

Motor System Structural components Inflammation

Rajko Bisevac ND, ABAAHP, FAARFM
purelifehealth@yahoo.com

MOTOR SYSTEM

- ▶ The motor system is the part of the nervous system that controls voluntary movement. It consists of the **brain, spinal cord and nerves** that connect these structures to the effector **muscles**.
- ▶ The human body has about **600 skeletal muscles**, which produce movements at body **joints**. The brain gives commands to the muscles through nerves.

STRUCTURE

- ▶ **Connective Tissues**
 - ▶ **Cartilage**
 - ▶ **Bones**
 - ▶ **Muscles**
- 

THE REAL CULPRIT?

1. STRUCTURAL DAMAGE
 2. NITRIC OXIDE
 3. GLYCOBIOLOGY & GLYCOCALYX
- 

LARGE PICTURE: Connecting the dots!

1. STRUCTURAL DAMAGE
 2. LIPIDS
 3. NITRIC OXIDE
 4. GLYCOBIOLOGY & GLYCOCALYX
- 

LARGE PICTURE: Connecting the dots!

1. STRUCTURAL DAMAGE – **SULFATED POLYSACCHARIDES**
2. LIPIDS
3. NITRIC OXIDE
4. GLYCOBIOLOGY & GLYCOCALYX

SULFATED POLYSACCHARIDES?

- ▶ Complex group of sugars with many important biological properties. These polymers
- ▶ Sulfated polysaccharides encompass a diverse group of anionic polymers, occurring in many different groups of organisms, from *macroalgae* to mammals.
- ▶ Act as an antioxidant, anti-inflammatory, anticoagulant, anticancer, antiviral, antidiabetic, and antithrombotic agent. They alter HUMAN IMMUNE SYSTEM.
- ▶ In the post-genomic era, science is still challenged to explain the biosynthesis of complex polysaccharides and glycoconjugates. Unlike nucleic acids and proteins, the information needed for their biosynthesis is not clearly contained to this day within the genome of the various organisms
- ▶ **Therapeutic importance of sulfated polysaccharides from seaweeds: updating the recent findings**
- ▶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3433884/>

FIBERS, SULFATED COMPONENTS

- ▶ Dietary fibres ameliorate decreased synthesis of heparan sulphate
- ▶ <https://pubmed.ncbi.nlm.nih.gov/12770644/>

- ▶ Research on saccharides and dietary fiber pectin in foods Ideal diet to extend our healthy life expectancy
- ▶ https://www.gifu-u.ac.jp/en/about/pub_news/g_lec/special_35_3.html

SELF-SUFFICIENT SYSTEM

- ▶ USA contributes to 30% of the world's waste
 - ▶ SWEDEN – Astonishing 99% recycling rate. Up from 96%.
 - ▶ Close to zero waste.
- 

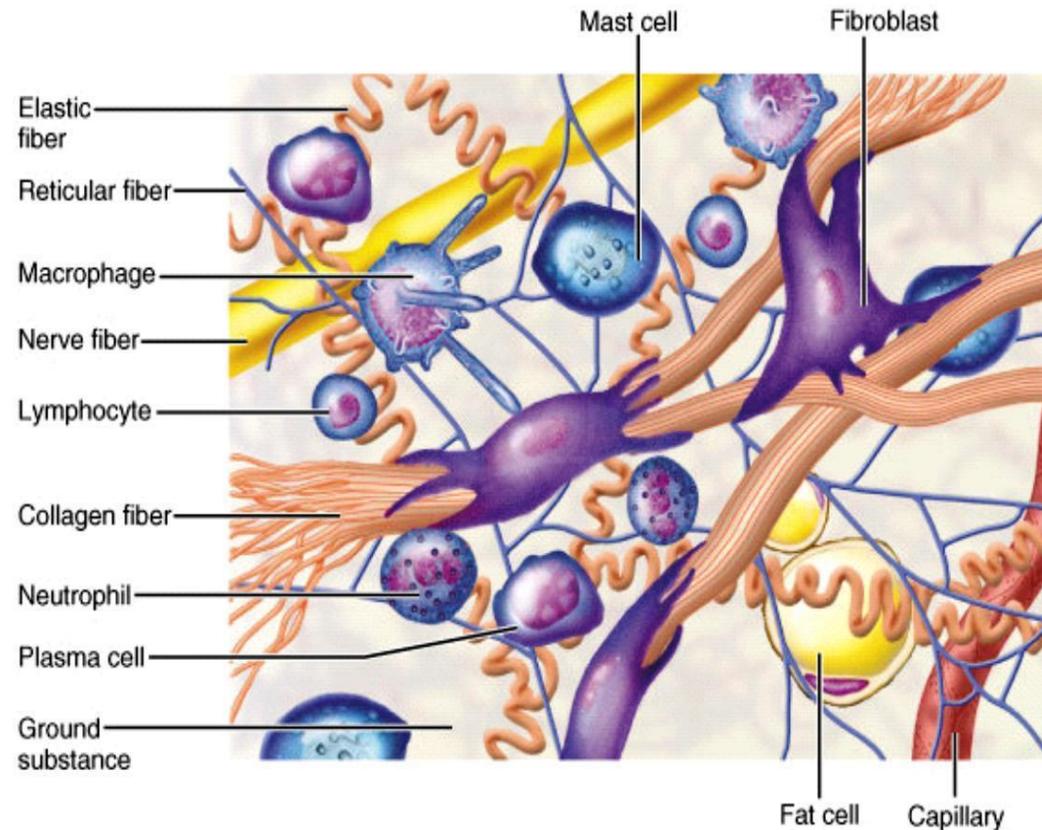
Connective Tissue

- ▶ Connective tissue is found everywhere in the body. It fills the spaces between organs and tissues and provides structural and metabolic support for other tissues and organs.
- ▶ Most abundant and widely distributed tissues
- ▶ Subtypes:
 - Fat tissue, dense fibrous tissue, cartilage, bone, blood, and lymph
- ▶ Functions
 - Binds together body tissues
 - Supports the body
 - Provides protection

Characteristics

- ▶ Variations in blood supply
 - Vascularized – contains a good blood supply
 - Avascular – poor blood supply, heal slowly (ex.tendons, cartilage)

- ▶ Made of
 1. Cells
 2. Ground substance
 3. Extracellular Matrix



1. Cells in Connective Tissue

- ▶ **Fibroblasts** – most common – responsible for secreting extracellular matrix including fibers: collagen, elastin, or fibronectin
- ▶ **Adipocytes** – fat storing cells
- ▶ **Macrophages** – phagocyte
- ▶ **Mast cells** – contain heparin proteoglycan and histamine
 - play a key role in allergic reactions
 - Causes bronchioles vasodilation and constriction
 - Digestion (HCL), neurotransmitter, control pain, happiness, mood, memory, BP, Motivation, sleep/wake cycle, sexual function, IMMUNE function.
- ▶ **Plasma cells** – derived from B-cells, found in lymph, important in developing immunity

Immune Cells

2. Ground Substance

- ▶ Translucent, viscous, gel-like substance in the extracellular space that contains all of the components of the extracellular matrix except for fibrous materials
 - ▶ Made mostly of water
 - ▶ Active in the development, movement, and proliferation of tissues and tissue metabolism
- 

3. Extracellular Matrix (ECM)

- This is what makes connective tissue different from any other tissue. **Variations** in the composition of ECM determine the properties of the connective tissue.
 - Ex. A calcified matrix can form bone or teeth.
- Three classes of biomolecules:
 - Structural proteins– collagen, elastin
 - Specialized proteins – fibronectin, laminins, integrins
 - Glycosaminoglycans (GAGs) – link together to form proteoglycans

Importance of Extracellular Matrix

- ▶ The ECM soaks up water, like a sponge due to the properties of the GAG: **aggrecan**, producing the high water content (75%).
- ▶ The **collagen** fibers form a network which has a very high tensile strength, and which entraps the aggrecan molecules.
- ▶ When you stand up or walk, the weight of your body is supported by the **cartilaginous ends of the long bones**. In this state your weight compresses the cartilage, literally squeezing the water out, until the force produced by the osmotic swelling is equal to the compressive force generated by your weight.

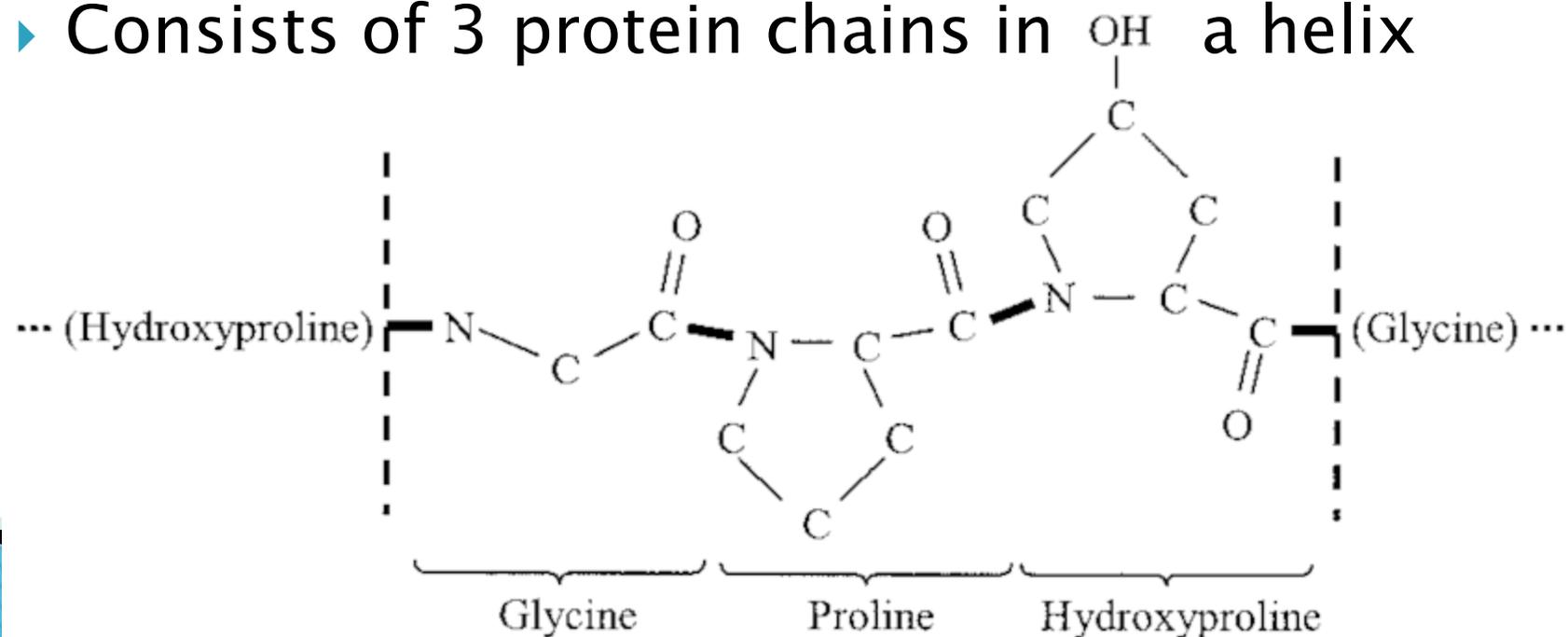
Structural Proteins of ECM

- ▶ Collagen and Elastin
- ▶ Good at resisting tensile forces
- ▶ They vary in diameter and pattern
 - Ex. Tendon fibers run parallel to resist forces in the direction in which muscle produces force
 - Bone fibers are arranged in alternating parallel layers



