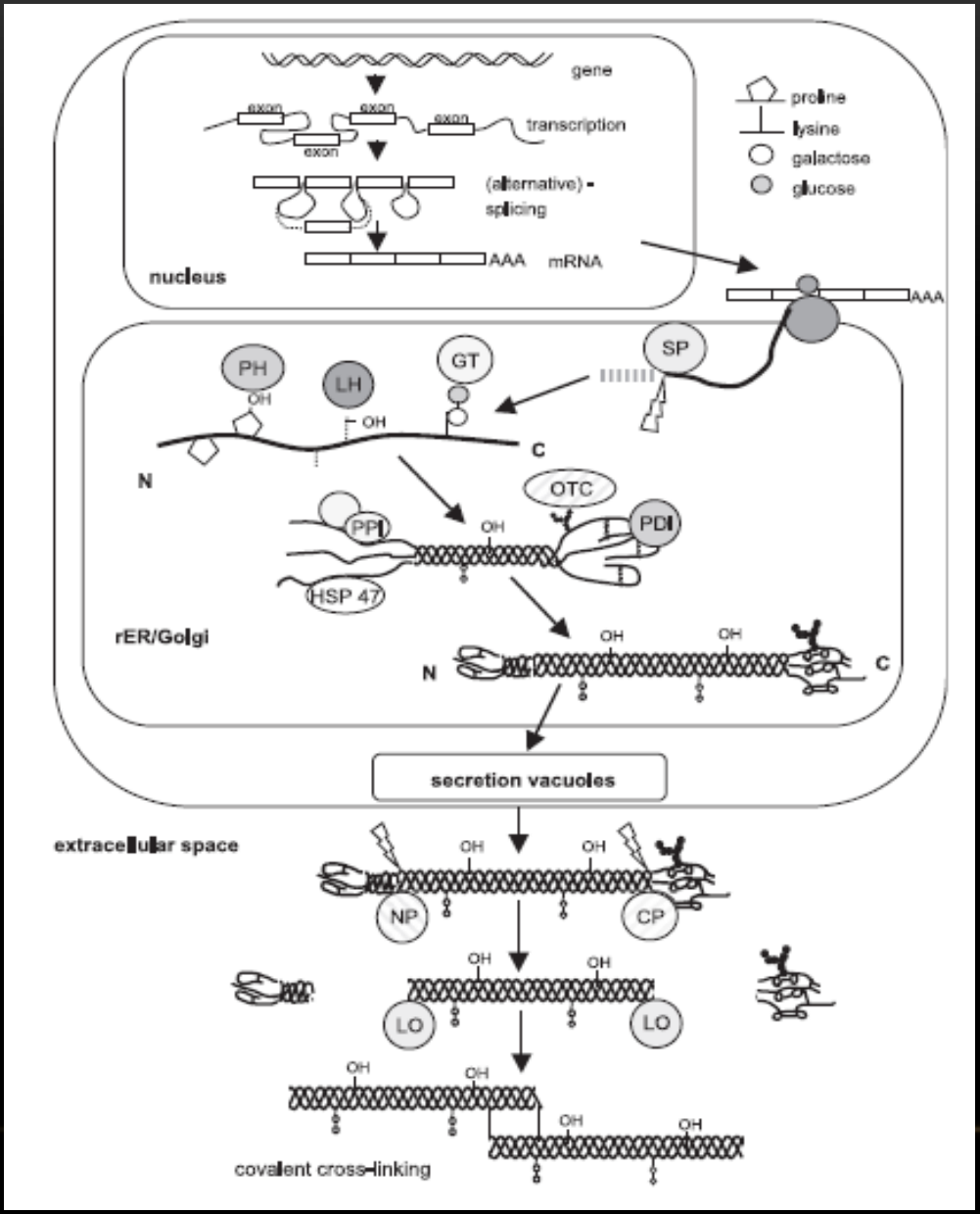
  Cross-linkage is a slow process and the tensile strength of collagen steadily increases over a long period

REGULATION OF COLLAGEN:

- It is necessary not only to control the amount of collagen production , to control the fiber architecture.
- Most important step at which regulation of collagen production occurs is at the gene level.
- The magnitude of collagen synthesis is dependent upon the levels of the mRNA for its α chain.
- These levels are largely determined by the rate of transcription, some substance such as TGF-β, elevate mRNA levels by increasing their stability.
- Collagen synthesis can be regulated posttranslationally by the extent of prolyl hydroxylation because an under hydroxylated collagen molecule is unstable at physiologic temperature and is degraded rapidly.

SOME MEDIATORS THAT AFFECT COLLAGEN SYNTHESIS

Mediator	Major Source	Collagen Synthesis
Growth factors		
PDGF	Platelets, macrophages, smooth muscle cells, epithelium	↑
TGF-β*	Platelets, macrophages	↑
FGF	Platelets, macrophages, matrix	↑
IGF	Serum, matrix	↑
Cytokines/lymphokines		
IL-$1_{\alpha,\beta}$†	Macrophages, most cells	↓
IFN-γ	Lymphocytes	↓
TNF-α	Monocytes/macrophages	↓
Hormones		
Glucocorticoids‡	…	↓
Others		
PGE_2	Monocytes/macrophages	↓


gene
exon
exon
exon
exon
transcription
(alternative) - splicing
AAA mRNA
nucleus
proline
lysine
galactose
glucose
AAA
PH
OH
LH
OH
GT
SP
C
N
OTC
PDI
PPI
OH
HSP 47
rER/Golgi
OH
OH
N
C
secretion vacuoles
extracellular space
OH
OH
NP
CP
OH
OH
LO
LO
OH
OH
OH
OH
covalent cross-linking

DEGRADATION AND REMODELING OF COLLAGEN

- Degradation of collagen and other matrix elements is a key component of normal tissue remodeling.
- It also contributes greatly to pathologic alterations.
- Collagen takes place by 2 different ways

  - intracellular degradation

  - extracellular degradation

- Mechanisms involved in degradation of collagen

extracellular degradation

- Secretion by cells of enzymes that sequentially degrade collagen and other matrix molecule

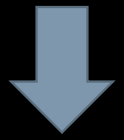
- Intracellular degradation:

fibroblast that are in intimate contact with the fibers

identify the alteration in the structure of collagen

cleave the fibrils and phagocytose of fibrils

forming phagosome then the phagolysosome



further degraded by the lysosome enzyme especially cathepsin

- Collagen degradation is primarily mediated by collagenases.
- These are specialised enzyme that have evolved specifically to hydrolyze collagen because their triple helical structure is resistant to most common proteinases.
- Collagenases belond to a family of enzymes called MMP

