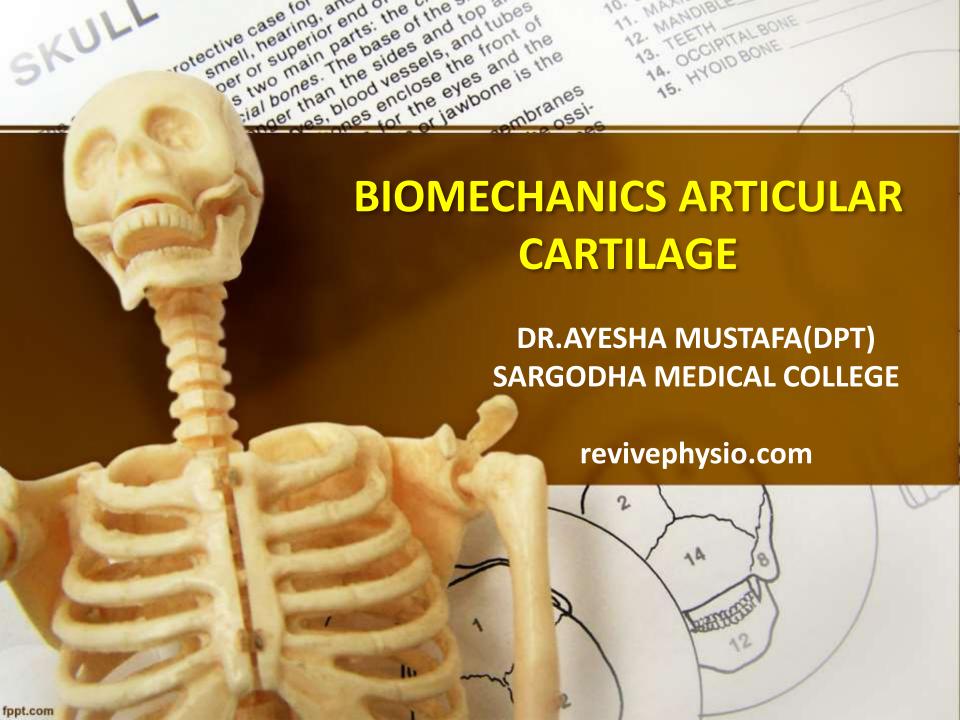


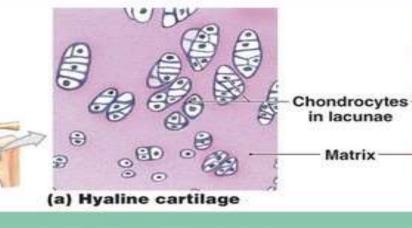
رسول الشصلي الشدعليه وسلم في ارشاد فرمايا: جس کا وضوئیں اس کی نماز نبیں ، اور جو محض وضو کے شروع میں اللہ کا نام نہ لے (بسم الله نه يراه)، اس كاوضوفيين_ (سنن ابوداؤد،جلد ا، ،حدیث 101)



HYALINE CARTILAGE

LOCATIONS: Between tips of ribs and bones of sternum; covering bone surfaces at synovial joints; supporting larvnx (voice box), trachea, and bronchi; forming part of nasal septum

FUNCTIONS: Provides stiff but somewhat flexible support; reduces friction between bony surfaces

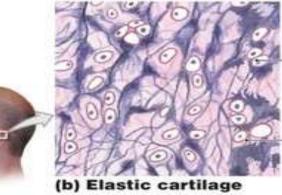




ELASTIC CARTILAGE

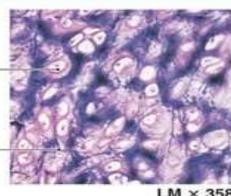
LOCATIONS: Auricle of external ear; epiglottis; auditory tube; cuneiform cartilages of larynx

FUNCTIONS: Provides support, but tolerates distortion without damage and returns to original shape



Chondrocyte in lacuna Elastic fibers in matrix

Matrix-

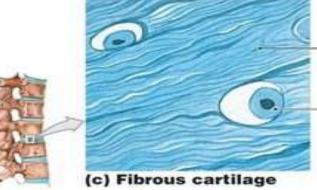


LM × 358

FIBROUS CARTILAGE

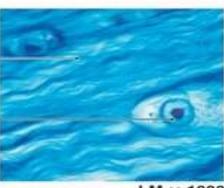
LOCATIONS: Pads within knee joint; between pubic bones of pelvis: intervertebral discs

FUNCTIONS: Resists compression; prevents bone-to-bone contact; limits relative movement



fibers in matrix Chondrocyte in lacuna

Collagen



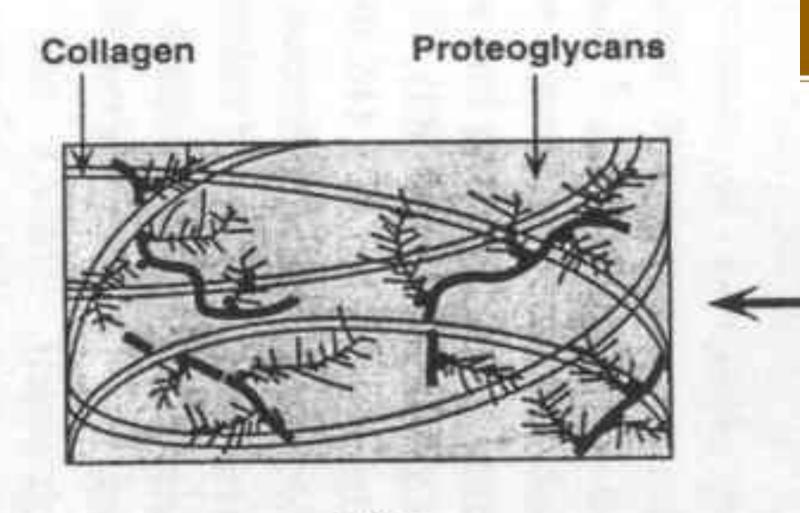
LM × 1000

Functions of articular cartilage

- Diarthrodial joint- Fibrous capsule- Inside lined with synovium which secretes synovial fluid.
- 1:;Distributes joint load over wide area reduction of stresses on contacting surfaces.
- 2::Allow movement of opposing joint surfaces with minimal friction and wear.

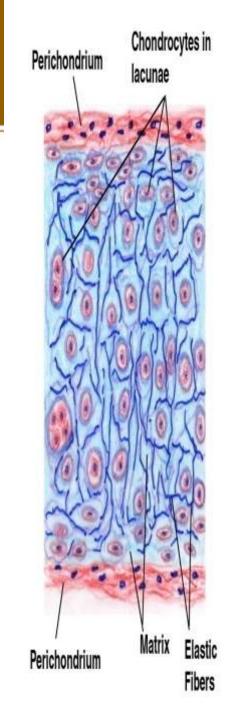
Cartilage

- Microstructure (Solid and Fluid Phase)
- Mainly composed of extracellular matrix (ECM)
- ECM largely comprised of water, proteoglycans, glycoprotein, and collagens
- Low cellularity with only cell type being chondrocytes
- No blood vessels, lymphatic channels or nerves in cartilage



Ultra (10⁻⁸ m-10⁻⁶ m)

- Chondrocytes less than 10% of the tissue volume
- Zonal distribution
- Manufacture, secrete, organize and maintain organic components of ECM.
- Responsible for increase ECM volume in growing cartilage and maintenance of the ECM in mature cartilage
- Respond to various stimuli (growth factors, matrix molecules, loads, hydrostatic pressures)
- No response to neural or hormonal systems



Organic matrix (wet portion)

- Composed collagen fibrils, mostly type 2 collagen, with minor amounts of 5, 6, 9,11 types = 15 22% by wet weight.
- Enmeshed in Concentrated solution of Proteoglycans
 (PGs)= 4 7% by wet weight.
- 60-80% water, inorganic salts and small amounts of proteins, glycoproteins and lipids.
- PGs and collagen fibrils form the structural components of significant strength & support the internal mechanical stresses.