Collagen

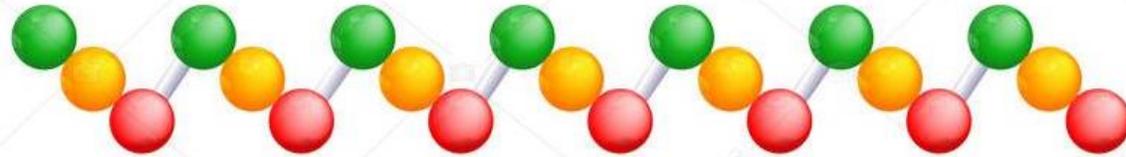
- ▶ Collagen is the most common fibrous protein in the ECM
- ▶ It's the most abundant protein in mammals
 - ▶ 25% of total protein mass
- ▶ Composed primarily of Glycine and Proline and contains sugar groups
- ▶ Consists of 3 protein chains in a helix



COLLAGEN

1. Primary structure

Amino acid sequence



2. 3 polypeptides coil to form Tropocollagen

Collagen molecule



3. Tropocollagens bind together to form a fibril

Collagen fiber



4. Many fibrils bind together to form a collagen fiber

Many types of Collagen

| Type | Location | Type | Location |
|------|---|--------|---|
| I | <u>Skin, Bone, Tendon (Non cartilage)</u> | XV | Associated with collagens close to basement membranes |
| II | <u>Cartilage, Vitreous humor</u> | XVI | Many tissues |
| III | Extensible conn. Tissue (skin, lung, vascular system viz. <u>Artery</u>) | XVII | Epithelia, Skin hemidesmosomes |
| IV | <u>Basement membrane</u> | XVIII | Close structural homologue of XV |
| V | <i>Along with Type-I</i> | XIX | Rare, Rhabdomyosarcoma |
| VI | Muscle | XX | Corneal epithelium |
| VII | <u>Dermal epidermal junction</u> | XXI | Many Tissues |
| VIII | Endothelium | XXII | Tissue junctions |
| IX | <i>Along with type II</i> | XXIII | Limited in tissues, mainly transmembrane and shed forms |
| X | Hypertrophic cartilage | XXIV | Developing cornea, Bone |
| XI | <i>Along with type II</i> | XXV | Brain |
| XII | <i>Along with type I</i> | XXVI | Testis, Ovary |
| XIII | NM Junction & Skin | XXVII | Embryonic Cartilage |
| XIV | <i>Along with type I</i> | XXVIII | BM Around Schwann cells |

Most Common Collagen Types

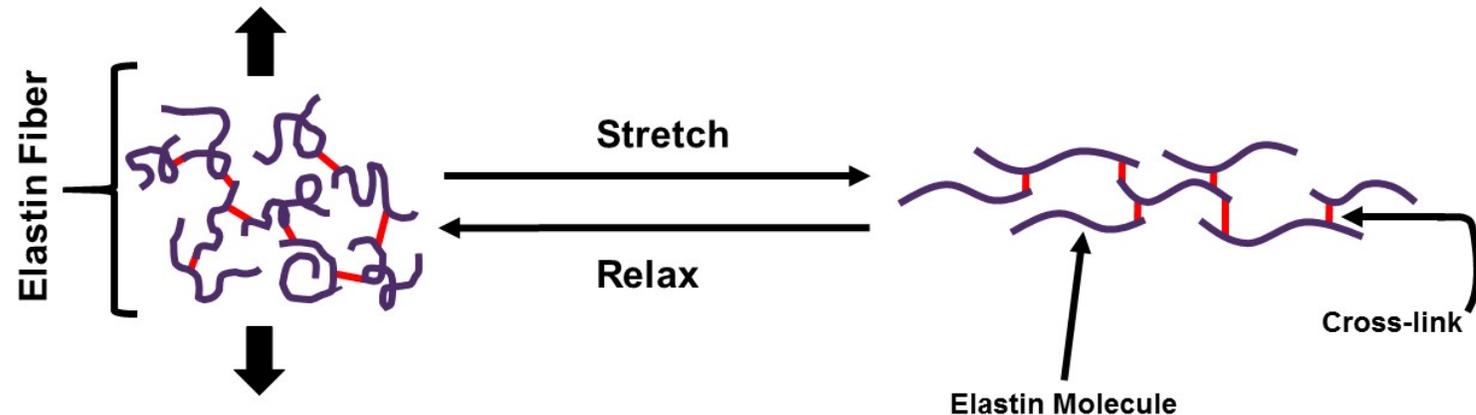
- ▶ Type I – most common – 90% of all collagens
 - Found in bone, hair, skin, nails, tendon, ligaments, cornea
 - Not in cartilage
 - Densely packed fibers wound into triple-helix
 - As it degrades, it becomes most noticeable in skin
 - Notice wrinkles, fine lines, loss of elasticity
- ▶ Type II – found primarily in cartilage
 - Loosely packed fibers wound into triple-helix
 - Provides cushion in cartilage for bones and joints

Most Common Collagen Types

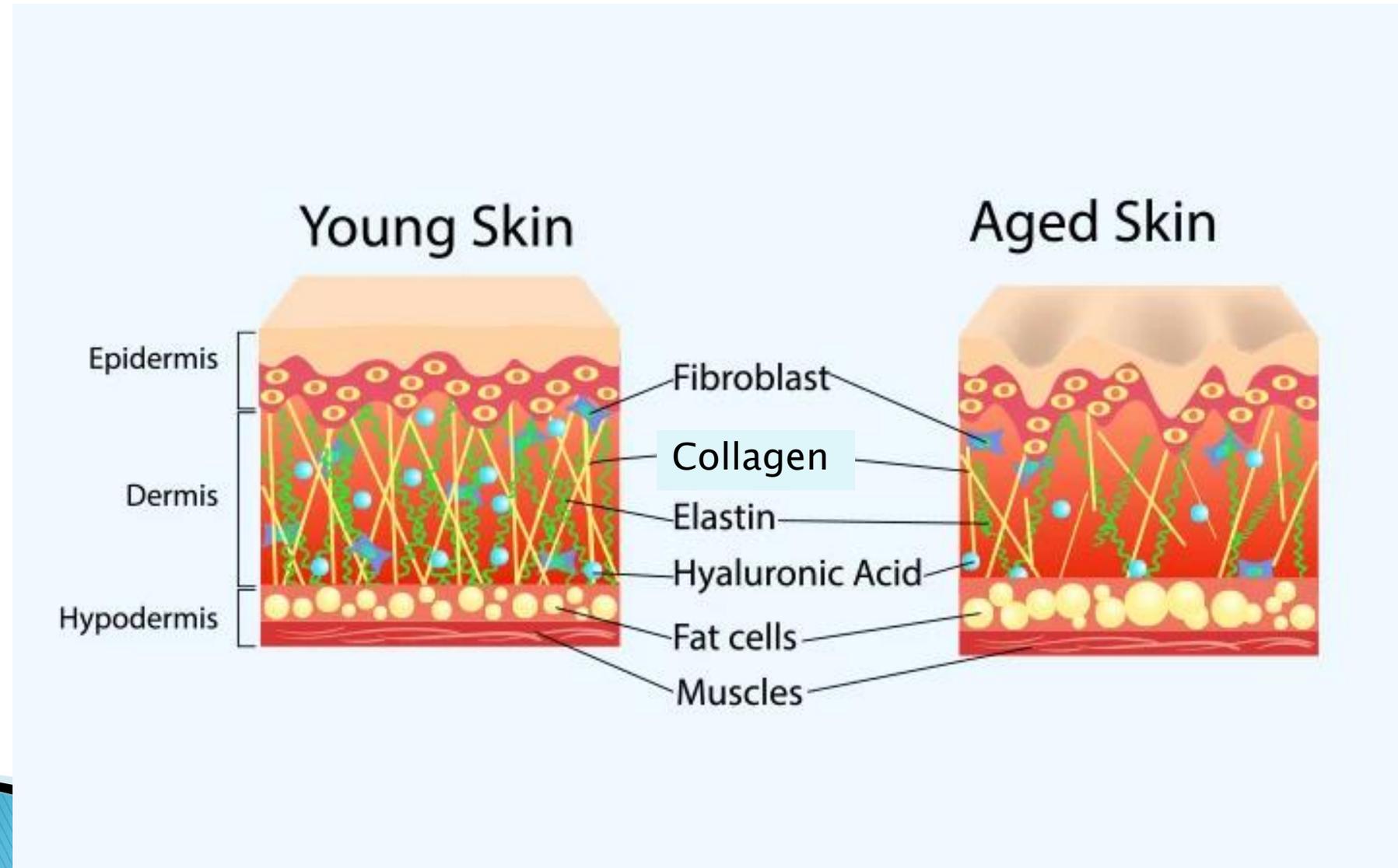
- ▶ Type III – often found alongside Type I
 - Makes up muscles, organs, arteries, and some connective tissue in liver, spleen, blood vessels, and internal organs such as uterus
- ▶ Type IV – does not form triple-helix
 - Creates a web-like pattern
 - Makes up the thick layer outside of cells giving them structure
 - Also found in skin, liver, kidneys, and some organs
- ▶ Type V – helps form cell surfaces and hair
 - Also needed to form cells that create placenta

Elastin

- ▶ Major protein in connective tissue found in elastic structures
- ▶ Gives snap back property to structures when they are stretched
- ▶ Major protein component of blood vessels
- ▶ Half-life of elastin is 70 years
- ▶ Loss of elastin in skin decreases flexibility and reduces wound healing ability



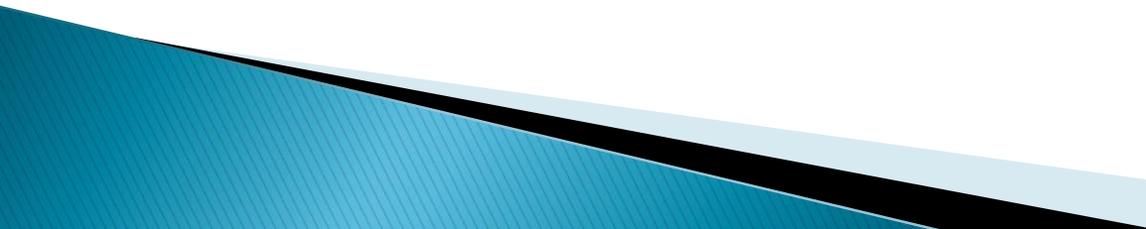
Collagen vs Elastin



Collagen vs Elastin

| COLLAGEN | ELASTIN |
|---|---|
| Main structural protein found in skin and connective tissue | Major structural protein in connective tissue of elastic structures |
| Third most abundant protein in the body | Less abundant than collagen |
| Found in connective tissue, skin, blood vessels, cornea, muscles, bones | Found in blood vessels and skin |
| Gives strength to structures | Makes structures elastic |
| Produced throughout life until aging begins | Mainly produced in fetus, and is no longer produced after puberty |
| Deficiencies: osteogenesis imperfect, chondrodysplasias, Ehlers–Danlos syndrome | Deficiencies: Marfan's syndrome, atherosclerosis, emphysema |