Enzyme	MMP Type	Source	Specificity
Collagenases			
Collagenase-1	MMP-1	Connective tissue cells, macrophages	Type I, II, III, VII, VI collagens
Collagenase-2	MMP-8	PMN	Same as collagenase-1
Gelatinases			
72-kd, gelatinase-A	MMP-2	Connective tissue cells	Gelatin, types IV–VII, X, XI, elastin
92-kd, gelatinase-B	MMP-9	Connective tissue cells	Same as gelatinase-A
Stromelysins			
SL-1	MMP-3	Many cells, tumor cells	Proteoglycans, laminin, collagen types III–V, IX, X
SL-2	MMP-10	Many cells, tumor cells	Same as SL-1
SL-3	MMP-11	Tumor cells, stromal cells	?
Others			
PUMP-1 (matrilysin)	MMP-7 Macrophages	Connective tissue cells	Fibronectin, laminin, type IV collagen, gelatin, proteoglycans
Metalloelastase	MMP-12	Macrophages	Elastin, fibronectin
Membrane type MMP	MT-MMP	Cell membrane	Progelatinase-A

DISTRIBUTION OF COLLAGEN IN PERIODONTIUM

Gingiva:

- collagen are the most abundant biochemical component of gingival connective tissue (more than 60% of total tissue protein).
- They are arranged in 2 forms:

type I collagen – arrange as large dense bundle of thick fibers in the major species

Type III collagen – arranged in a loose pattern of short thin fibers mixed with a fine reticular network.

- Type V collagen – accounts less than 1% of the total collagen.
- Type VI collagen – seen in microfibrils throughout the lamins propria.
- Type IV collagen – present in the basement membrane in lamina lucida along with laminin.

_ also present in internal basal lamina serves as an interface through which junctional epithelium is attached to root surface.

- Periodontal ligament:
- predominantly type I, III and V collagen.
- Type VI collagen – micro fibrils
- Type IV – basement membrane to which anchoring fibrils are attached that contains type VII collagen
- Type XII involved in three dimentional organisation of the extracellular matrix .
- Type XIV – is asssociated with the major collagen fibrils.

- Cementum:
- predominantly contains Type I & III collagen
- Some trace of type V & VI.

- Alveolar bone:
- 94 to 98% is mainly type I collagen.
- During its formation in the osteoblast large procollagen precursor undergoes important post translation modification. Suitably located proline and lysine residues are hydroxylated to hydroxyproline and hydroxylysile

Oral tissue	Collagen type	Function
Alveolar bone	Type I	Resist mechanical shear from any direction
Periodontal ligament	Type I, III	Flexibility and strength to the tissue[3]
Cementum	Type I	Regulating periodontal tissues during development and regeneration[2]
Dentin	Type I	Accommodation of minerals in the holes and pores of fibrils
Pulp	Type I, III	Provide strength to connective tissue
Gingiva	Type I, IV	Provide strength to connective tissue[4]
TMJ	Type I, II and III	Structural component of intra-articular disc and provide reinforcement and mechanical stability under compression[5]

COLLAGEN DISORDERS

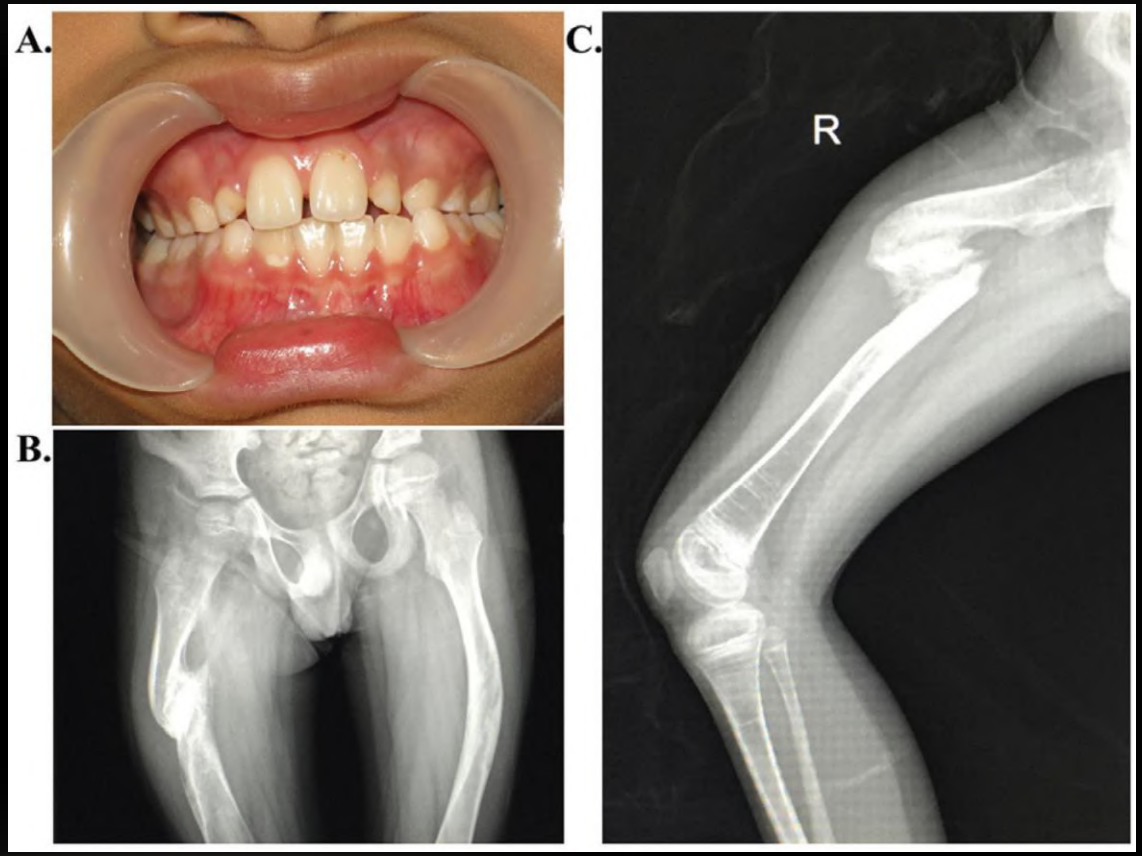
- Heritable / Genetic collagen disordes:
  - Ehlers -Danlos syndrome
  - Osteogenesis imperfecta
  - Stickler syndrome
  - Alport syndrome
  - Epidermolysis bullosa
  - Marfan syndrome

- Autoimmune collagen disorders
  - Systemic lupus erythematosus
  - Systemic sclerosis
  - Oral submucous fibrosis
- Miscellaneous
  - Scurvy

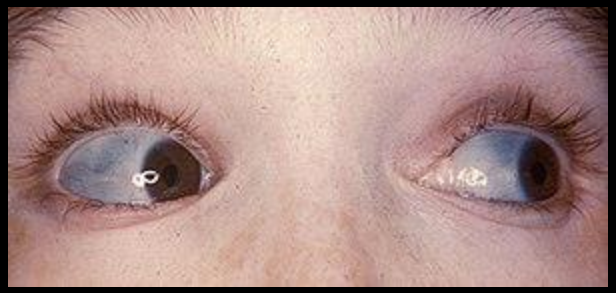
❖ Osteogenesis Imperfecta: (Brittle bone disease)

The disease is characterized by

- extremely fragile bones
- reduced bone mass
- blue sclera,
- hearing loss and
- scoliosis.