PERCENTAGE OF WET WEIGHT Water Inorganic Matrix Organic Matrix PERCENTAGE OF DRY WEIGHT Collagen Proteoglycan Elastin Glycoproteins and Other

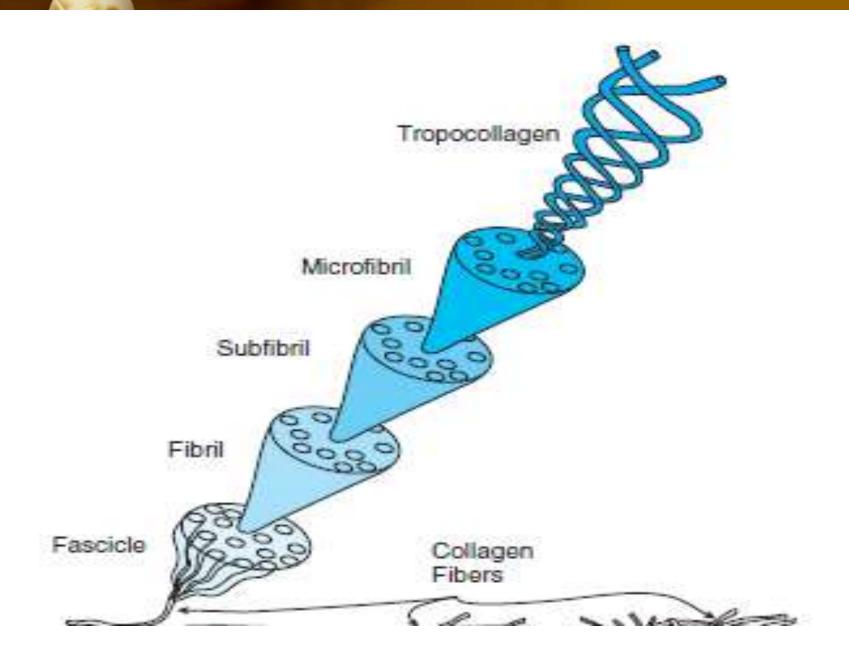
FIBROCARTILAGE

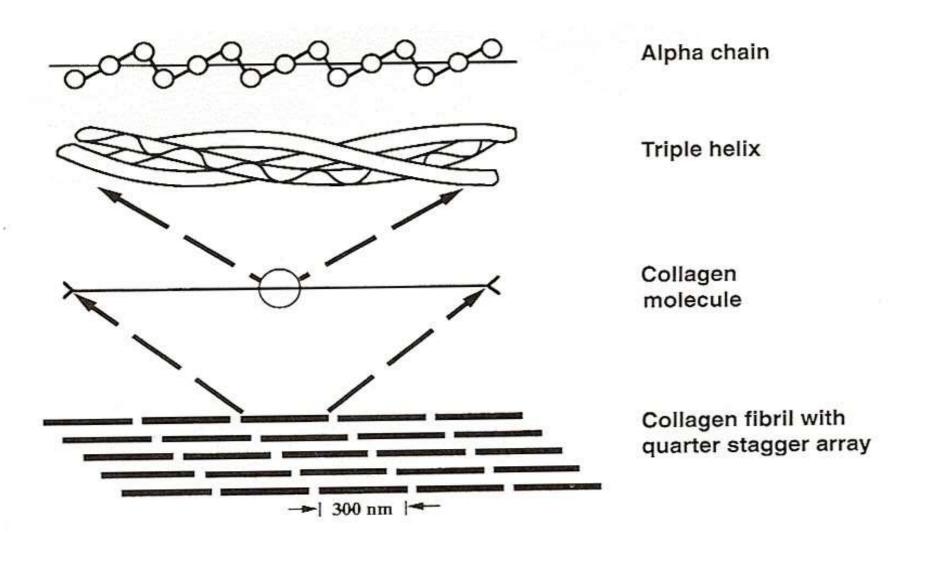
BONE

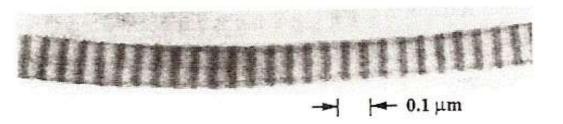
HYALINE CARTILAGE

Collagen

- Made up of molecules (tropocollagen--1.4 nm) that polymerize to form fibrils (25- 40 nm).
- Alpha triple helical structure
- Comprises over 50% of the dry weight
- Major type is type II (95%),......
- Provides tensile and sheer properties of the tissue and immobilizes proteoglycans in the ECM
- Tightly cross linked intra and inter-molecularly



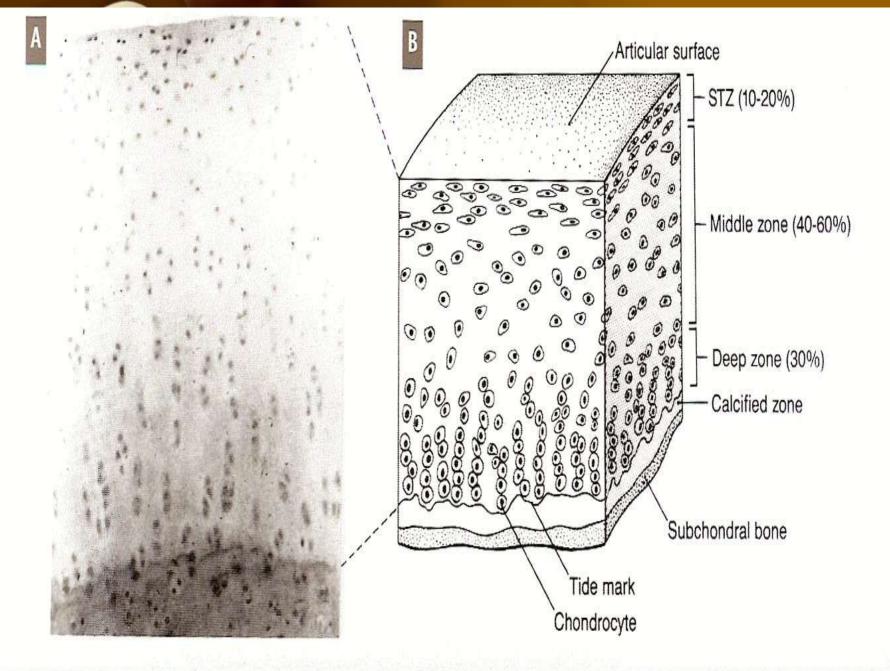




Fibril with repeated banding pattern seen under electron microscope

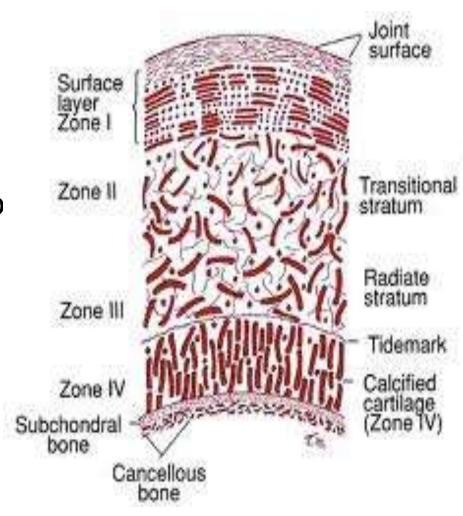
Structure and Composition

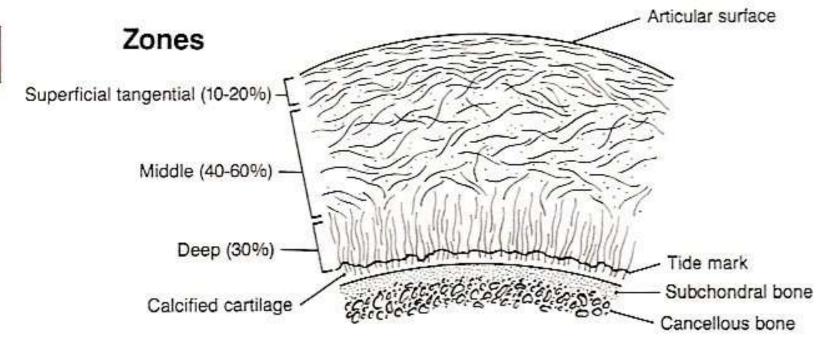
- Collagen is inhomogeously distributed within the articular cartilage
- Layered structure/ character- four distinct zones
 - The superficial tangential zone
 - The transitional or middle zone
 - —The deep zone
 - The zone of calcified cartilage



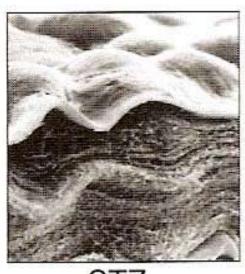
Superficial zone

- The Superficial Zone-Collagen fibrils parallel to joint surface
- Chondrocytes elongated and elliptical with parallel to joint
- Low Proteoglycans content
- High water content
- 10-20 % of total thickness.

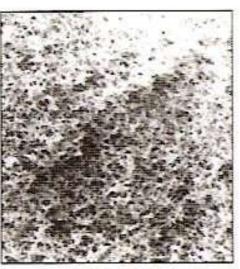




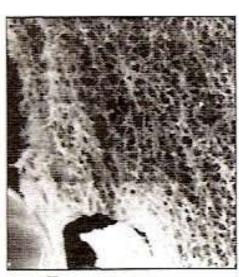
В



TZ Mid



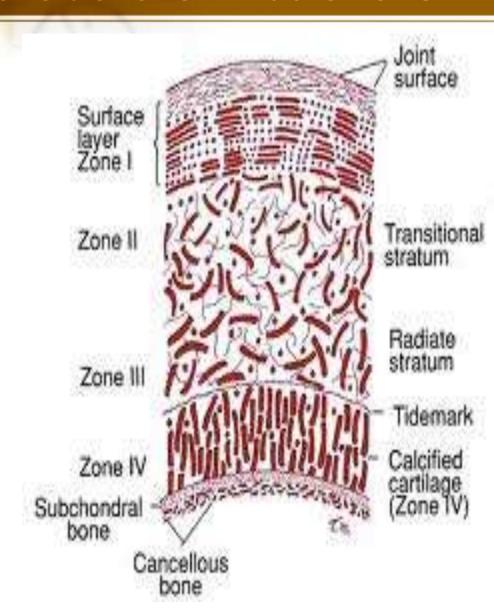
Middle zone



Deep zone

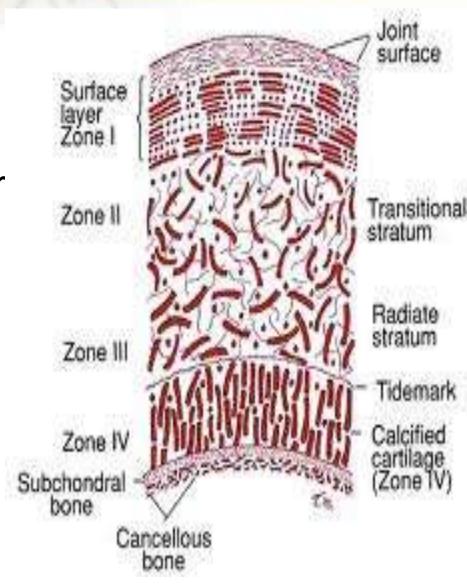
Transitional or middle Zone

- Less organization of larger diameter collagen fibrils
- Chondrocytes more rounded
- Greater distance between the less organized and homogenous fibres.
- 40 60% of total thickness.