Collagen: Hydrolyzed vs Gelatin vs Peptides

- ▶ Full-length collagens are broken down into collagen peptides in a process known as **collagen hydrolysis**.
 - ▶ **Collagen peptides** are the constituent of hydrolyzed collagen.
 - ▶ **Hydrolyzed collagen** is the final product of the complete hydrolysis of collagen.
 - ▶ Partial hydrolysis of collagen makes **gelatin**.
 - ▶ The main feature of hydrolyzed collagen is its ability to be readily absorbed by the digestive system when compared to regular collagen protein or even gelatin.
- 

Glycosaminoglycans (GAGs)

- ▶ 10% of the extracellular matrix
- ▶ Unbranched, polysaccharide chains
- ▶ One sugar residue is always an amino sugar
- ▶ (ex. N-acetylglucosamine)
- ▶ The other sugar residue is usually glucuronic acid or iduronic acid
- ▶ GAGs are
 - highly negatively charged (attract cations like sodium)
 - Inflexible
 - Strongly hydrophilic

4 main groups of GAGs

1. Hyaluronic acid

- most simple, as it does not contain sulfated sugars
- Longest chain
- Made by an enzyme complex at the cell surface

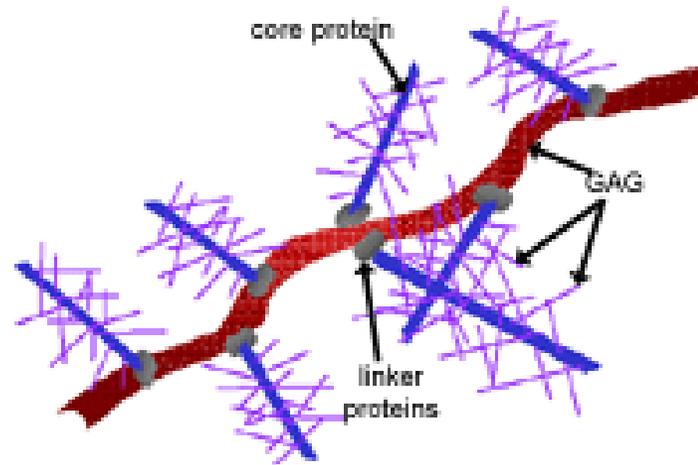
2. Chondroitin sulfate

3. Heparin sulfate

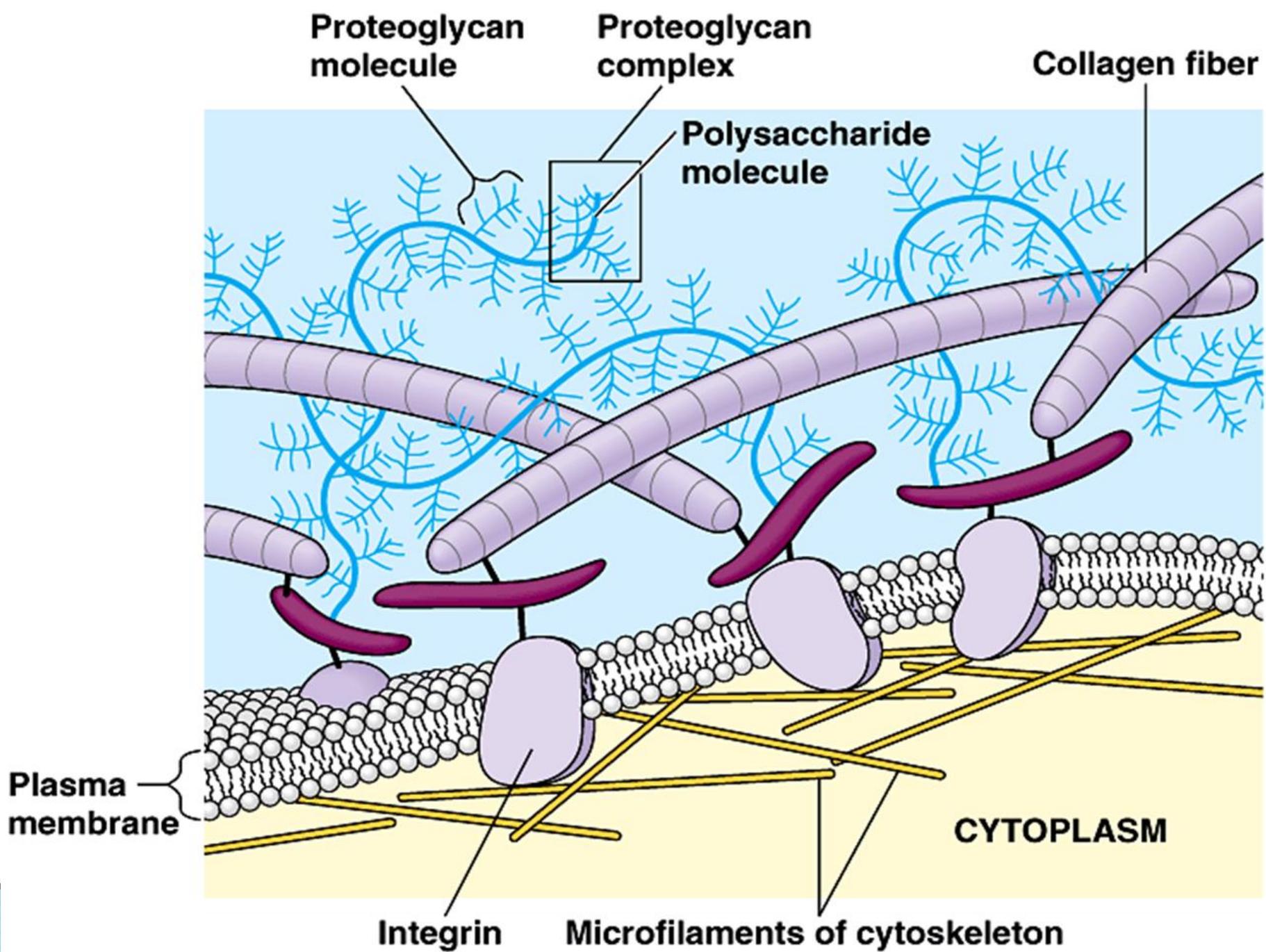
4. Keratin sulfate

- Sulfated
- Complex
- Small
- Secreted by the cell
- Always found attached to a protein forming a **proteoglycan**

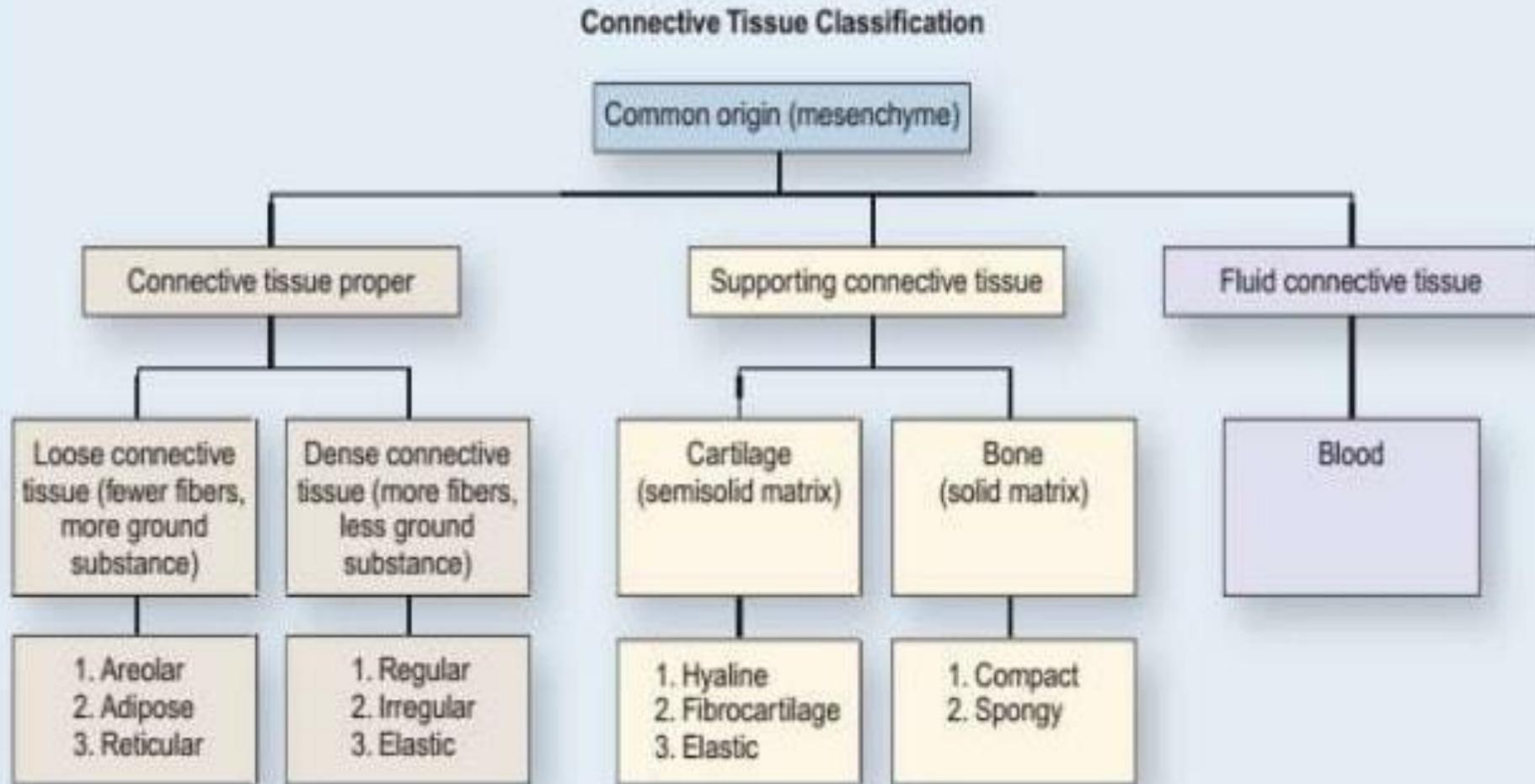
Proteoglycans



- ▶ They are Glycosaminoglycans that are attached to a 'core' protein
- ▶ All GAGs except hyaluronic acid attach to a protein in this way
- ▶ They form pores of different sizes to regulate the sizes of molecules that move through the matrix
- ▶ One important proteoglycan is aggrecan, which is a major component of cartilage