- This is due to mutations in one of the two genes, COL1A1 and COL1A2, which encode the two chains of type I collagen, the major protein of bone.
- The most common mutations of this disease is due to substitution of glycine with a bigger amino acid.



EHLERS-DALNOS SYNDROME (RUBBER MAN SYNDROME)

- Heterogeneous group of heritable disorders of connective tissue characterized by

  articular hypermobility

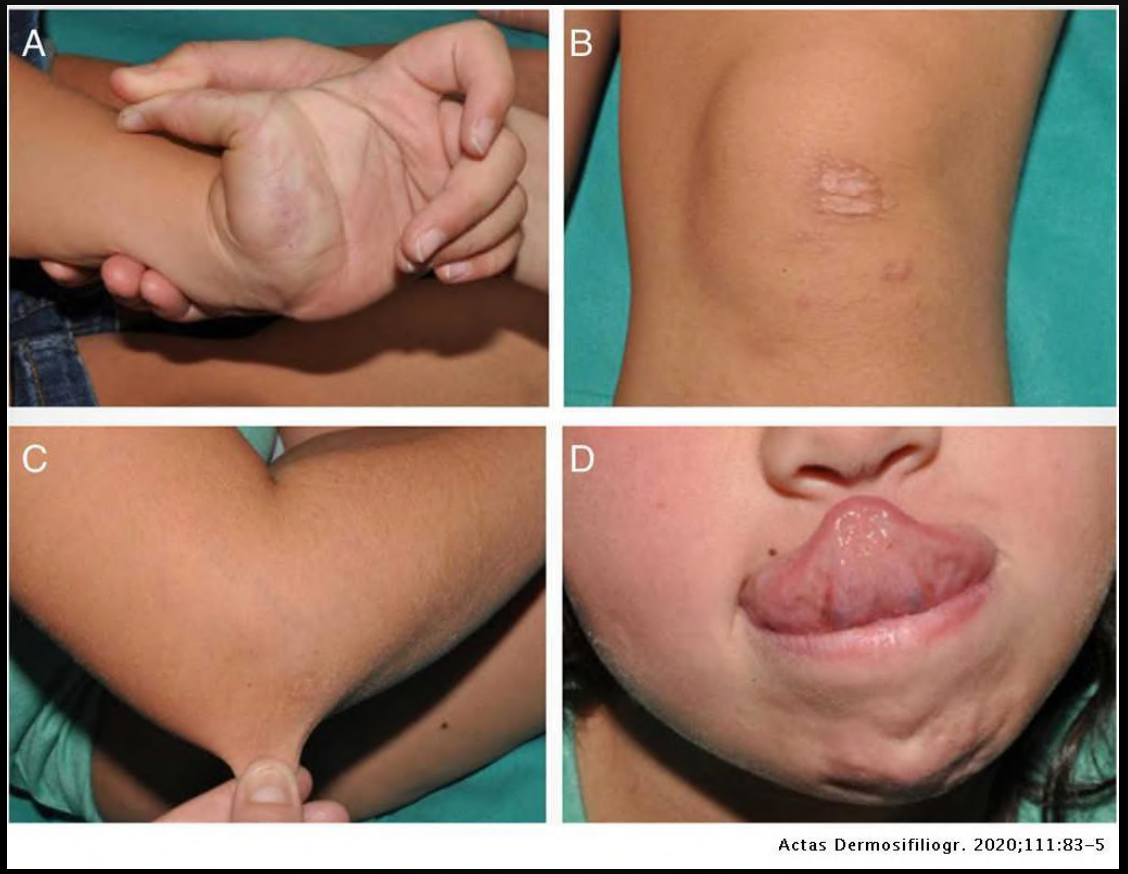
  skin hyperextensibility, and

  tissue fragility affecting skin, ligaments, joints, blood vessels, and internal organs.

- Cause- mutations in the COL5A1 and COL5A2 genes encoding the α1 and α2 chains of type V are defined.

- Oral manifestation:

- Gorlin sign
- Early onset generalized periodontitis resulting in the premature loss of deciduous and permanent teeth.
- The gingiva is fragile and hemorrhage may be difficult to control during surgical procedures.
- Absence of the inferior labial and lingual frenula has been reported in EDS II, EDS III and suggested to be a highly specific and sensitive marker for these disorders.


A
B
C
D
Actas Dermosifiliogr. 2020;111:83-5

- CHONDRODYSPLASIAS:

Approximately 50 mutations that leads to this condition has been reported.

CF: Heterogenous group of disease.

Abnormal growth and development of cartilage.

Exhibit abnormalities in type II collagen- containing tissues such as growth plates ,nucleus pulpous and viterous humor.

3 major forms of this disease :

Achondrogenesis/Hypochondrogenesis

Spondyloepiphyseal

dysplasia Stickler Syndrome.

❖ ALPORT SYNDROME:

Progressive hereditary nephritis associated sensoneuronal deafness and occular abnormalilties.

It has an X linked inheritance pattern.

Characterized by splitting and thinning of the glomerular basement membrane.

Pathogenesis:

Point mutations in triple helical and C-propeptide domains.

Multiple exon deletions

Affected Gene: COL4A5 GENE.

- Dystrophic epidermolysis bullosa:

Molecular defects is seen in type VII collagen gene.

In this disease the dermal epidermal integrity is affected due to abnormal or absent anchoring fibrils.

Pathogenesis: Mutations in COL7AI gene.

- Marfan's Syndrome:

- This is the most common hereditary group of connective tissue disorders.
- Manifestations include ocular, skeletal, cardiovascular, and dural lesions. There is defect in organisation of collagen.
- There is more amount of soluble collagen.

Symptoms : Skeletal dolichostenomelia (long, narrow extremities)

scoliosis (abnormal spinal curvature)

pectus excavatum (deeply depressed sternum)

flat foot (pes planus) due to the medial deviation of the medial malleolus

Rheumatoid Arthritis:

- Systemic inflammatory autoimmune disorder primarily attacks the synovial membrane of the minor joints in successive episodes, leading to joint stiffening.
- Pathogenesis:
- Occurs in patients with a genetic predisposition (HLA-DRB1 0401, 0404 and0101).
- Initial viral infection somehow stimulates autoreactive Th1 cells.
- This generates autoantigens, This causes B cells to form autoreactive antibodies(rheumatism factors).