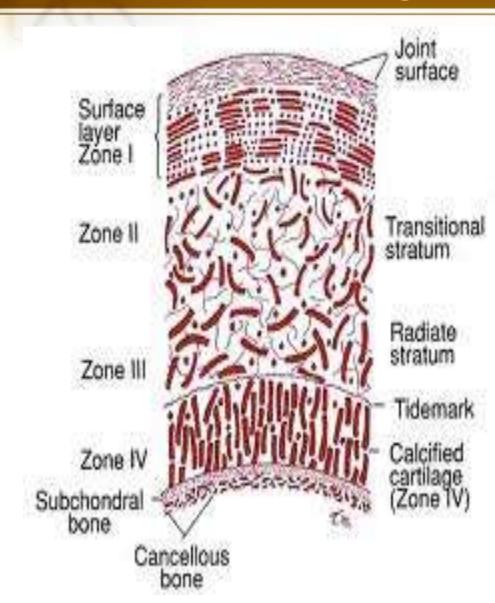
Deep Zone

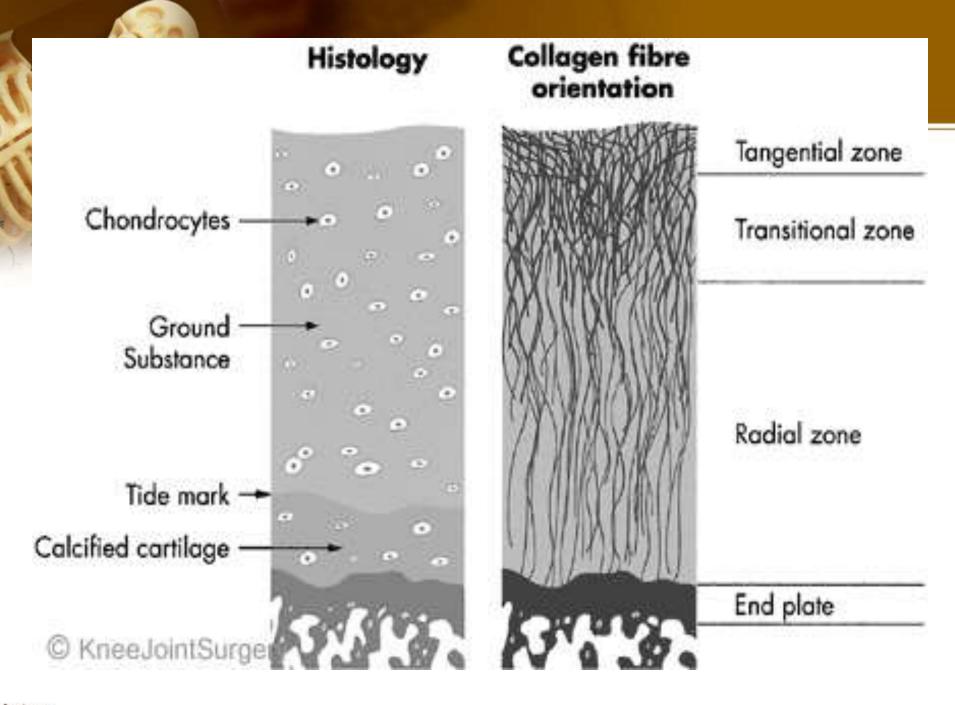
- Even larger diameter collagen fibrils organized perpendicular to joint
- Highest proteoglycan content
- Lowest water content
- Chondrocytes spherical
- 30 % of total thickness



Zone of Calcified Cartilage

- Separates the articular cartilage from subchondral bone- interlocking root system anchoring the cartilage to the underlying bone.
- A line called the tidemark can be seen with histological stains and separates this zone from the deep zone
- Like rings in a tree, the number of tidemarks increase with age





- Anisotropic fibre orientation, varying collagen fiber arrangment due to
- ☐Zonal variation, highest at the surface then constant throughout the deeper zones. This compositional Layering= distribution of stresses more uniformly.
- The most important property is tensile stiffness and strength,,,, not tested on single fiber, tested on high collagen structures.
- So strong collagen tension (strong resistance)
- Large slenderness ratio: Ratio of length to thickness..

- Anisotropic is material properties differ with the direction of loading.
- Often is thought that this anisotropy is related to the varying collagen fiber arrangements within the planes of articular surface.
- However, that variations in collagen fiber cross link density, as well as variations in collagen PG interactions also contribute to articular cartilage tensile anisotropy,
- In tension, this anisotropy is usually described with respect to the direction of the articular surface split lines.

Mank Wai!



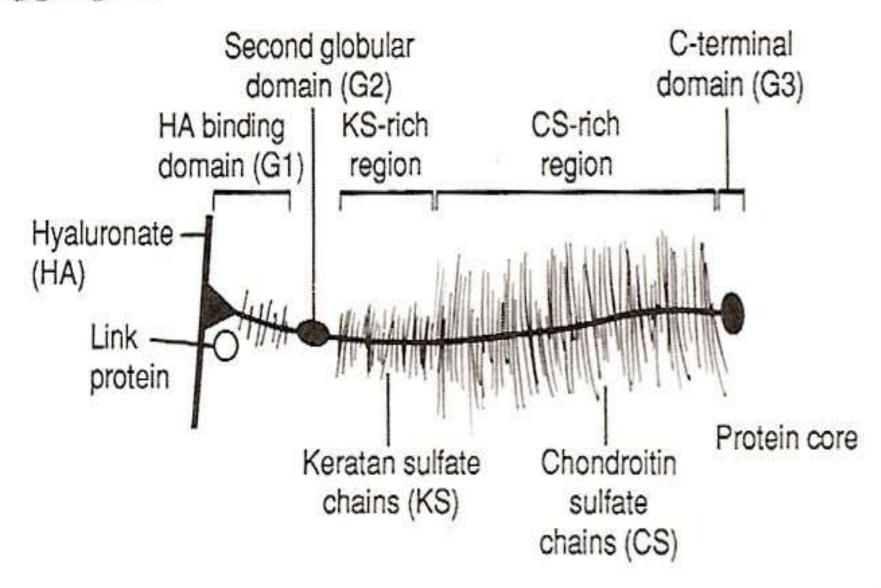


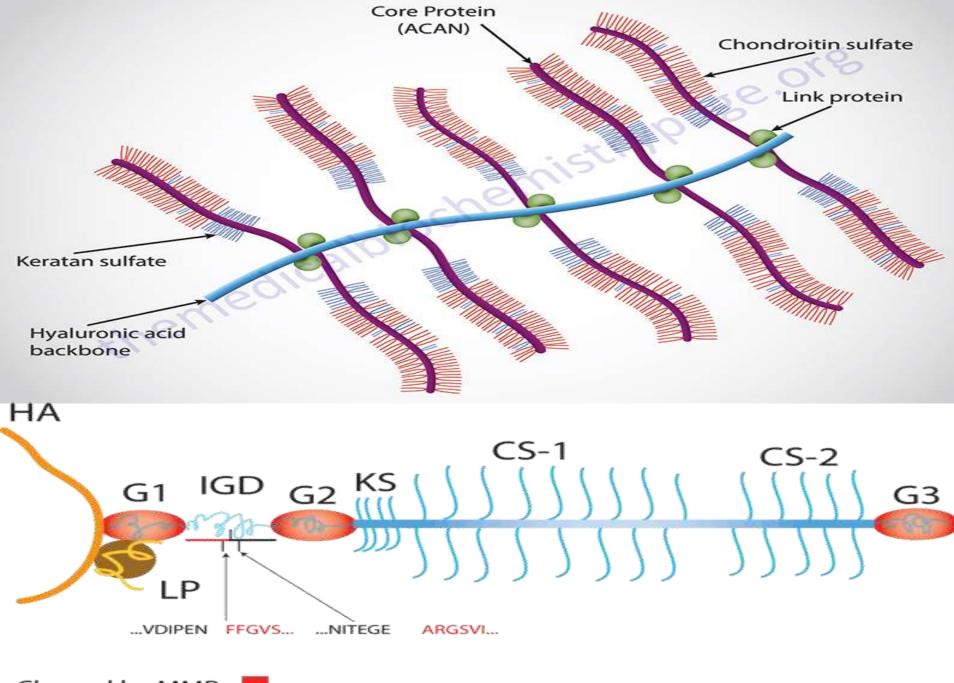


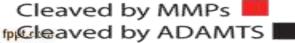
- Protein core
- Hyaloronic acid
- Hyaloronic molecule binding region (HABR).
- Link protein= stabilization
- Chondroitin sulphate (CS)= 25-30 disaccharide units
- Keratan Sulphate= small=13 disaccharide units.