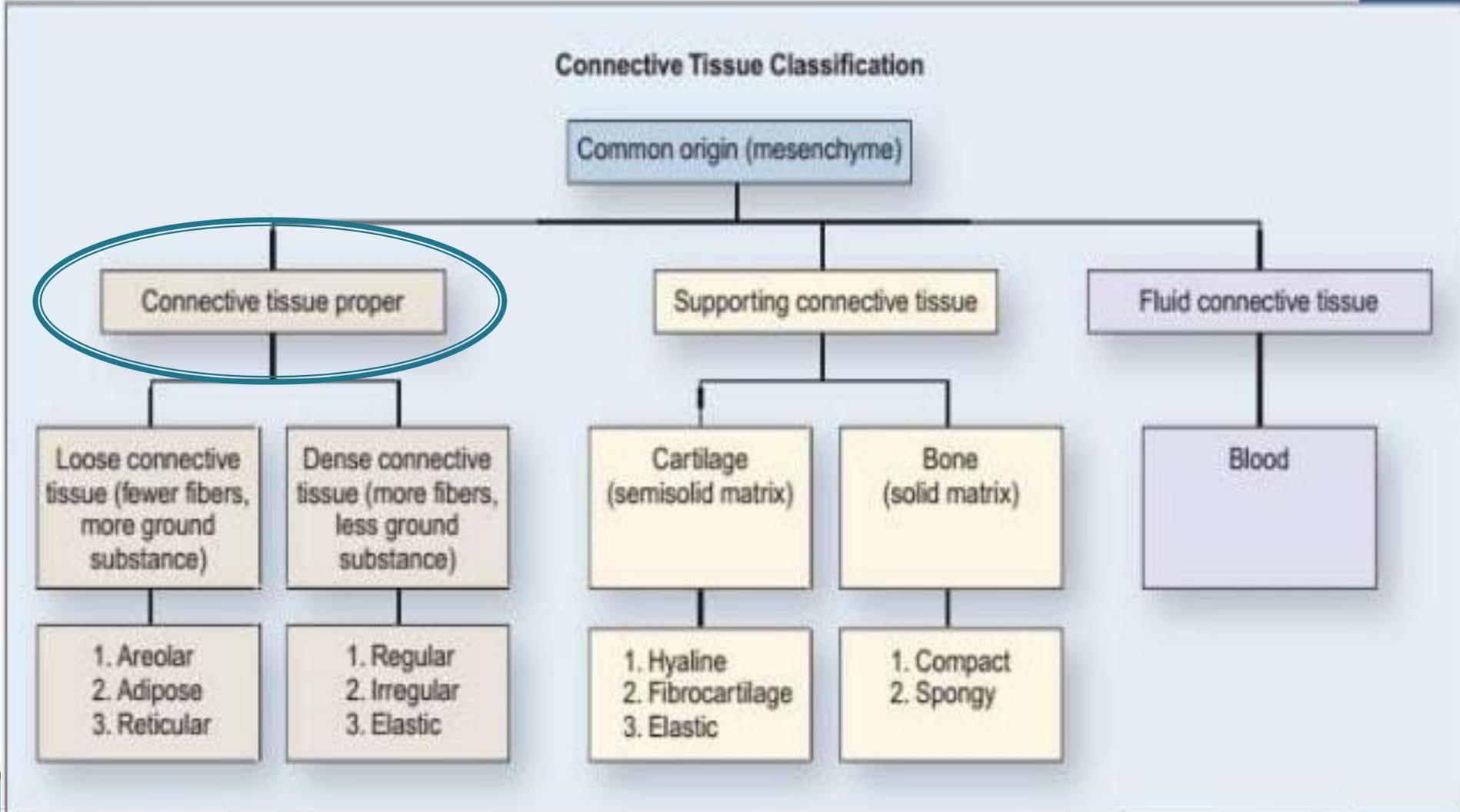
Classification of connective tissue

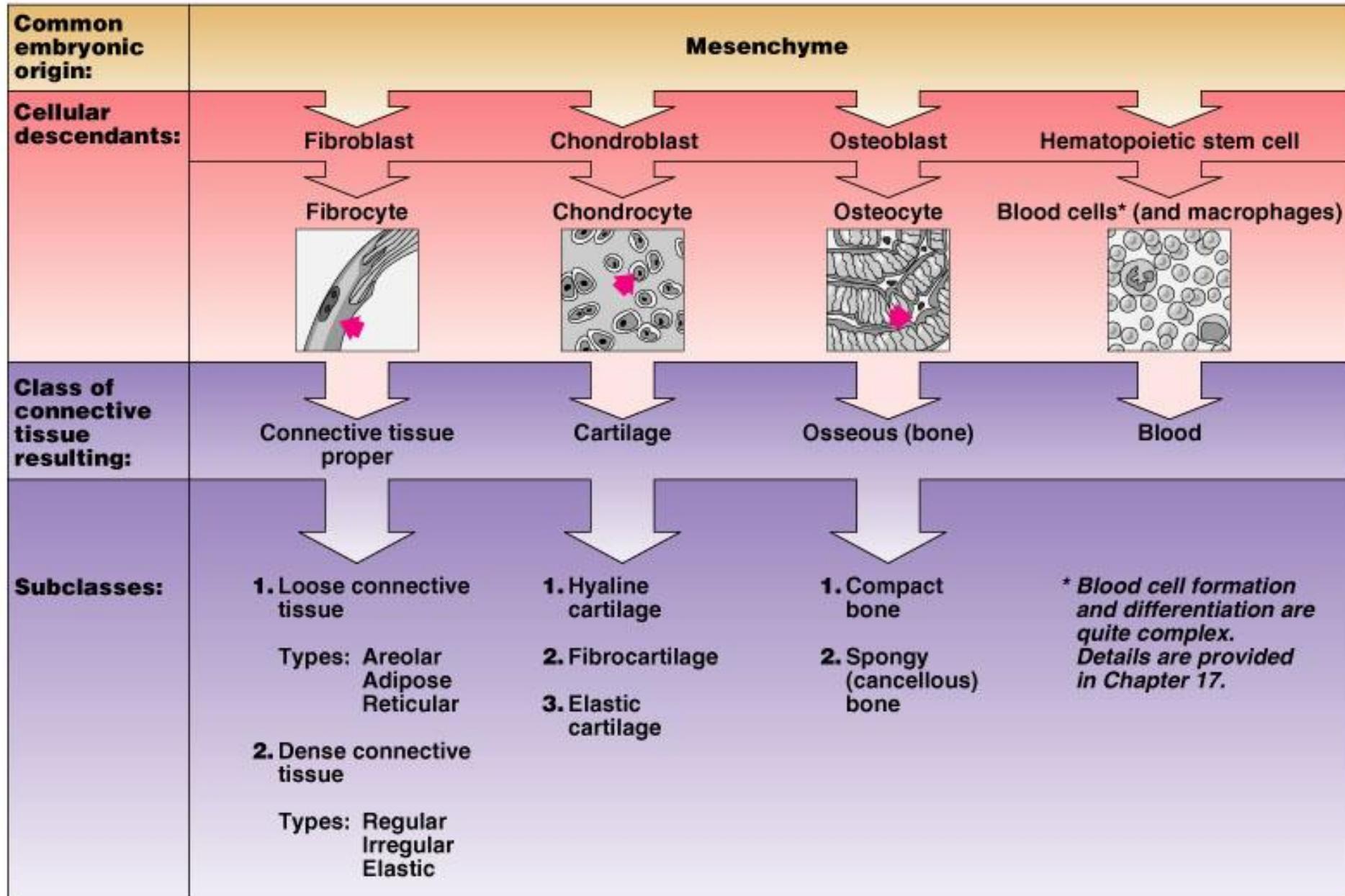


Volume of Finished Cartilage

- ▶ 10–20% – Collagen Fibers
 - ▶ 65–80% – Water
 - ▶ 10–25% – Proteoglycan–hyaluronic acid aggregates
- 