  -anti-idiotypes (primarily IgM against IgG) ,

  -antinuclear antibodies, and

  -anti-collagen type II antibodies

- These antibodies cross-link to form deposits on collagen fibers (fibrinoid necrosis), leading to formation of rheumatoid granulomas.
- This activates the complement system which perpetuates the inflammation
- . It affects the TMJ causing loss of vertical dimension. Indirectly have perio complications like dys functionally excessive occlusal forces in the molar regions and loss of bone support from extrusion of the anterior teeth.

Sjogren's syndrome:

- Systemic autoimmune disorder with symmetrical involvement of the salivary and lacrimal glands and desiccation of the conjunctiva and oropharynx.
- Clinical triad of – xerostomia, keratoconjunctivitis sicca, rheumatoid arthritis.

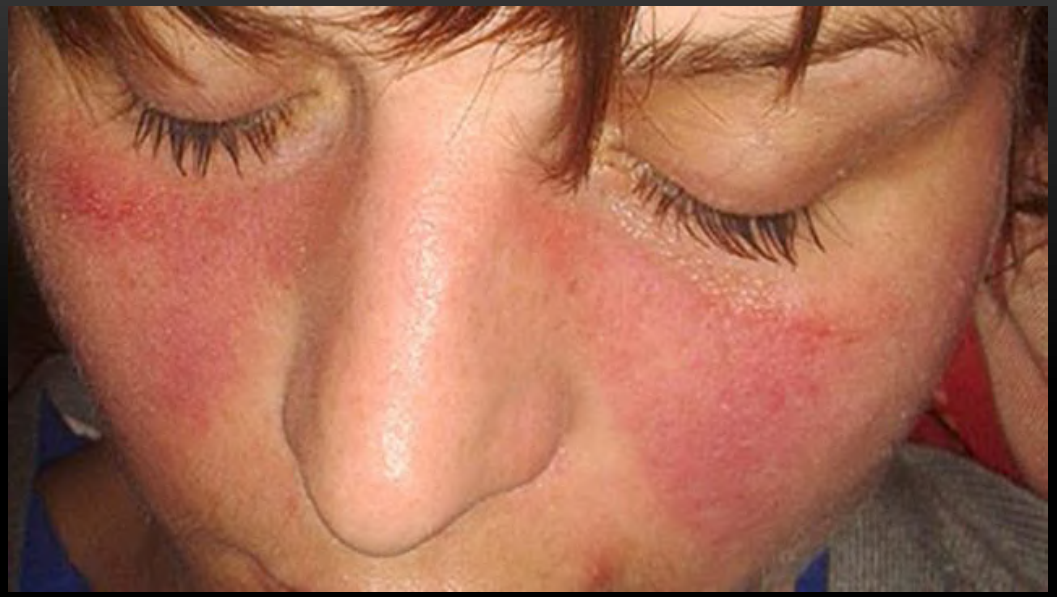
❖ Primary form involves an isolated keratoconjunctivitis sicca syndrome.

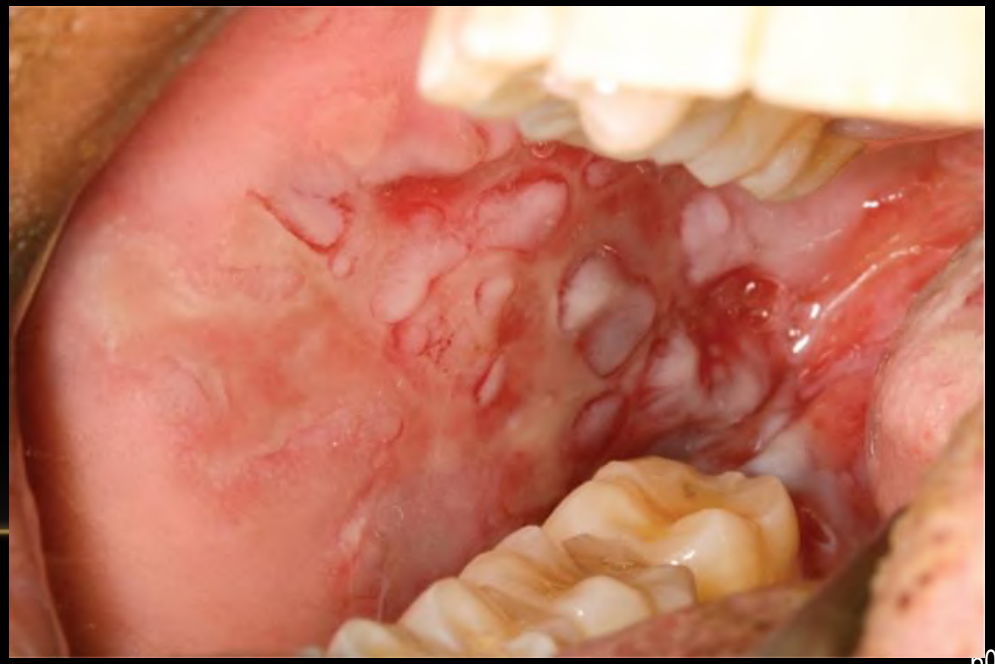
❖ Secondary form involves a keratoconjunctivitis sicca syndrome in conjunction with other autoimmune disorders such as rheumatoid arthritis or systemic lupus erythematosus.

- Pathogenesis: Patients with a genetic predisposition (primarily HLA-DR3) form autoreactive antibodies mainly against splicosomal proteins as well as against the excretory epithelia of the salivary and lacrimal glands.

SYSTEMIC LUPUS ERYTHEMATOSIS

- Lupus erythematosus is a multifactorial autoimmune collagen vascular or connective tissue disease, which may affect the oral mucosa in either its cutaneous and systemic forms with varied prevalence .
- Oral lesions include ulceration, pain, erythema and hyperkeratosis. Other oral complaints are xerostomia, stomatodynia, candidiasis, periodontal disease and dysgeusia.





Progressive systemic sclerosis:

- Systemic immunologic disorder that begins with progressive sclerosis of the dermal connective tissue and spreads to the vascular connective tissue of internal organs.
- CF: There is progressive fibrosis of skin and mucosa and limited jaw opening
- Pathogenesis: The disorder is characterized by two mechanisms: — Formation of immune complex and, presumably induced by it, — Excessive formation of abnormal collagen and microfibrils

SCURVY

- A deficiency in vitamin c is known as scurvy.
- Key function od ascorbic acid is its involvement in the synthesis of collagen fibers from proline via hydroxyproline
- Other metabolic reactions for which vitamin C is required are the hydroxylation of lysine into hydroxylysine in collagen

- The α-chains of the tropocollagen molecules are unable to form stable helices and the tropocollagen molecules are incapable of aggregating into fibrils.