- large protein plysaccharide molecule composed of protein core to which GAGs attached.
- They contain smaller to even larger aggrecans,
- Aggrecans has ability to attach hyaluronan molecule through a specific HA-binding(HABR).
- BINDING STABALIZED by link protein & stabalization crucial to function of articular cartilage, without it PG molecule escape from tissues.

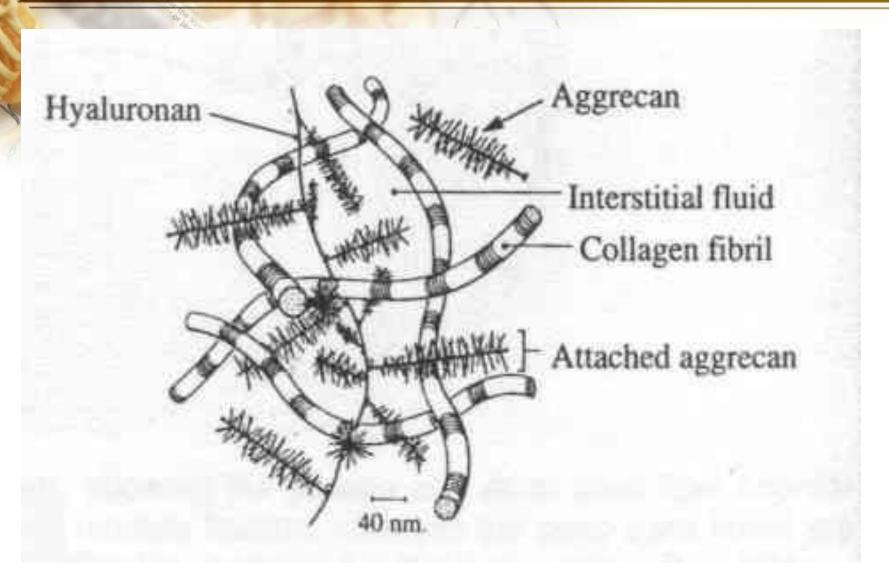
Proteoglycan Aggregate

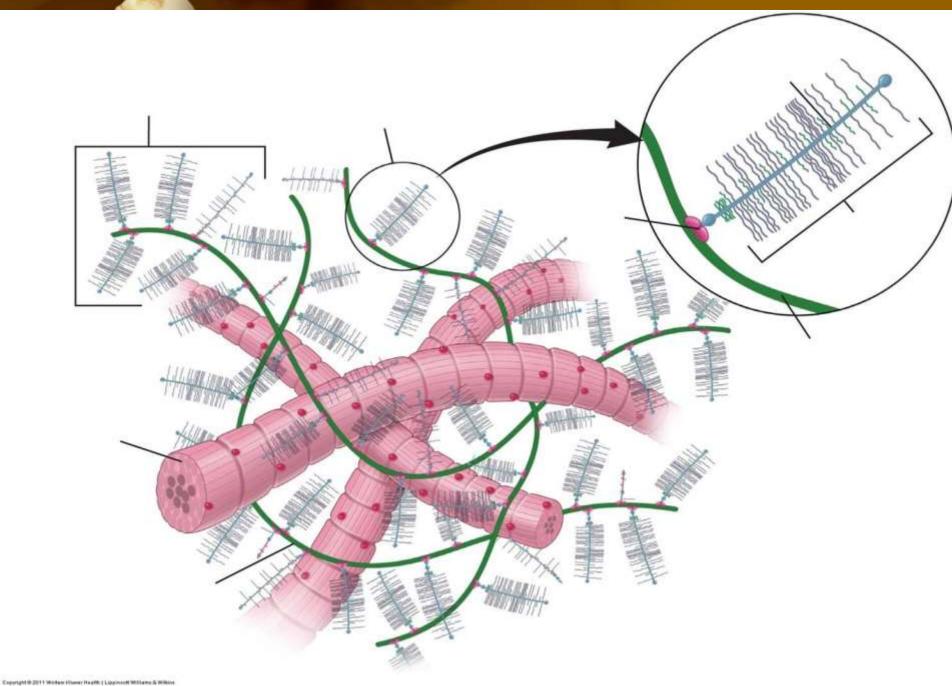






Proteoglycan: protein with bound side chains (glycosaminoglycans)

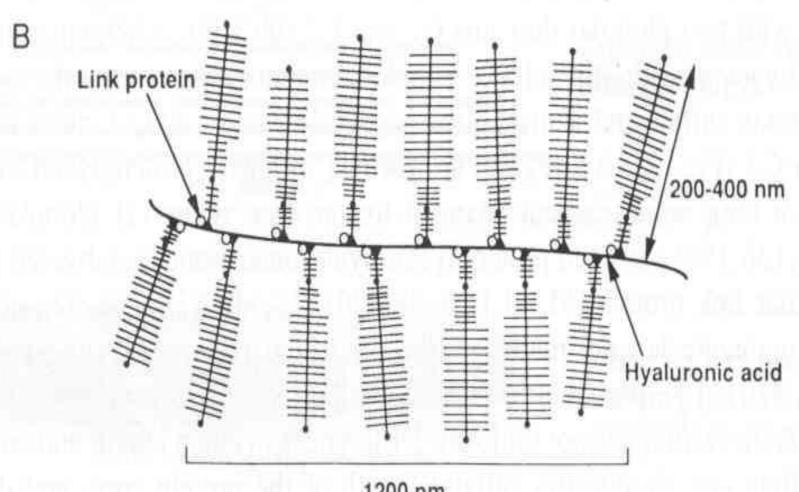




- Aggrecans ::::consist of an approximately 200 nm long protein core to which approximately 150 GAG chains covalently attached.
- Aggregation promotes immobilization of PGs adding structural stability and rigidity to ECM
- Heterogeneous distribution of GAGs.
- Rich region in KS
- Region rich in CS
- Three globular regions. G1, G2, G3

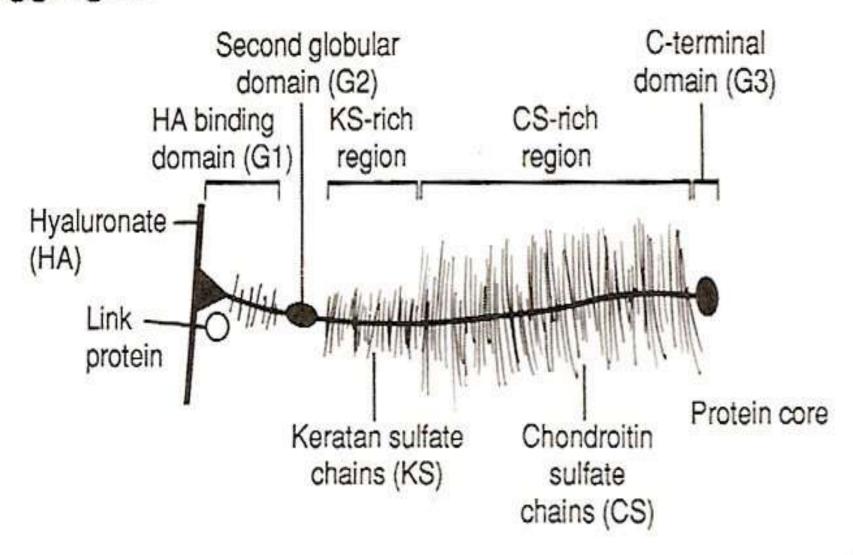


Proteoglycan Aggregates/ Aggrecan



- G1= between HABR and small amount of Keratan Sulphate, few oligosaccharides
- G2= between HABR and rich KS region
- G3= core protein C terminus
- Aggregates may have several hundred Aggrecans attached non covalently to the central HA core via their HABR and each site is stabilized by LINK protein.

Proteoglycan Aggregate



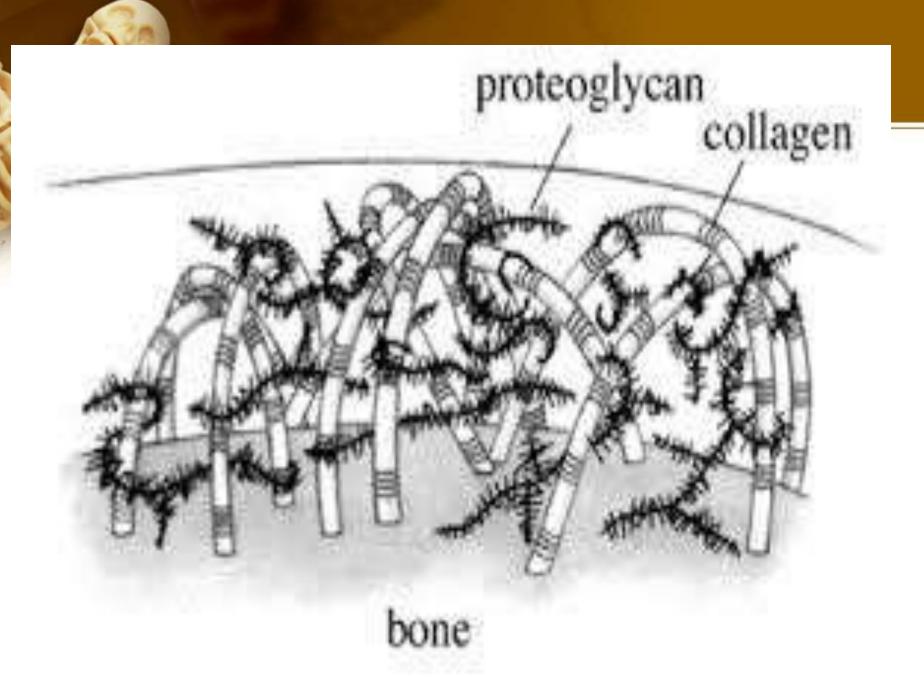
- Aggrecans are polydisperse=vary in length, Molecular weight, and composition.
- Two distinct populations of Aggrecans.
- 1) Present throughout life and rich in CS
- 2) Present only in adult cartilage and rich in KS.
- With Cartilage maturation= water content, carbohydrate/protein ratio, CS decrease.
- KS increase with the age....