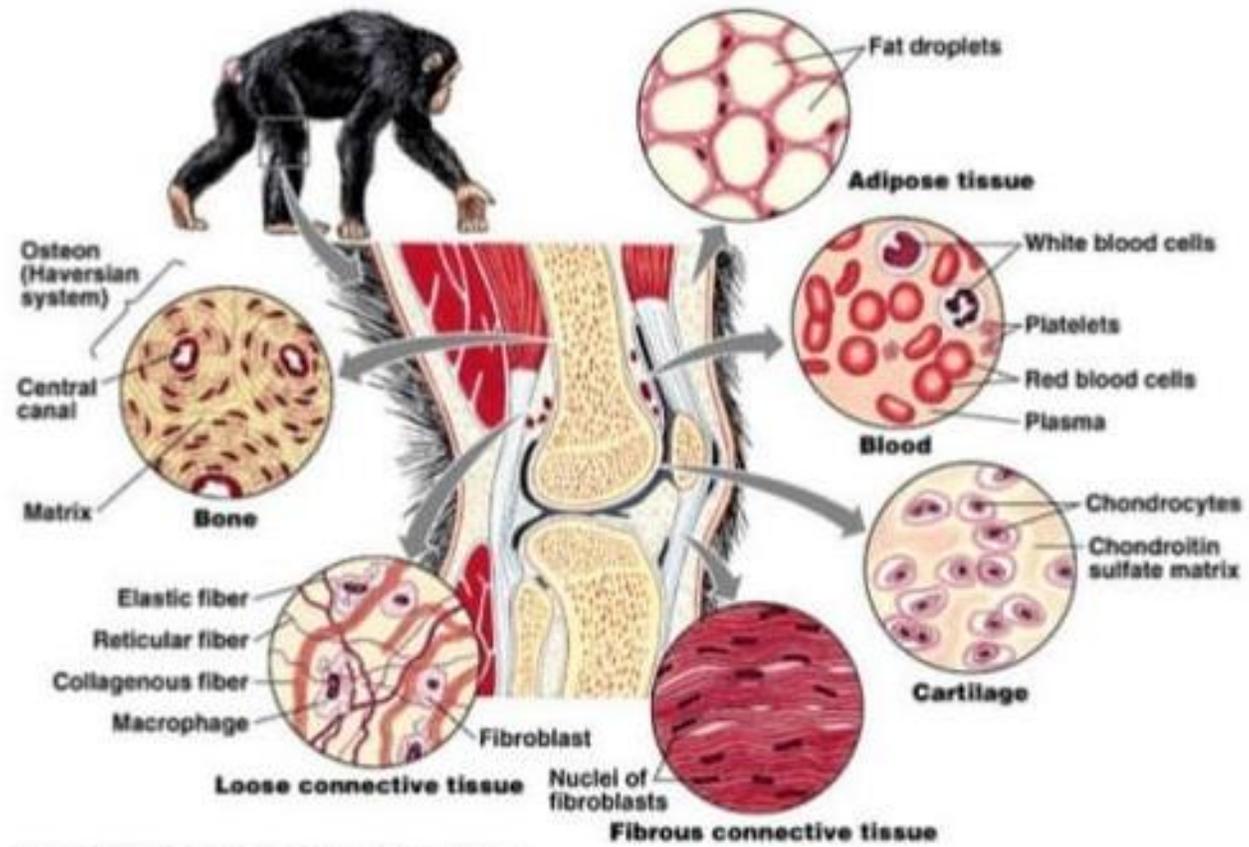
Classification of connective tissue





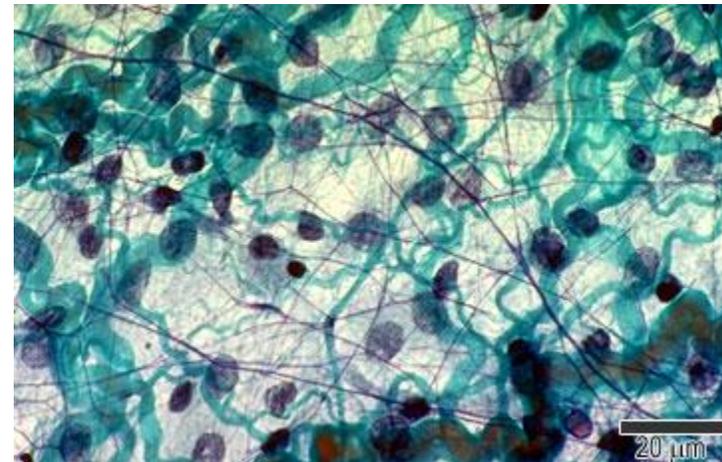
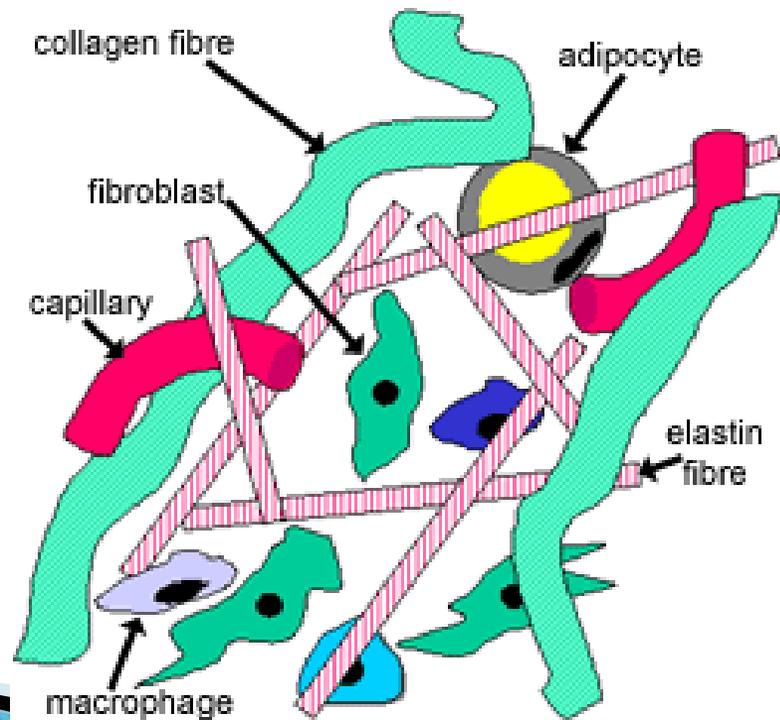
Types of Connective Tissue

1. Loose Connective Tissue
2. Dense Connective Tissue
3. Cartilage
4. Blood (lymph)
5. Bone



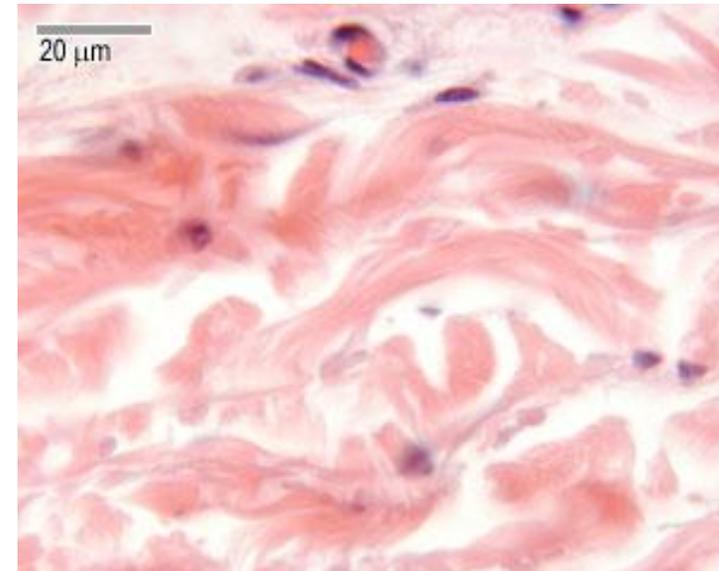
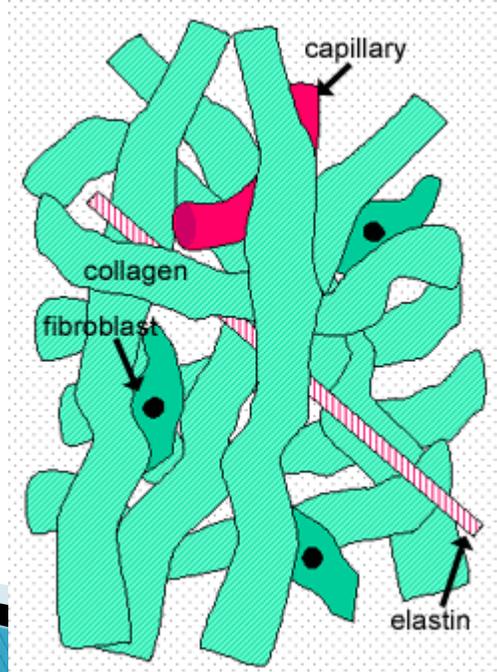
Connective Tissue Proper

- ▶ Loose connective tissue
 - Contains many cells, a loose arrangement of fibers, and moderately viscous fluid matrix

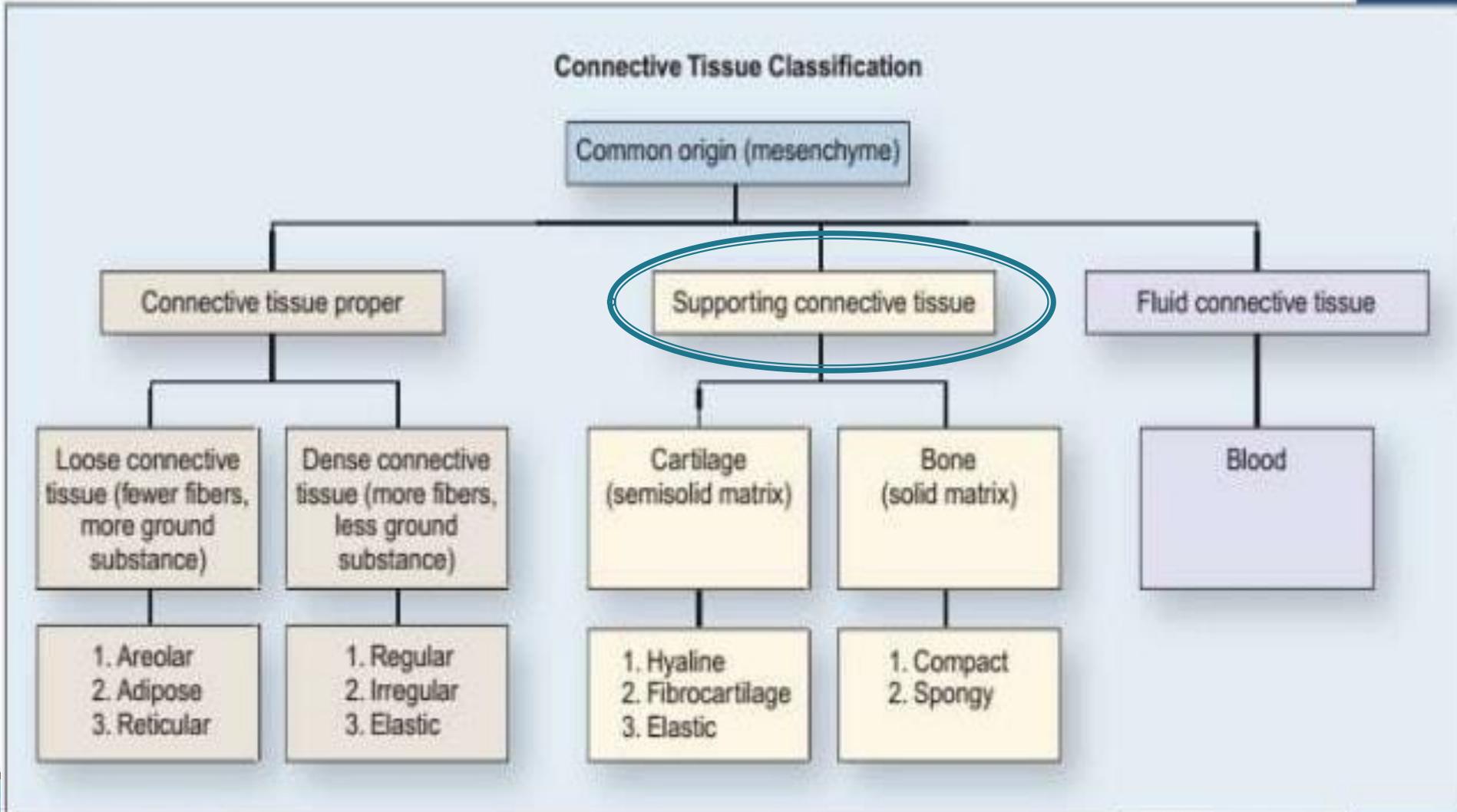


Connective Tissue Proper

- ▶ Dense Irregular Connective Tissue
 - Contains a dense woven network of collagenous fibers (and some elastic) in a viscous matrix.
 - Found in joint capsules and muscle fascia
 - Forms the dermis of skin
 - Impact resistant