- Avitaminosis C is associated with the failure of wound healing or the rupture of capillaries due to intrinsic intercellular weakness with lack of connective tissue support of the capillary walls.

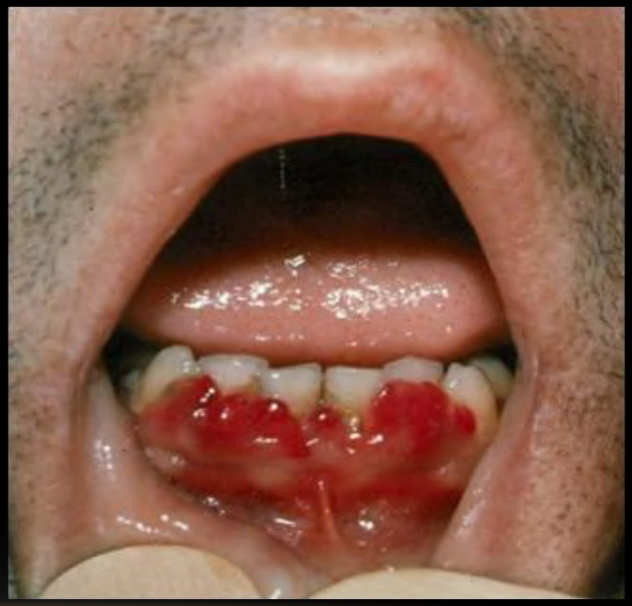
oral signs may be cardinal:

Fetid odor and loosened teeth

gingivae are boggy, ulcerated

bleed with the interdental and marginal gingiva becoming bright red,

Smooth, swollen and shiny.



ALTERATION OF COLLAGEN IN GINGIVA

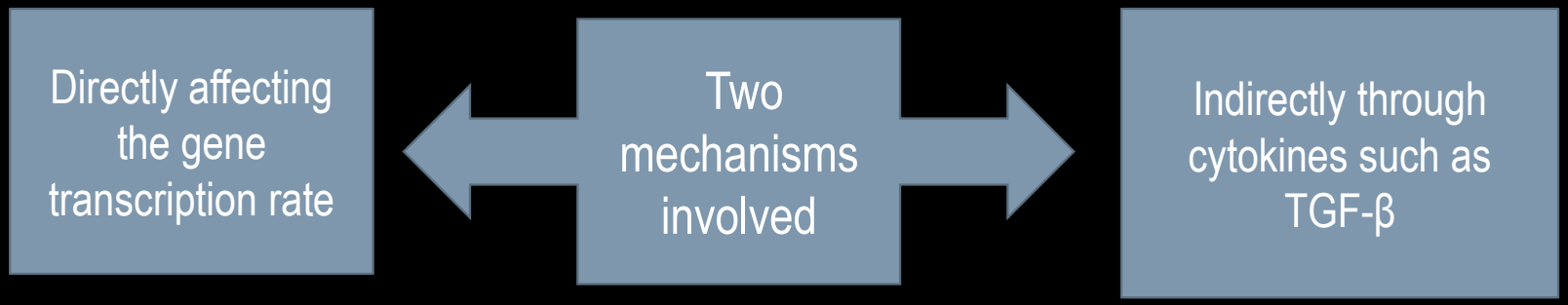
ALTERATION IN GINGIVITIS AND PERIODONTITIS

- In gingivitis tissue destruction begins within the perivascular extracellular matrix where most of the collagen with in the foci of inflammation is degraded.
- Quantitative and qualitative changes occur in gingival collagen.
- In gingiva collagen becomes more soluble (indicate new and active synthesis)

- Type I & II collagen destroyed at foci of inflammation.
- The ratio of collagen types are altered.
- Type V collagen increases and its amount may exceed that of type III.
- A new collagen species, type I trimer can be detected in inflamed gingiva.

GINGIVAL ENLARGEMENTS

- Type I & III collagen ratio becomes different with loss of type I and elevated levels of type III.



❖ **Hereditary Gingival Fibromatosis:**

- **It is** also called elephantiasis gingivae, hereditary gingival hyperplasia, and hypertrophic gingiva.
- It is characterized by progressive enlargement of the gingiva.
- exhibit an autosomal dominant or recessive mode of inheritance.

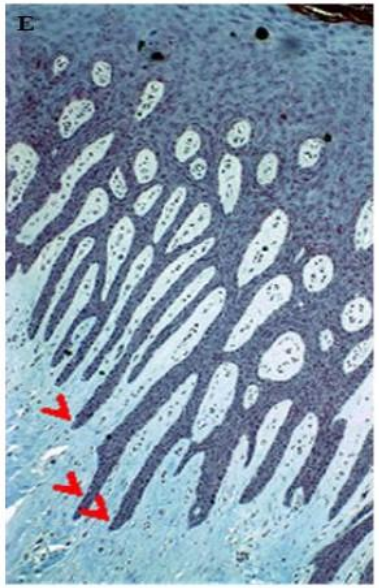
Oxidative stress in gingival hereditary fibromatosis: in vivo and in-vitro assays