- CS/KS ratio= 10:1 at birth
- 2:1 in adult cartilage
- Sulfation of CS also undergo age related changes.
- Decrease in hydro-dynamic size of Aggrecans either Due maturation or weight bearing demands.

Water

- Most abundant component
- Most concentration near the articular surface= 80 %
- 65% in deeper zone
- Free mobile cations(Na, K, Ca)
- Essential for appropriate function of articular cartilage
- Moved through the ECM by a pressure gradient
- Resistance to flow by small pore size within the ECM creates a pressurization of the fluid
- Flow through the ECM provide nutrient transport and source of joint lubrication

- A small percentage of the water is intracellularly', and approximately 30% associated with collagen fibrils.
- The interaction between collagen, PG, and water, via osmotic pressure, have an important Function in regulating the structural organization of the ECM and its swelling properties.
- Most of the water thus occupies the interfibrillar space of the ECM and is free to move when a load or pressure gradient applied.

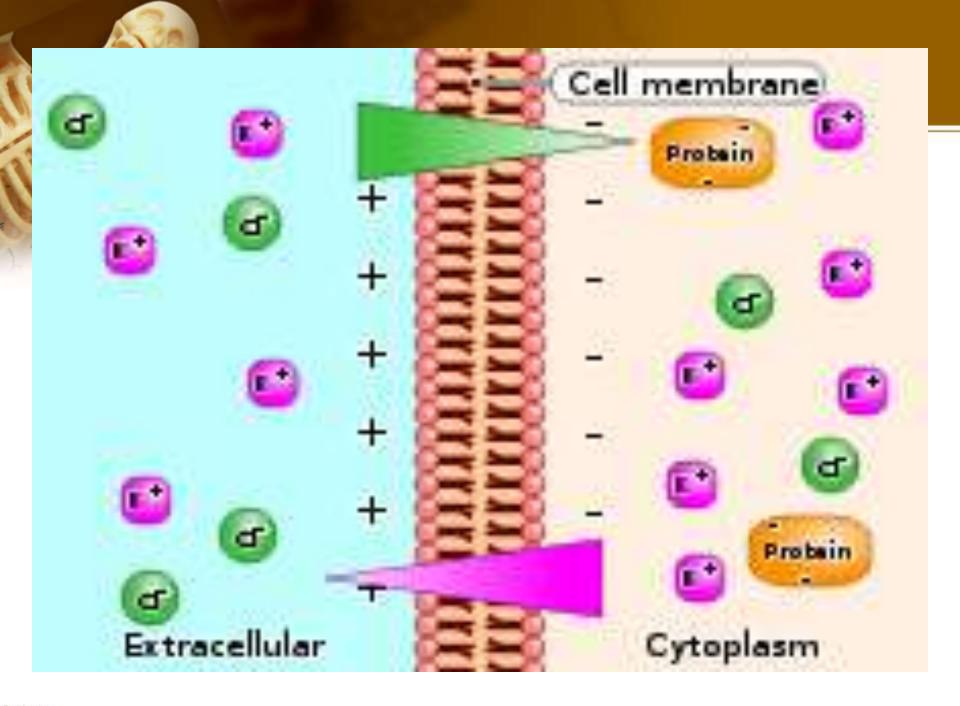


Structural and physical interaction among cartilage Components.

- The chemical structure and physical interactions of the PG aggregates influence the properties of the ECM.
- The sulfate and carboxyl charge groups on the CS and KS chains dissociate at physiological pH, leaving a high concentration of fixed negative charges that create strong intramolecular and intermolecular charge-charge repulsive forces;
- colligative sum of these forces is equivalent to the Donnan osmotic pressure

- these charge-charge repulsive forces tend to extend and stiffen the PG molecules into the interfibrillar space formed by collagen network,
- Magnitude of repulsion is one million, million, million, million, million, million, million, million, million, million....
 times greater than gravitational forces.
- charged body cannot persist -→ discharging or attracting counter-ions to maintain
 electroneutrality,

- Attract various counter-ions and coions (mainly Na', Cal., and C I") into the tissue...
- The total concentration of these counter-ions and co-ions is given by Donnan equilibrium ion distribution law
- Inside the tissue, the mobile counter-ions and coions form a cloud surrounding the fixed sulfate and carboxyl charges, thus shielding these charges from each other--→diminish large electrical repulsive forces.
- The net result is the swelling pressure



Swelling pressure:

- The Donnan osmotic pressure theory' has been extensively used to calculate the swelling pressures of articular cartilage
- By Starling's law, this swelling pressure is, in turn. resisted and balanced by tension developed in the collagen network,...

 this swelling pressure subjects a "pre-stress" of even in the absence of external loads

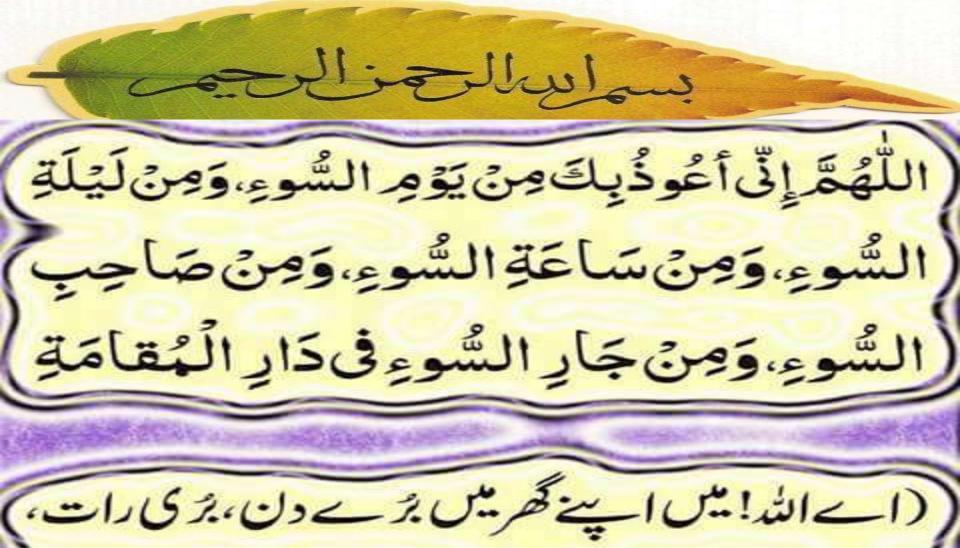
- A compressive stress applied to the cartilage surface, deformation primaly in the PG molecule
- This external stress causes the internal pressure in the matrix to exceed the swelling pressure and thus liquid will begin to flow out of that tissue.
- As the fluid rush out, the PG concentration increases, which in turn increases the Donnan osmotic swelling pressure or the charge-charge repulsive force and bulk compressive stress until they are in equilibrium with the external stress.
- In this manner, the physiochemical enable it to resist compression.

- This mechanism complements the role of collagen strong in tension but week in compression.
- PGs in collagen interactions serve as a bonding agent between the collagen fibrils in maintaining the ordered structure and mechanical properties of to form networks of strength
- the density and strength of the interaction sites also depend on LP between aggrecans and aggregates, as well as collagen.

- There are fewer aggrecanes, and more biglycans and decorins, in the superficial zone of articular cartilage.
- Thus, there must be a difference in the interaction b/w these PGs and the collagen fibrils from the superficial zone than from those of the deeper zones.
- Interaction b/w PG and collagen not only' plays a direct role in the organization of the ECM but also contributes directly' to the mechanical properties of the tissues.

- when articular cartilage is subjected to external loads, the collagen-PG solid matrix and interstitial fluid function together in a unique way to protect against high levels of stress and strain developing in the ECM.
- Furthermore, changes to the biochemical composition and structural organization of ECM, such as during osteoarthritis (OA), are paralleled by changes to the biomechanical properties of cartilage., Leading to wear of AC.