Classification of connective tissue

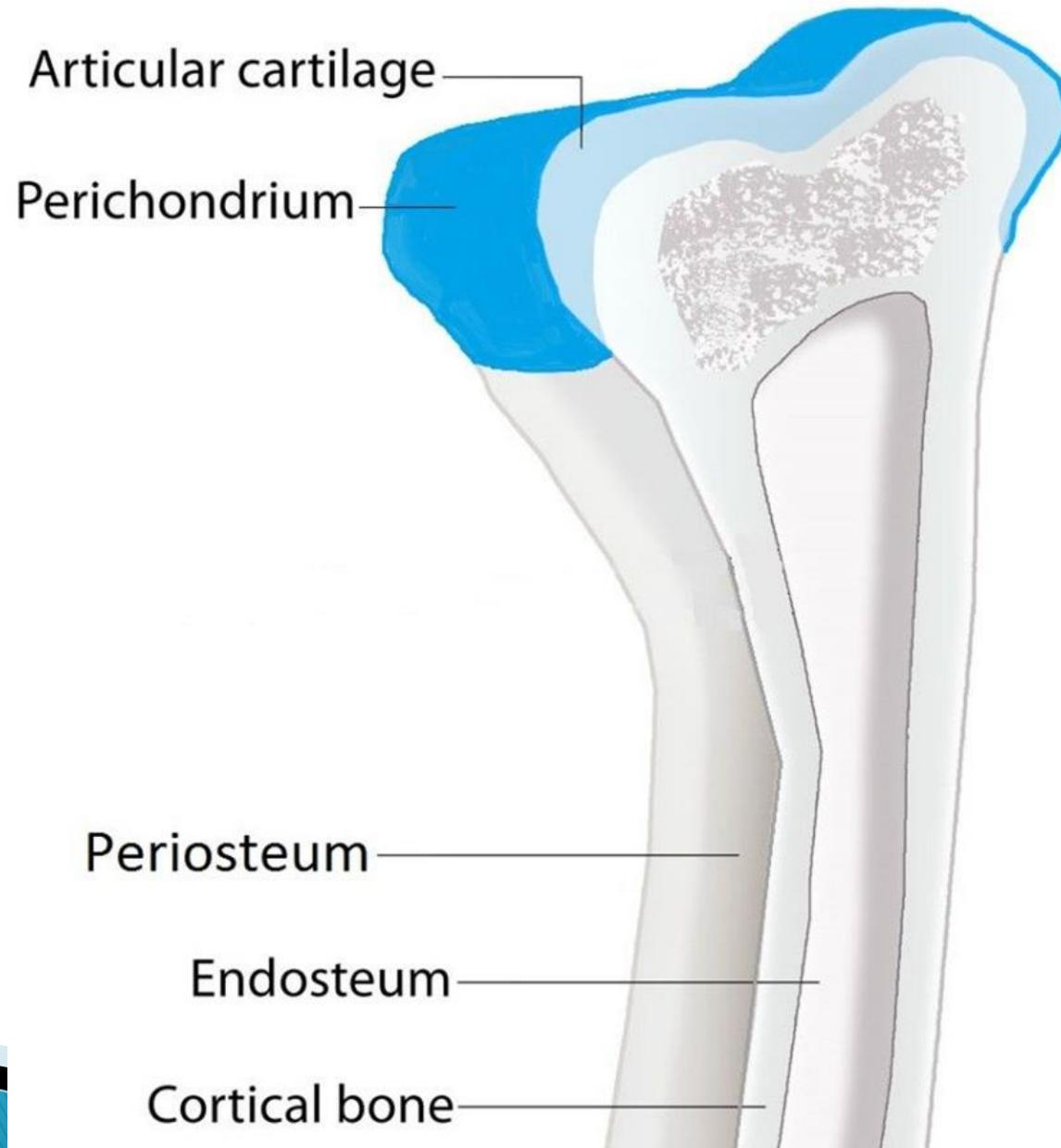


Supporting Connective Tissue

1. Cartilage

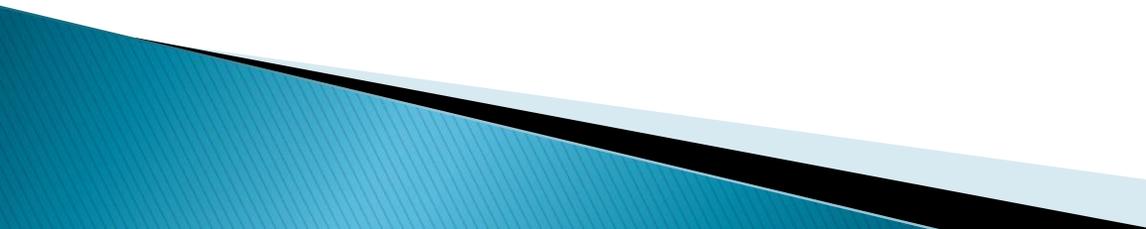
- Consists of dense collagen fibers and elastic fibers within the ground substance
- Surface of most cartilage is contained within a membrane called the **perichondrium**
- Unlike other CT, cartilage contains no blood vessels except in the perichondrium from which it receives its nutrients

THE PERICHONDRIUM

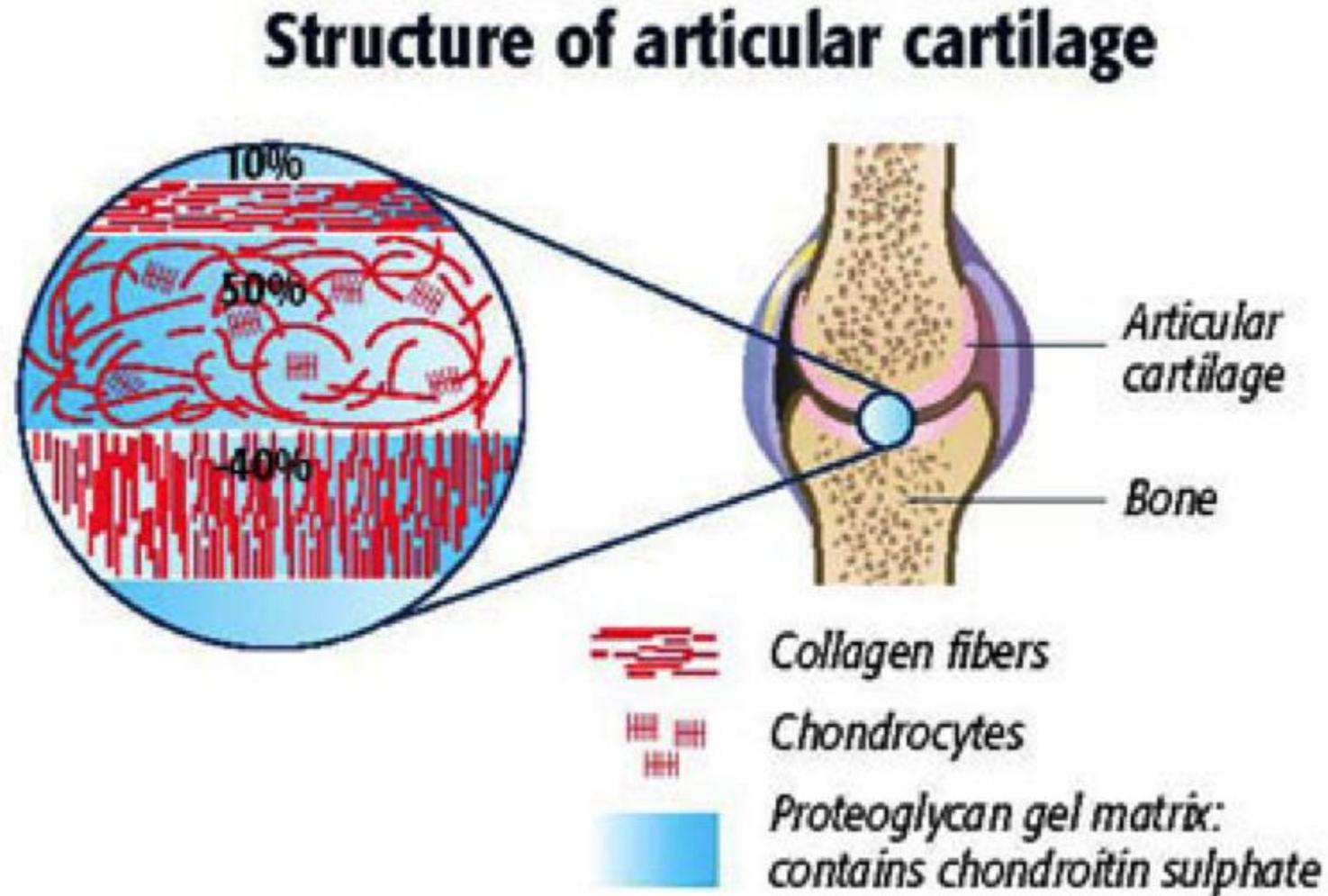


3 Types of Cartilage

1. **Hyaline – Most abundant cartilage**
 - Found in trachea, costal cartilages, larynx, nose
 - Covers surfaces of bones at the joints, especially where damage may lead to arthritis
 - Provides flexibility, support, and a smooth, low friction surface for bones moving within joints
2. **Fibrocartilage – Strongest of the 3 types**
 - Found in menisci, discs, pubis symphysis, tendons
 - Provides support and rigidity and attaches to surrounding structures. It is tough with strong fibers.
3. **Elastic cartilage**
 - Provides support and helps maintain shape

- ▶ Cartilage has limited repair capabilities, because of poor vascularization and due to the fact that chondrocytes do not travel to the repair site. Rather, cartilage repair is dependent on diffusion of nutrients and matrix repair materials, which requires motion.
 - ▶ Damaged hyaline cartilage is usually replaced by fibrocartilage, a type of scar tissue, rather than the original hyaline cartilage.
- 

- ▶ Chondrocytes are the cells that make up cartilage, and their matrix contains chondroitin sulfate.



Cartilage Nutrients

▶ Chondroitin Sulfate (Purified)

- Use with disc and ligament injury, mitral valve prolapse, cartilage problems, free radical problems, to increase the total white blood count, and in any tissue where a lack of elasticity is a known problem (vessel, artery, heart valves, etc.).
- Biotics purified CS is predigested and readily absorbed over 90% vs 5% with other commercial, non-purified forms.

- **Purified Chondroitin Sulfates**
- **Chondro-Plus (no Glucosamine)**
- **ChondroSamine Plus (Glucosamine HCl)**
- **ChondroSamine-S (Glucosamine Sulfate)**
- **Osteo-B II**
- **Osteo-B Plus**

Cartilage Nutrients

- ▶ Glucosamine Sulfate or HCl
 - Stimulates chondrocytes to generate ground substance, chondroitin. Use together with purified chondroitin sulfates for added cartilage healing.
 - CondroSamine–Plus (Glucosamine HCl)
 - ChondroSamine–S (Glucosamine sulfate)

Products should be considered for osteo and rheumatoid arthritis, joint inflammation, cartilage repair and any other condition where increased sulfur intake is needed. Contains components extracted from shrimp and crab shells and should not be used by patients who are allergic to these foods.

Cartilage Nutrients

- ▶ **CHONDRO PLUS** – Source of manganese, purified chondroitin sulfates and vitamin B-12 (synergist to manganese). Excellent for ligament, disc and cartilage support, athletic injuries, long-term preventive support for athletes or people engaged in strenuous activity.
- ▶ In acute situations and with disc lesions add **Intenzyme Forte** and **Carbamide Plus** (addresses inflammation and helps to disperse edematous fluid normally present with disc injury).

Cartilage Nutrients

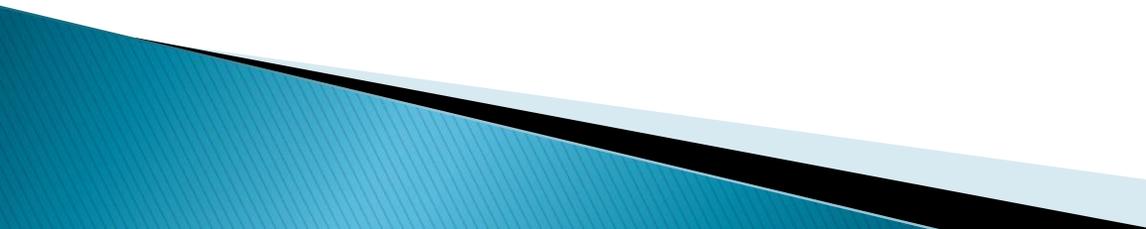
- ▶ **CARBAMIDE PLUS** -Carbamide Plus is a combination of Carbamide (USP urea) along with herbal diuretics and enzymatically processed organic beet, tillandsia (Silver Spanish Moss), rice bran along with vitamins, minerals, amino acids, molasses, SOD and catalase.
- ▶ Carbamide reduces the electrical conductivity of water and will denature proteins.
- ▶ This causes the release of free calcium phosphate into the blood which reacts with sodium bicarbonate to provide calcium bicarbonate an important blood buffer.