Oxidative stress

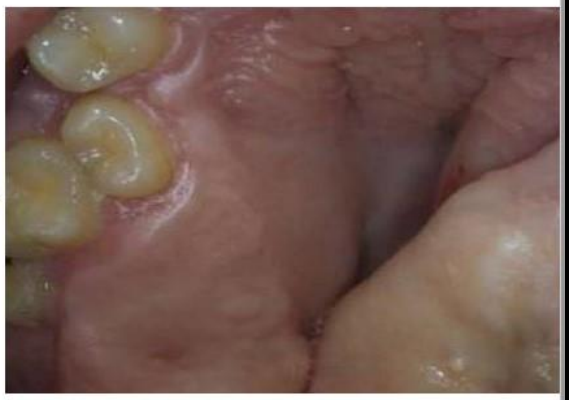
Decreasing CoQ10

Collagen synthesis

Dense fibrous tissue,
Basal lamina disruption



Fibromatosis



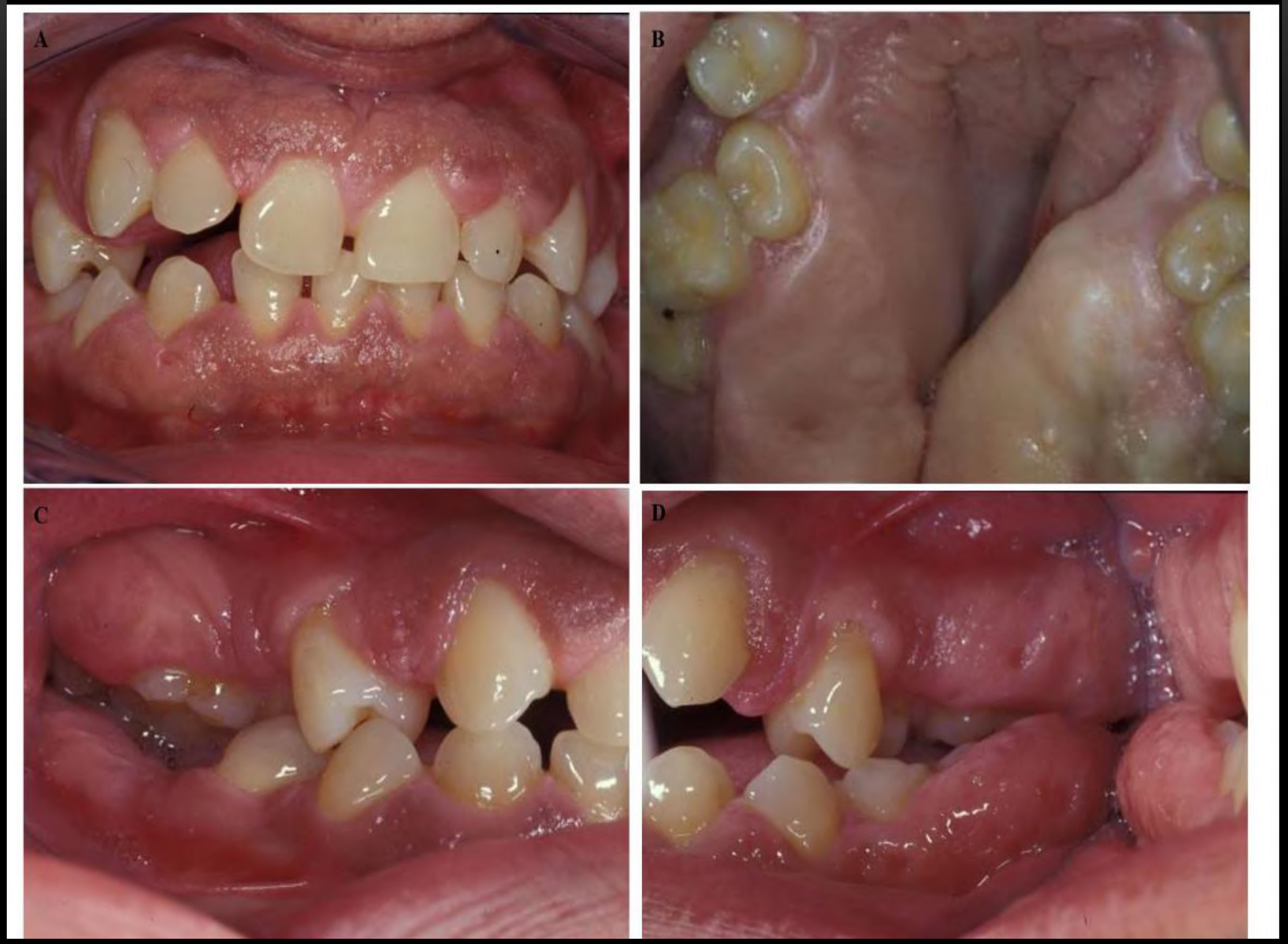
- recessive pattern usually linked to other syndromes: Cowden, Jones, Goltz-Gorlin, Murray-Puretic-Drescher, Ramon,Rutherfurd, Cross
- other systemic diseases: cherubism, hypothyroidism, chondrodystrophy, growth hormone deficiency, hypertrichosis, epilepsy, mental retardation, craniofacial dysmorphism or leukemia.

Oral manifestations of HGF

- thick and fibrous gingiva
- enlarged tissues are firm, pink and nodular in appearance and may show exaggerated stippling
- tissues are non-erythematous, except for locally caused inflammation, and have no tendency to bleed

Histologically

- increased amount of randomly arranged bundles of collage
- Hyperplastic dense fibrous connective tissues that are formed by thick bundles of collagen fibers, small calcified particles, islands of osseous metaplasia, ulceration of the overlying mucosa, and inflammation


A
B
C
D

❖ DRUG INDUCED ENLARGEMENT:

- A) Phenytoin

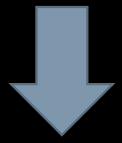
fibroblasts become sensitive → increased production of collagen.

The enzyme collagenase secreted by phenytoin sensitive fibroblasts is relatively inactive to degrade collagen.

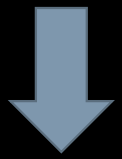
an imbalance in production and degradaton results in the over accumulation of collagen and hence increase in bulk of connective tissue.

- B) Calcium channel blockers:

interaction between Nifedipine & gingival fibroblasts



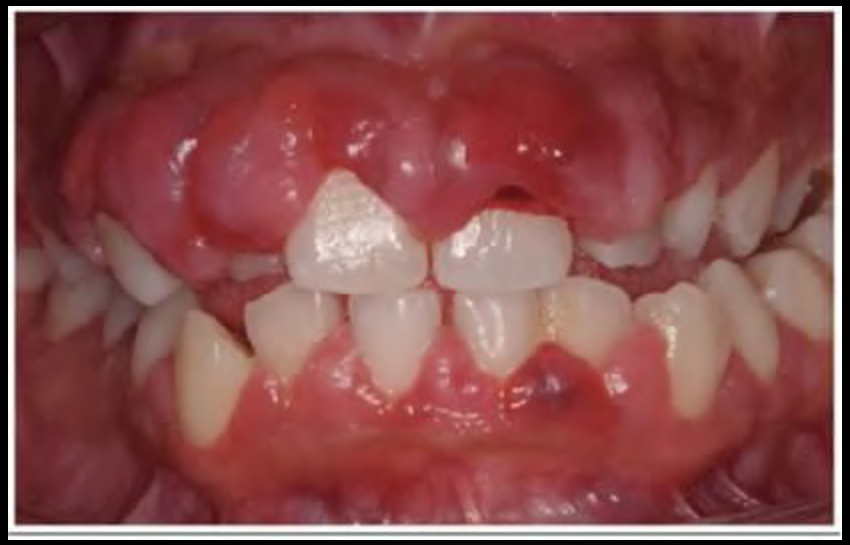
overproduction of collagen and extracellular ground substance



increase in the size of gingiva

- C) Cyclosporin induced:

cyclosporin reacts with gingival fibroblasts to enhances protein synthesis



ALTERATION IN DIABETES MELLITUS

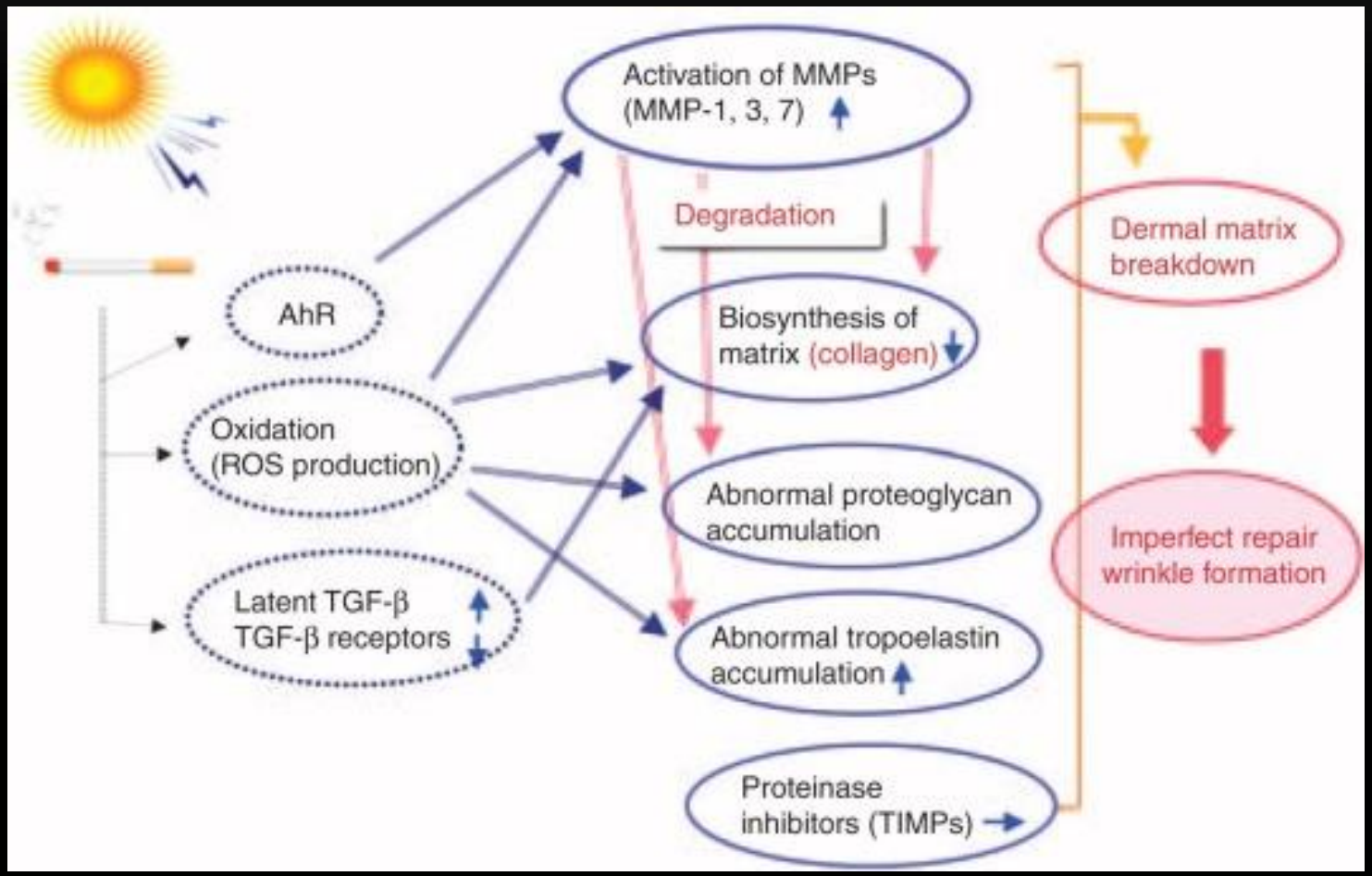
- In hyperglycemic state numerous protiens and matrix molecules undergo a non enzymatic glycosylation process resulting in accumulation of glycation end products (AGEs).

collagen cross-linked by AGE formation → less soluble →

less likel to be normal for repaire or replace

- increased expression of MMP 8 & 9 is seen in diabetic patients.

IN SMOKERS:

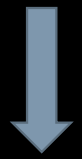

Activation of MMPs
(MMP-1, 3, 7)
Degradation
Dermal matrix
breakdown
AhR
Biosynthesis of
matrix (collagen)
Oxidation
(ROS production)
Abnormal proteoglycan
accumulation
Imperfect repair
wrinkle formation
Latent TGF-β
TGF-β receptors
Abnormal tropoelastin
accumulation
Proteinase
inhibitors (TIMPs)

POTENTIAL BEHAVIOR

stress

increases in cortisol and β endrophin concentration

regulates expression of MMP – 1, 2, 7 & 11 and TIMP – 1 in gingival fibroblasts



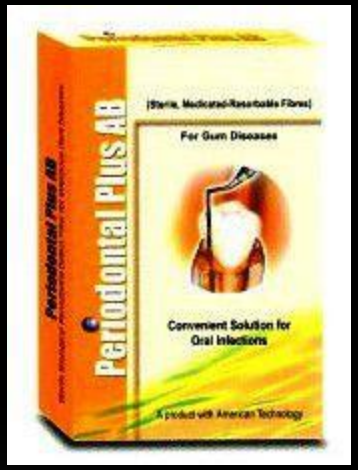
periodontitis - Patricia et al in 2007

BIOMEDICAL APPLICATIONS

- **Drug delivery- For LDD in periodontal pockets:**

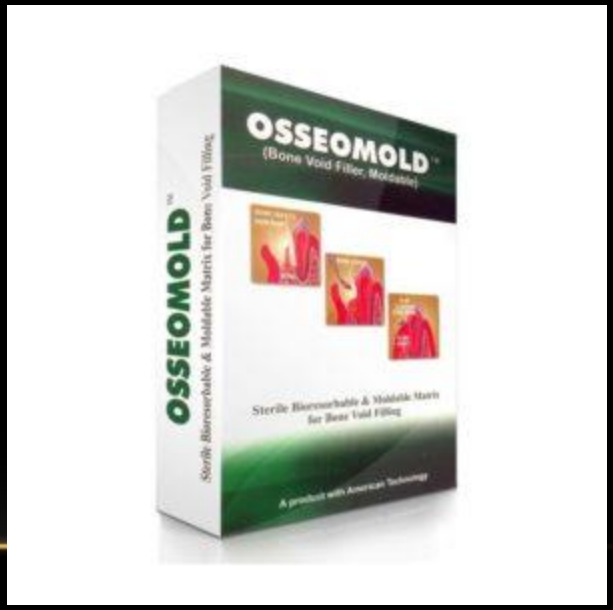
- **high concentration of drug can be maintained at the target site**

- **drug can be loaded in to collagen membrane by hydrogen bonding, covalent bonding or simple entrapment.**