(اے اللہ! میں اپنے گھر میں بڑے دن ، بڑی رات ، ربڑی گھڑی سے ، بڑے ساتھی اور بڑے ہمسایہ سے تیری پناہ ما نگتا ہوں)

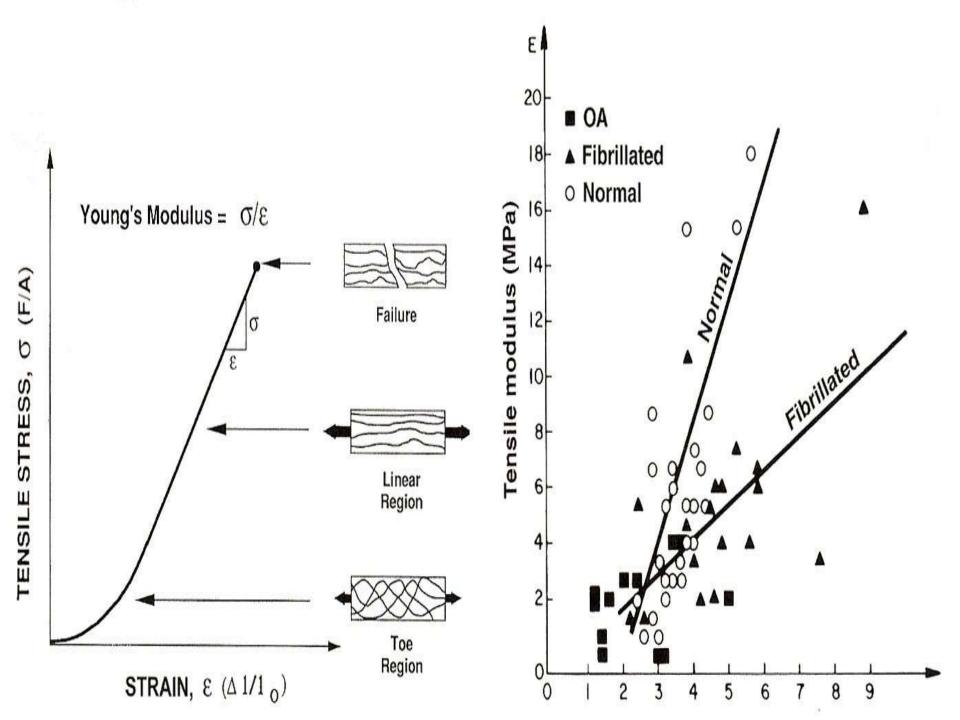


Behavior of articular cartilage under uniaxial tension

- highly complex.
- In tension the tissue is strongly anisotropic
- Superficial zone= tough wear resistance.
- Stiffer and stronger in the direction parallel to the split line patterns than perpendicular to it.

Viscoelastic behaviour in tension

- Intrinsic mechanical response of collagen solid matrix in tension depend on biphasic fluid flow effects.
- Perform slow low strain experiment allowing stress relaxation to occur till equilibrium in each increment of strain.
- Displacement rate of 0.5 cm/minute is used and pulled to failure.



- Stress-strain curve:::;Negation of viscoelastic solid properties of ECM.
- With increasing strain AC tends to stiffen.
- Initial toe region = collagen fibre pull out and realignment.
- **Linear region**= stretching of straightened aligned collagen fibres.
- **Failure** = All fibres contained within the specimen are ruptured.

• Change in :molecular structure of collagen, Organization of collagen fibres within the collagenous network, collagen fibre cross linking (e.g. in O.A)......?
Ans:

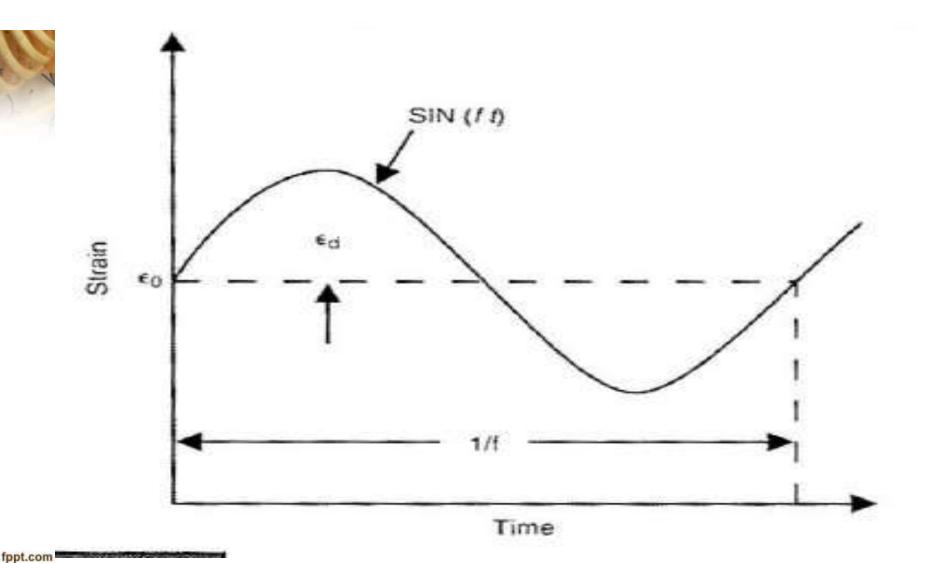
 Disruption of collagen network is key factor in initial events leading to OA.

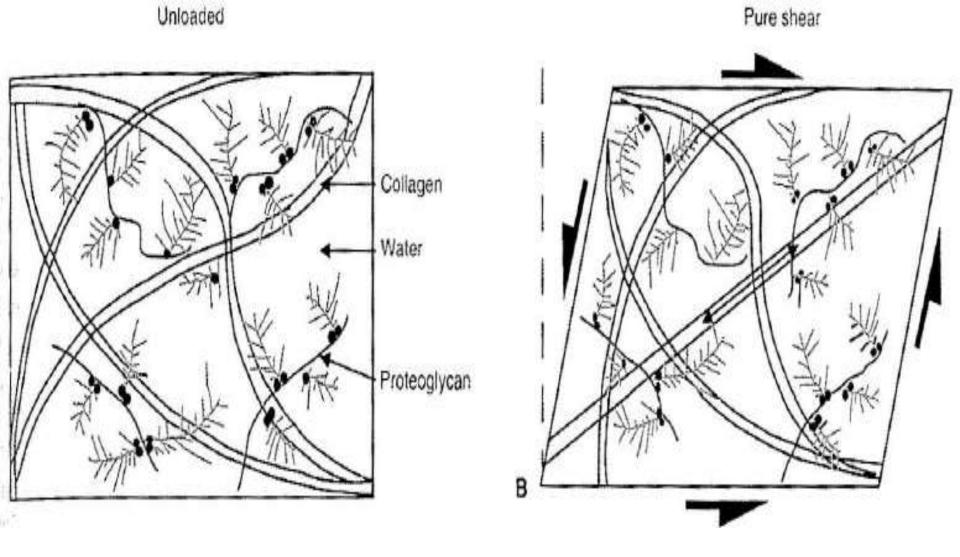
Behaviour of Articular cartilage in pure Shear

- In tension and compression only equilibrium intrinsic properties of the collagen can be determined because of volumetric change.
- If AC is tested in pure shear under infinitesimal strain conditions = no pressure gradient or no volumetric change & no fliuid will flow
- Steady dynamic pure shear experiment can be used to determine intrinsic VE(viscoelastic) properties of the collagen-PG solid matrix.

- In a steady dynamic shear experiment. the viscoelastic properties of the collagen-PG solid matrix are determined by subjecting a thin circular wafer of tissue to a steady sinusoidal torsional shear.
- In experiment of this type, the tissue specimen is held by a precise amount of compression between two rough porous platens.
- The lower platen is attached o a sensitive torque transducer and upper plate to mechanical spectrometer with servo controlled dc motor.
- Excitation signal by motors range .01 to 20 Hz. & it measures 2-20% change in viscoelasticity

Steady sinusoidal torsional shear imposed on a specimen in pure shear. The fluctuating strain in the form of a sine wave with a strain amplitude ϵ_{ij} and frequency f.





 cartilage subjected to pure shear. When cartilage is tested in pure shear under infinitesimal strain conditions. no volumetric changes or pressure gradients are produced; hence, no interstitial fluid flow occurs. This figure also demonstrates the functional role of collagen fibrils in resisting shear deformation.

- The measure of total resistance offered by viscoelastic material is called as dynamic shear modules.
- Phase shift angle is the measure of total energy dissipation within the material.
- The shear stiffness modules showed that shear stiffness in AC comes from the collagen and collagen PGs interactions only.....Not from the PGs itself.

SWELLING BEHAVIOR OF ARTICULAR CARTILAGE

- Swelling is ability of a tissue to gain or lose size or weight when soaked in solution
- AC swelling is physiochemical in that it results from the charged nature of the proteoglycans
- These negative charges requires counter ions (Na+, Ca++) for electro neutrality
- This results in higher ion concentration in the tissue than in the bathing solution

- Explanation according to the Triphasic nature of AC.
- Charged solid phase = Collagen-PG network
- Fluid phase= interstitial water
- Ion phase

 Donnan osmotic swelling pressure resists compression.