Cartilage Nutrients

- ▶ Proteins – proteins with AA needed for cartilage repair
 - Amino Sport
 - Whey Protein Isolate
 - Hydrolyzed Collagen Protein
 - Optimal Collagen

- ▶ Sulfur – MSM, Garlic Plus
 - If MSM or other sulfur containing products causes stomach distress, this is generally an indication of hypochlorhydria.
 - Always use Mo-Zyme with MSM; molybdenum activates MSM in the system.

Cartilage Nutrients

- ▶ EFAs
 - ▶ Vitamin C – promotes cartilage and connective tissue regeneration
 - ▶ Copper – needed for repair
 - ▶ Manganese –
 - part of various enzymes involved in cartilage and bone production
 - Plays an essential role in incorporating calcium into growing bones
 - Effectively reduces the loss of bone mass
- 

Cartilage Nutrients

- ▶ Manganese cont.
- ▶ Too much Mn can be toxic.
- ▶ If dosing high amounts of chondroitin sulfates, use Purified Chondroitin Sulfates, which does not contain Mn.
- ▶ Mn toxicity symptoms:
 - Loss of appetite, elevated BP, liver damage, neurological symptoms like memory loss, hyperirritability, hallucinations, blurred speech, involuntary laughing, hand tremors

Cartilage Nutrients cont.

▶ Additional considerations

- Gammanol Forte with FRAC – increases IGF
 - Useful for older clients when healing is impaired due to growth hormone or sex hormone deficiency.
 - With aging anabolic hormone levels decrease, which can result in painful, arthritic joints and slow healing time.
 - Consider glandular support also:
 - Women – Cytozyme-F or Cytozyme-O
 - Men – Cytozyme-M or Cytozyme-Orchic
 - Trachea glandular – as effective as shark cartilage at significantly lower levels

Cartilage and Motion

- ▶ It's important to maintain motion in affected joints
 - Manual therapy
 - Stretching
 - Strength exercises
 - Physical therapy
 - Yoga
 - swimming

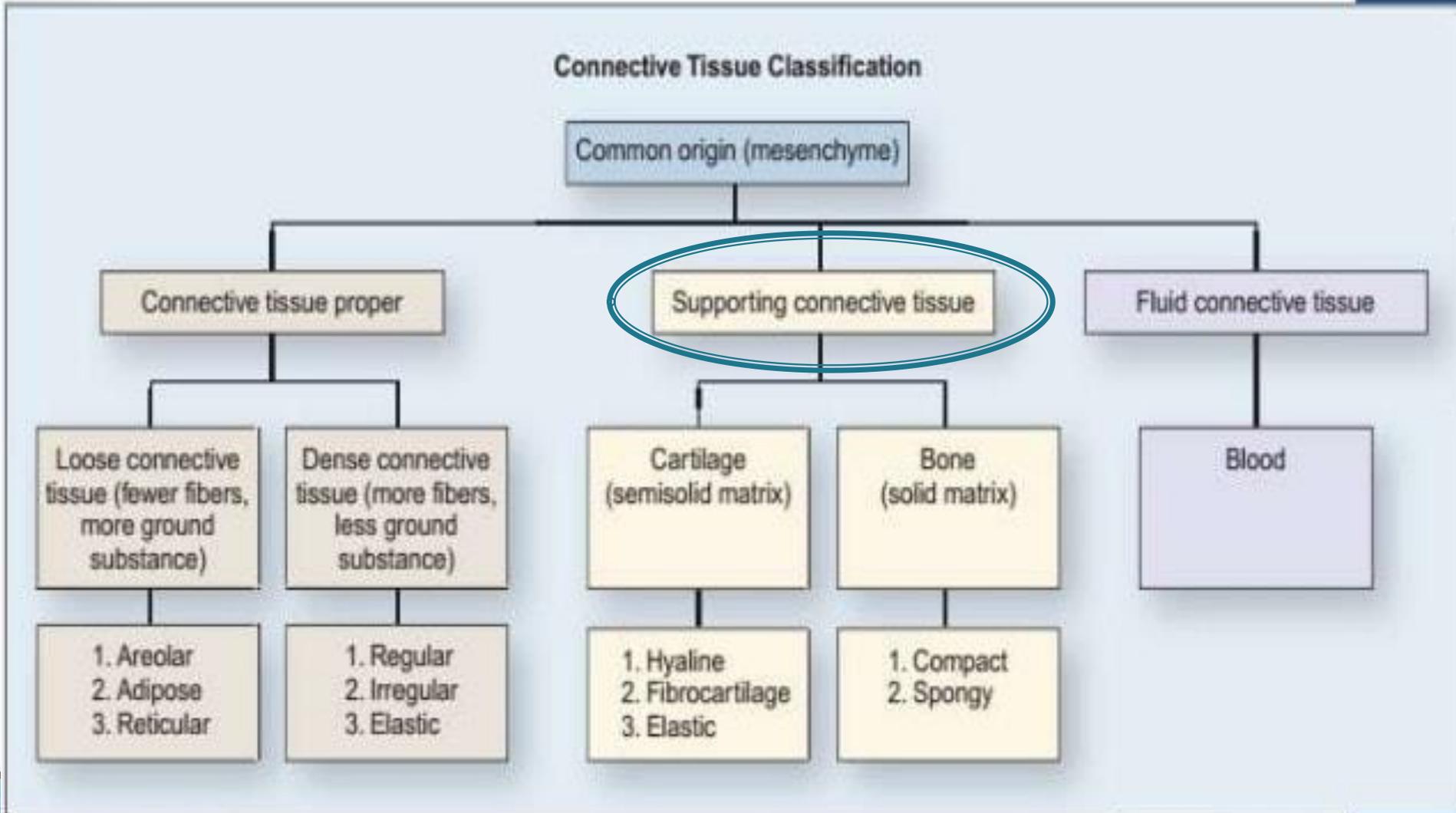
Cartilage and NSAIDs

- ▶ NSAIDs reduce pain and inflammation, but they inhibit cartilage repair and promote arthritic degeneration.
- ▶ NSAIDs are eliminated from the body via Phase II detox pathways that require sulfur.
- ▶ Continuous use of NSAIDs depletes sulfur stores, and sulfur is necessary for cartilage repair.
 - If taking NSAIDs, supplement with Sulfur!

Cartilage and Toxicity

- ▶ Toxins not eliminated from the body will be stored typically in
 - adipose tissue
 - in cellular tissue as lipofuscin (an end product of lipid and lipoprotein oxidation)
 - in connective tissue.
- ▶ When toxins are stored in CT, it loses structural integrity and functionality.

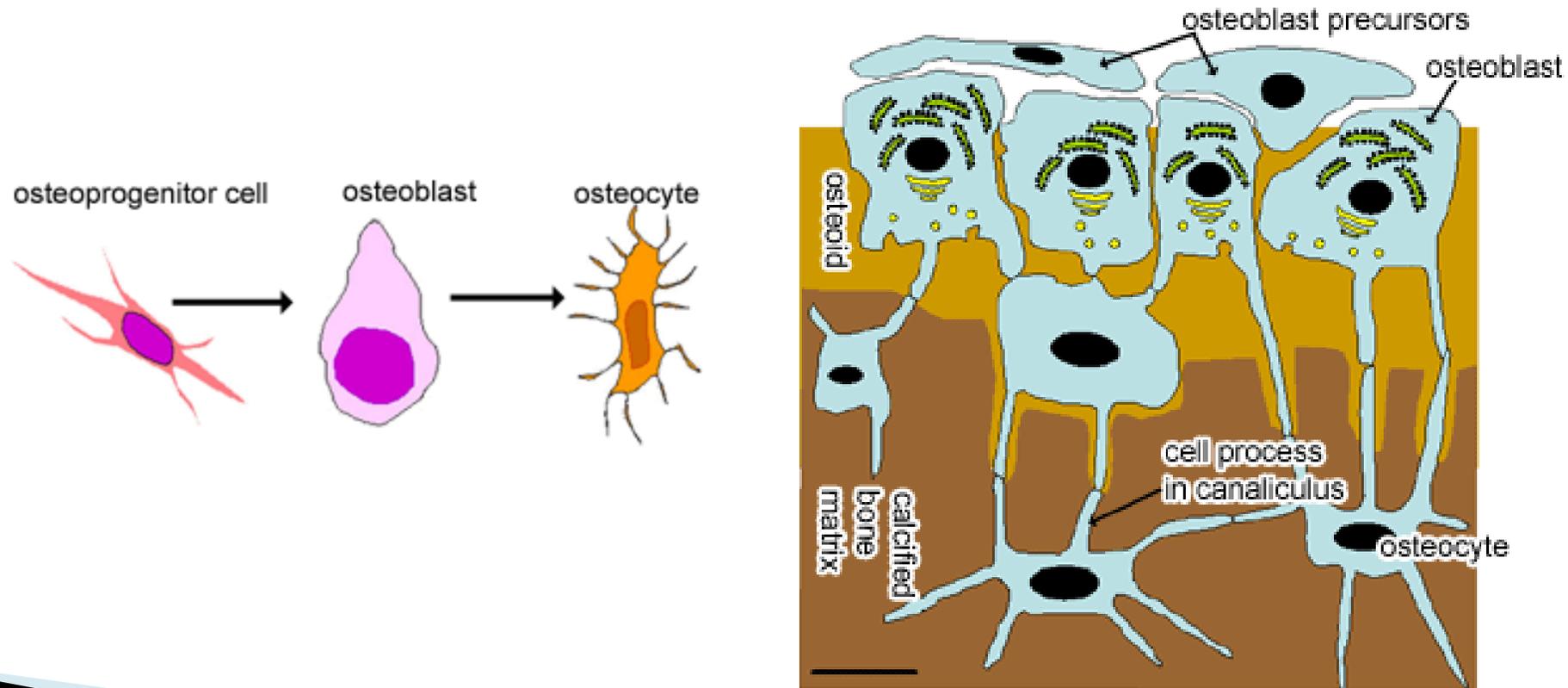
Classification of connective tissue



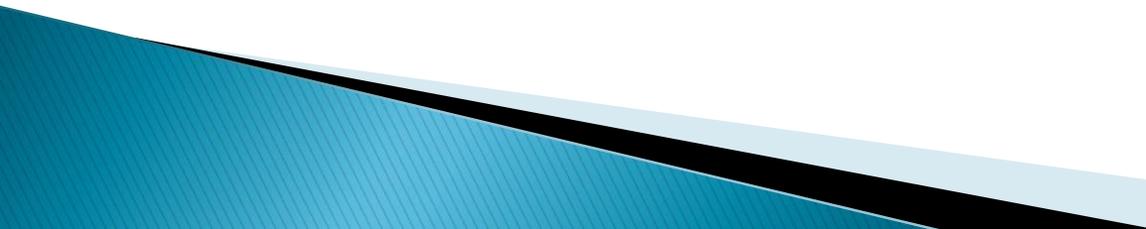
Supporting Connective Tissue

2. Bone

- Made of Cells and Extracellular Matrix

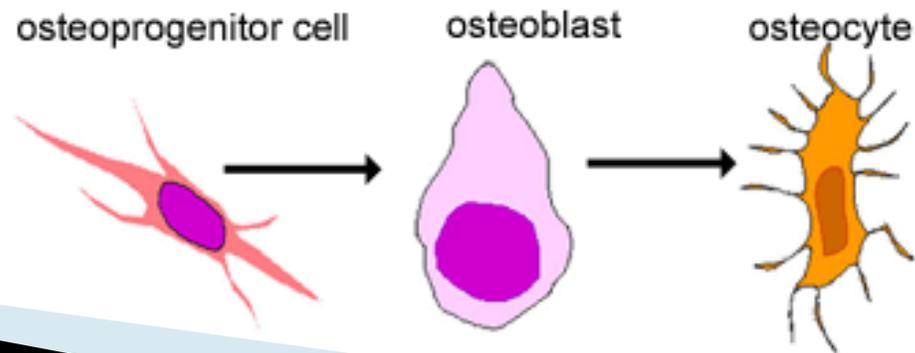


Bone function

- ▶ **Support** – bones make up a structural framework for the body, and provide attachment sites for muscles.
 - ▶ **Protection** – protection of internal organs – i.e. brain, heart and lungs,
 - ▶ **Assisting movement.**
 - ▶ **Mineral homeostasis** – the bone is a store for calcium and phosphorus
 - ▶ **Blood cell production** – takes place in the bone marrow.
- 