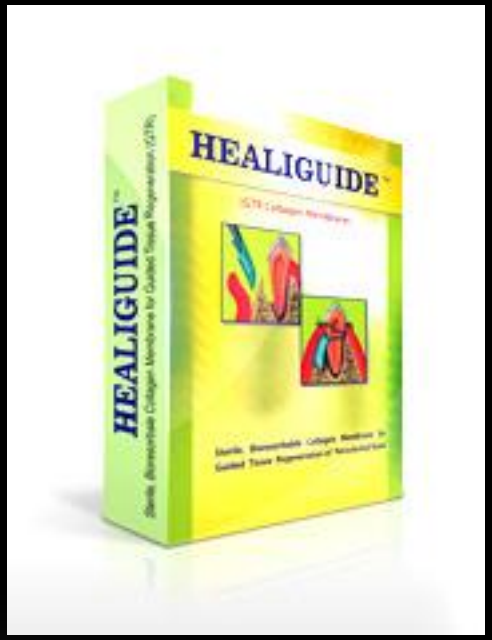
- **Tissue augmentation- recession coverage Collagen membranes are used as an alternative to connective tissue grafts in mucogingival surgeries**

- **Bone substitute- as bone grafts in intra-bony defects Collagen has been used as implantable carriers for bone inducing proteins Collagen itself is used as bone substitutes due to its osteo-inductive**
- **Osseograft/DMBM is one such de-mineralized bone derived Type-I collagen for bone void filling**



❖ Guided tissue regeneration- GTR membrane:

It is a procedure use barrier devices that are placed between the periodontal flap and the osseous defect to maintain a space for repopulation of the defect with cells heving regenerative potential



❖ Hemostat:

stimulated by the protien fibrinogen , the platelets then clump by binging to the collagen that becomes exposed following rupture of the endothelial lining of blood vessels.

collagen is therefore a natural hemostat.

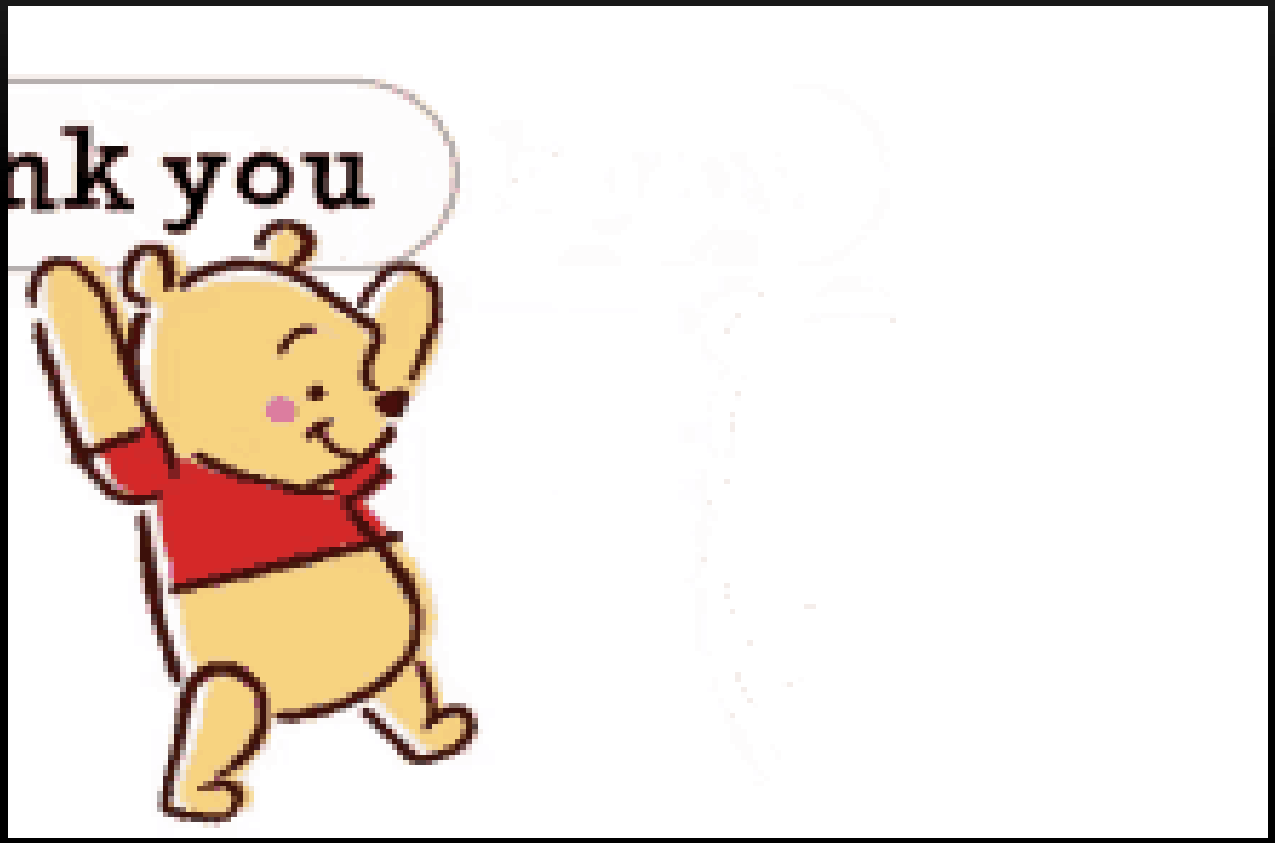
CONCLUSION

Collagens have ubiquitous distribution throughout the animal kingdom. Collagens serve important mechanical functions within the body, particularly in connective tissues and also exert important functions in the cellular microenvironment.

It is an important constituent of periodontium therefore knowledge of the structure, biosynthesis and interactions of collagen with other components, its regulation and degradation mechanisms and changes it undergoes with age and diseased state is essential, for the understanding of the functioning of the periodontium.

REFERENCES:

- K. Gelse ., et al.Collagens—structure, function, and biosynthesis. Advanced Drug Delivery Reviews 55 (2003) 1531–1546.
- P. Mark Bartold .Biology of the periodontal connective tissue.1998
- **Palwinder Kaur ., et al.**Collagen: Role in Oral Tissues: A Review. **International Journal of Science and ResearchMay 2014, 3(5).**
- **Simarpreet V Sandhu., et al.**Collagen in Health and Disease. Journal of Orofacial Research . March 2012
- **Akshat Pandey**., et al .**Oral Manifestations of Autoimmune Connective Tissue Diseases.** Indian Journal of Rheumatology.2018.
- **Lourdes Roman-Malo**., et all.Case Report **Fibroblasts Collagen Production and Histological Alterations in Hereditary Gingival Fibromatosis.mdpi 2019**, 7, 39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