- Mechano- electrochemical multi electrolyte theory.
- Ion gradient load results in an internal swelling pressure greater than that in the bath solution
- Donnan equilibrium ion distribution law says as the external bath ion concentration increases, the difference in total ion concentration between the tissue and the bath approaches zero.
- This causes loss of water in the interstitium and a shrinkage of the tissue, conversely the opposite is true

Equilibrium Swelling Behavior

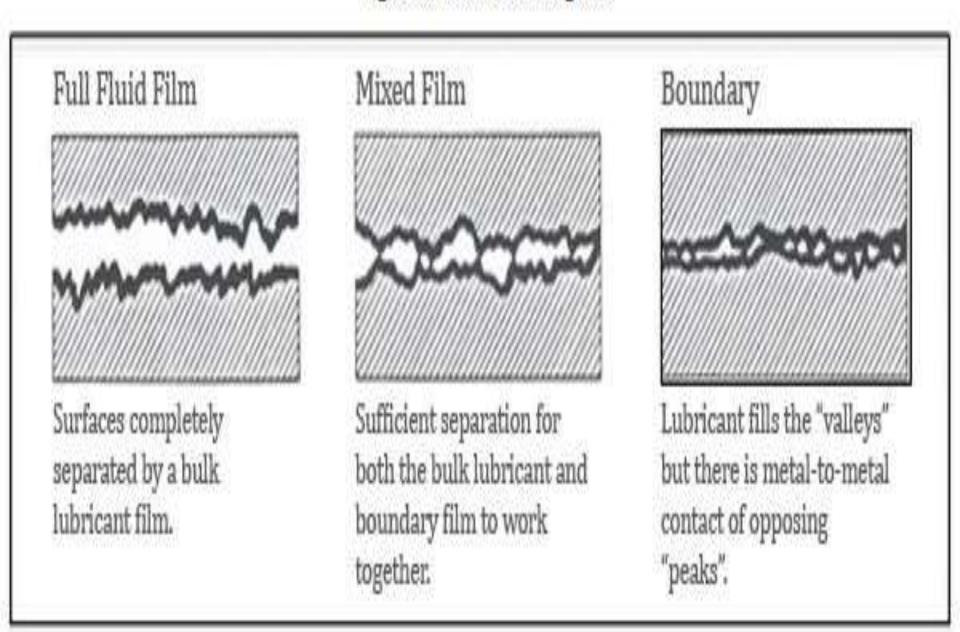
- Proteoglycans in AC are compacted to 1/5
 of their free-solution volume
- This trapping and entanglement in the interfibrillar space resulting in a strong cohesive matrix
- This makes a swelling pressure equilibrium

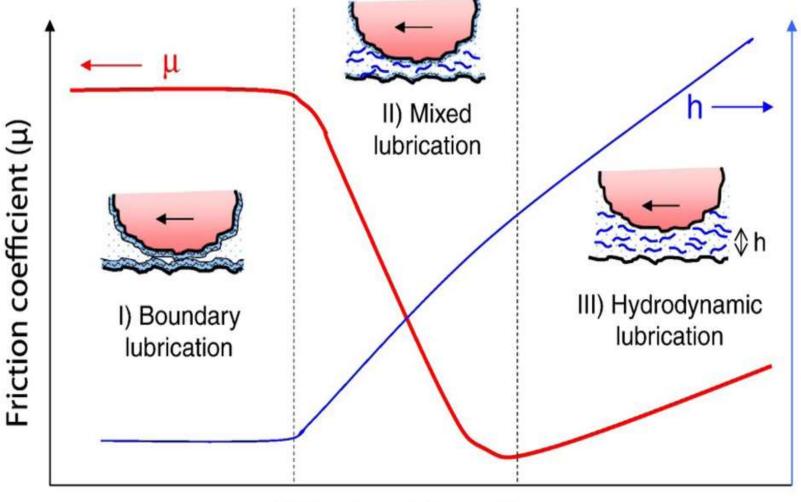
 If this matrix is damaged or disrupted (e.g. OA) then tissue will swell further and water content will increase

Lubrication of Articular Cartilage

- Engineering perspective= 2 fundamental joint lubrication mechanisms.
- Boundary Lubrication = single monolayer of lubricant molecules absorbed on each bearing surface.
- Fluid film lubrication = thin film providing surface to surface separation.

Figure 1: Lubrication Regimes





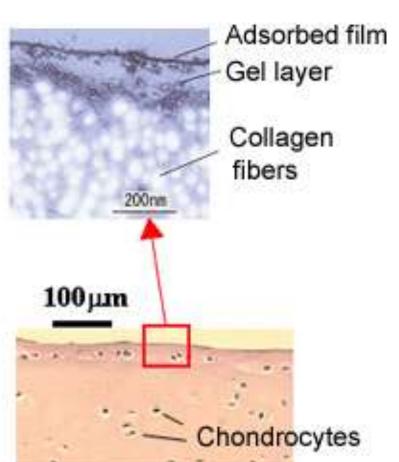
Velocity x Viscosity
Load

- Extremely low frictional co efficient for the synovial joints.
- Boundary lubricated surfaces have higher coefficient of friction than fluid film surfaces.
- Both mechanisms occur depending upon loading conditions.

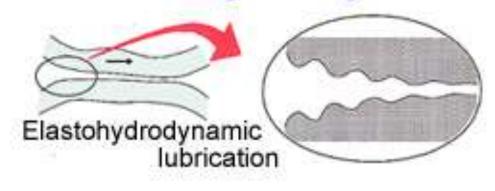
Fluid film lubrication

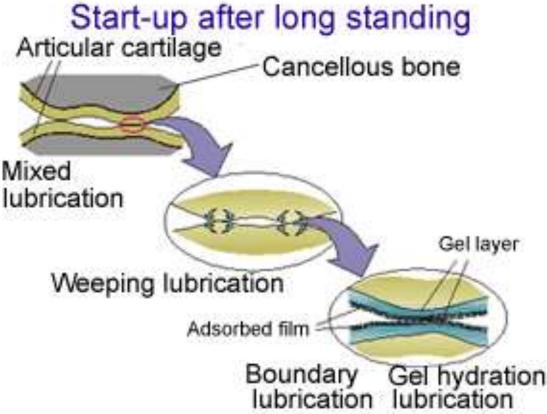
- separation of the bearing surfaces.
- Load supported by, pressure generated within the fluid film
- Engineering bearings= fluid film thickness less than 20μm – exceeds three times the roughness/decrease friction cofficent on the AC.
- If heavy & prolonged loading, incongruent gap geometry, slow reciprocating grinding motion, low synovial fluid viscosity then boundary lubrication takes over.

During walking



Cross-sectional image of natural articular cartilage





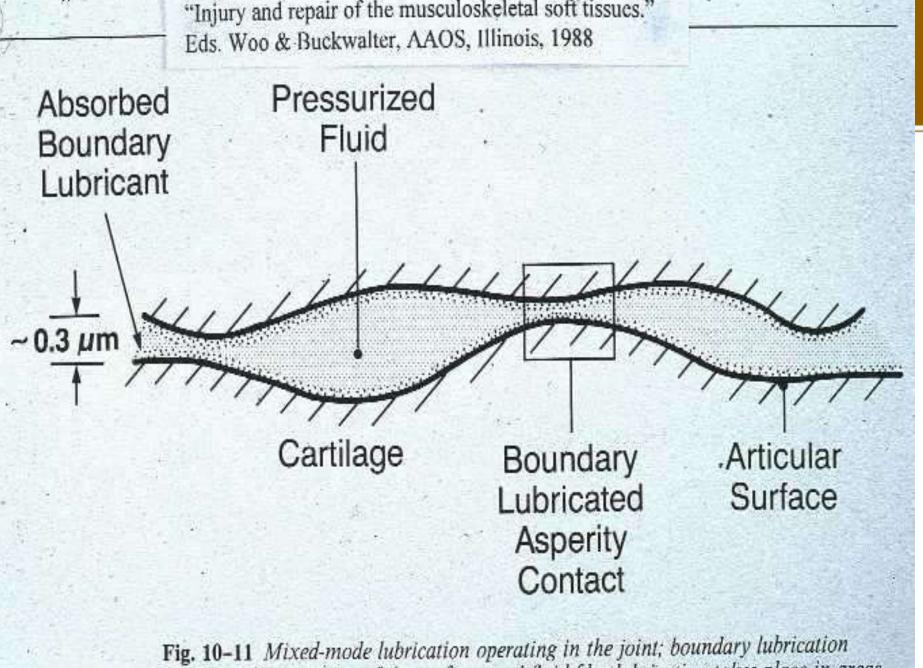


Fig. 10-11 Mixed-mode lubrication operating in the joint; boundary tubrication occurs at the asperities of the surfaces and fluid-film lubrication takes place in areas with more widely separated surfaces.