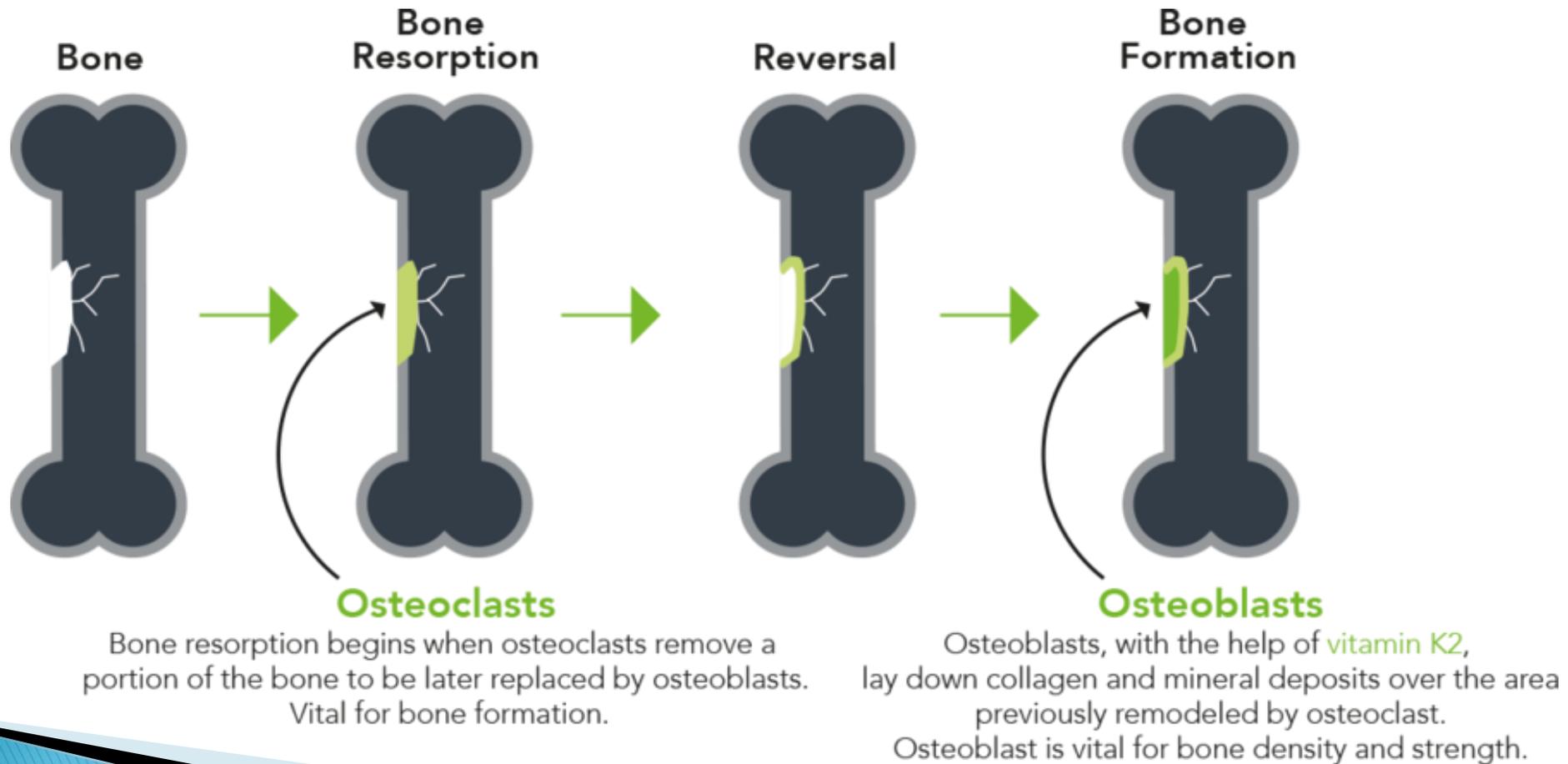
Types of Cells Found in Bone

- ▶ **Osteoprogenitor cells** are the 'stem' cells of bone, and are the source of new **osteoblasts**.
- ▶ **Osteoblasts**, lining the surface of bone, secrete collagen and the organic matrix of bone (osteoid), which becomes calcified soon after it has been deposited. As they become trapped in the organic matrix, they become **osteocytes**.
- ▶ **Osteocytes** maintain bone tissue. Fine processes from these cells ramify through bone, and form gap junctions with other osteocytes



Osteoblasts build and rebuild (think anabolic) that matrix and produce new bone material

Osteoclasts break down (think catabolic) and recycle bone tissue and the mineral matrix



Growth/Nourishment of Bone

- ▶ **Unlike cartilage**, bone has a very good blood supply. Bone is riddled with blood capillaries. The central cavity contains blood vessels and is a storage for bone marrow. All of the osteocytes in bone are within 0.2mm of a capillary. The tissue fluid from the capillary reaches the osteocytes through canaliculi.
- ▶ There are two ways in which bone can grow:
 1. **Endochondral** – formation of bone onto a temporary cartilage model or scaffold.
 2. **Intramembranous** – formation of bone directly onto fibrous connective tissue. There is no intermediate cartilage stage. This type of ossification occurs in a few specialized places such as the flat bones of skull (i.e. parietal bone), mandible, maxilla and clavicles.

- ▶ Bone is living DYNAMIC tissue continuously repairing and replacing itself with functional tissue!

- ▶ Bone remodels to stress and will change shape and density in response to the stress placed upon it, (known as Wolff's law.)
 - ▶ Healthy bone tissue requires some stressors so that it can regenerate itself.
 - ▶ Complete rest will result in body wasting – a loss of lean body mass and bone density
 - ▶ Brisk walking and other weight bearing activities are needed to build and maintain bone density
- 

Bone Maintenance

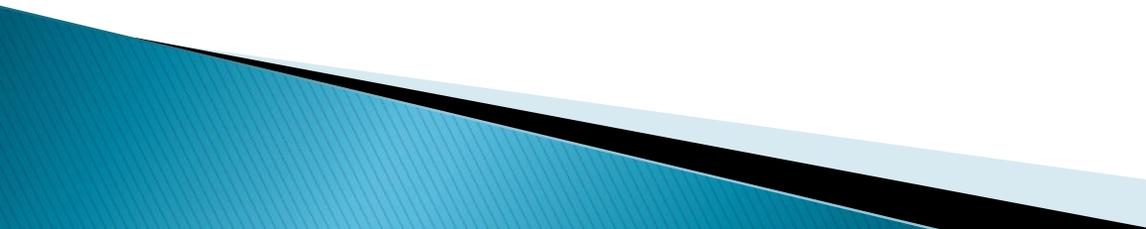
- ▶ Weight-bearing exercise
 - ▶ Strength training
 - ▶ Healthy diet
 - ▶ Sunlight, Vitamin D
 - ▶ Healthy fatty acids
 - ▶ Green leafy vegetables
 - ▶ Vitamin K
- 

- ▶ If OsteoClastic activity is increased over OsteoBlastic activity bone loss occurs..
- ▶ This can be easily measured with a is a simple urine test

First Tier Testing

- ▶ N-Telopeptide ...Urine test to assess and measure osteoclastic activity
- ▶ (Professional Co-op Services ~ 866-999-4041 ~ Cost \$49.00)

- ▶ Repeat the N-telopeptide to make sure dietary and supplement changes are affecting bone status every 30–45 days.
- ▶ The following tests are also valuable and supplementation should be added to the basic protocol based on what is found
- ▶ **Blood Chemistry Panel – Look for Inflammation** by testing:
 - ▶ Homocysteine
 - ▶ CRP
 - ▶ Fibrinogen
 - ▶ Sedimentation Rate

- ▶ Mineral Levels. Check:
 - ▶ RBC magnesium,
 - ▶ Zinc
 - Low alkaline phosphorous test below the midline of the laboratory range possible zinc need
 - Zinc taste test
 - ▶ Calcium /Phosphorous ratio should be 2.5 / 1
 - ▶ 25 (OH) Vitamin D...goal is 50–100 ng /ml
 - ▶ Kidney Function by looking at Creatinine
- 

▶ **Second Tier Testing**

- ▶ if the above protocols and testing are not affecting the Osteoclastic function consider the following tests and observations
- ▶ Check Adrenal Function using blood saliva or urine, Balance DHEA levels.
- ▶ **Stress will increase cortisol** whether it is emotional, chemical or physical = ↑ HPA axis = ↑ bone loss
- ▶ ANY glucocorticoid therapy will affect bone loss, even creams. Isocort and Cortef are forms of cortisol and can cause bone loss even on low dose

- ▶ **Second Tier testing continued:**
 - ▶ Hormone Panels:
 - ▶ Cortisol
 - ▶ DHEA
 - ▶ Testosterone
 - ▶ Estrogen
 - ▶ Progesterone
 - ▶ Parathyroid Hormone – PT
- 

Bone Support

- ▶ Osteo-B II – bone formula without Cu
- ▶ Osteo-B Plus – contains Cu
- ▶ Optimal EFAs Caps – support healing and reduces inflammation
- ▶ Additional:
 - Vitamin D, Ca, Mg, Vitamin K, Trachea glandular

Bone Fracture Healing

- ▶ Intenzyme Forte – reduces swelling, inflammation; removes cell debris
- ▶ Osteo B II or Osteo B Plus
- ▶ Vitamins D and K
- ▶ Also Ca and Mg, if needed

- ▶ Bone Pain and Inflammation
 - Optimal EFAs Caps, Vit D, Bio-Allay, KappArest,
 - Intenzyme Forte