Lubrication Processes for Articular Cartilage

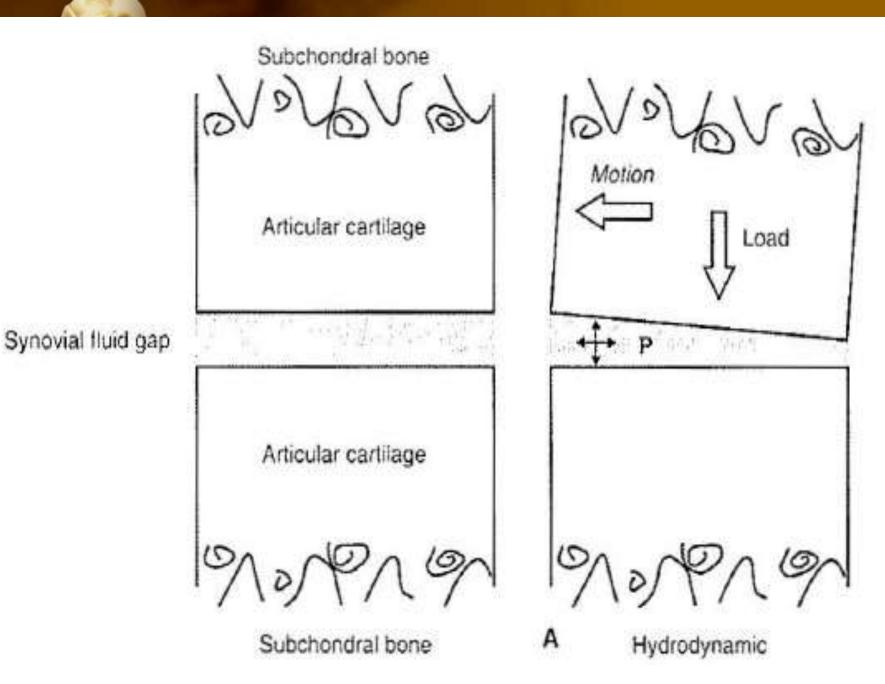
Hydrodynamic Lubrication

Squeeze-film Lubrication

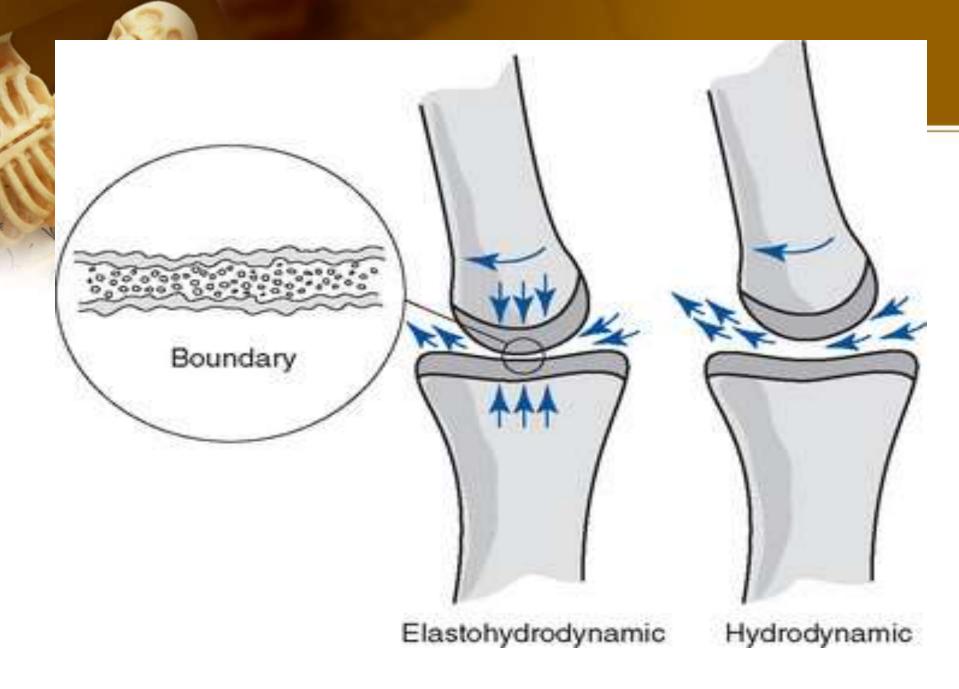
Mixed Lubrication

Two process film lubrication in weight bearing

• 1:::Hydrodynamic lubrication= non parallel bearing surfaces -(Slide over each other).- converging wedge of the fluid, fluid dragged into the wedge create lifting pressure.



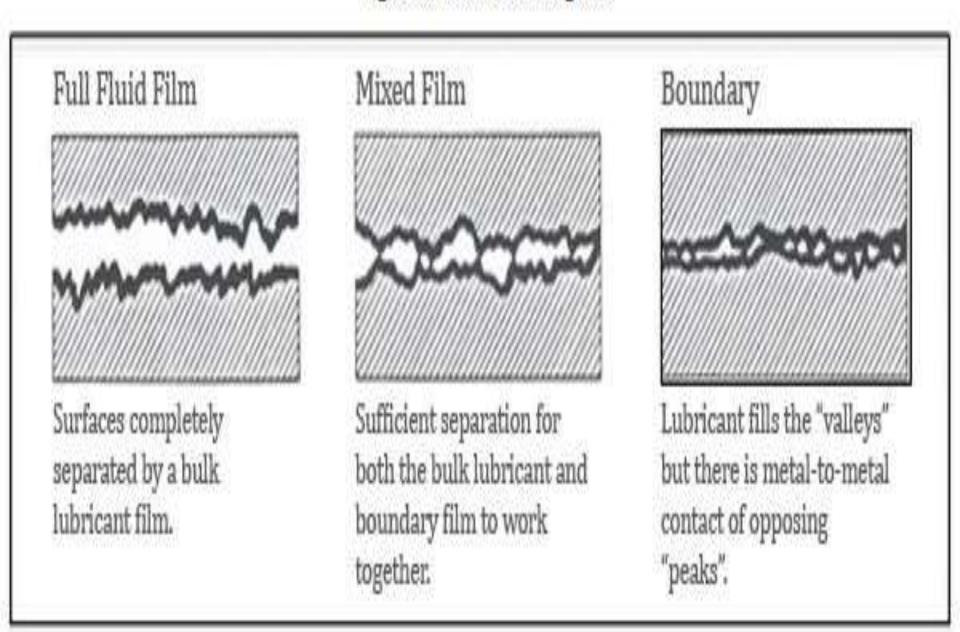
- 2:::Squeeze film lubrication = when bearing surfaces move perpendicular to each other- pressure generated within the fluid film, Sufficient to carry high loads for shorter durations.
- Eventually resulting in thinning of the fluid film contact of the peak surfaces.
- Elastohydrodynamic lubrication: in case of soft surfaces undergo either undergo sliding(hydrodynamic)/perpendicular(sqeez) action, pressure generated in fluid film deforms surfaces, increase surface area for bearing and fluid not escaped & long lasting film generated



Boundary lubrication

- Surfaces are protected by adsorbed layer of boundary lubricant preventing surface to surface contact, elimination of wear.
- Independent of physical properties of lubricant or the surface.
- **Dependent** upon the chemical properties of the lubricant. i.e. specific Glycoprotein LUBRICIN.= adsorbed as macromolecular monolayer to each articulating surface.

Figure 1: Lubrication Regimes



- Two macromolecule single-layers of two articulating AC surfaces ranging in combined thickness from 1 to 100nm, able to carry load and effective in reducing friction.
- Reduction of friction coefficient by a fraction of 3 to 6 folds quite modest as compared to earlier suggestive findings(60 folds)

Mixed lubrication

- Combination of fluid film and boundary lubrication
- 2 scenarios
- First= temporal co-existence of fluid film and boundary lubrication at spatially distinct locations.
- Second called BOOSTED LUBRICATION=
 shift of fluid film to boundary lubrication.

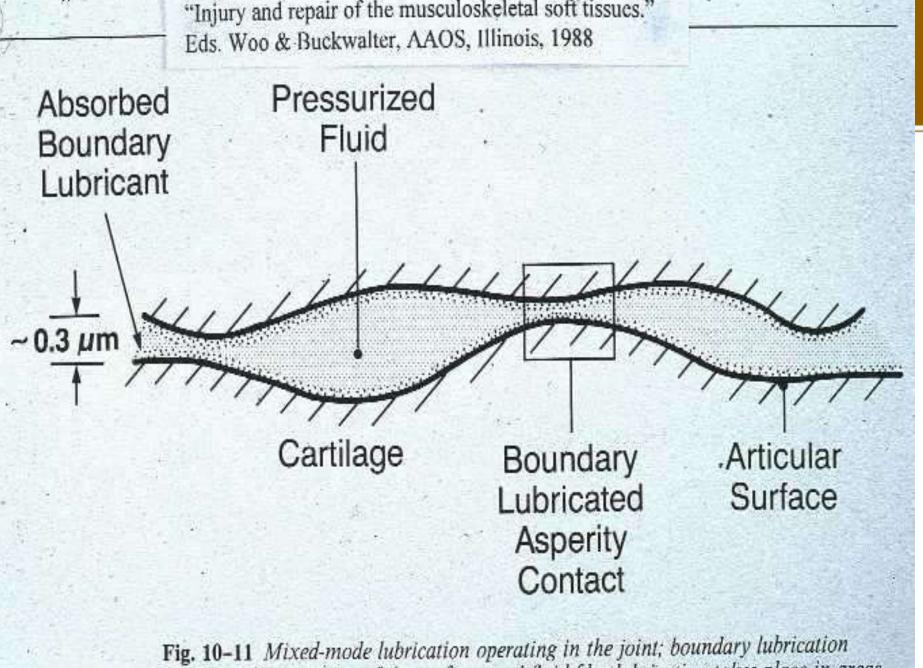
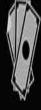


Fig. 10-11 Mixed-mode lubrication operating in the joint; boundary tubrication occurs at the asperities of the surfaces and fluid-film lubrication takes place in areas with more widely separated surfaces.

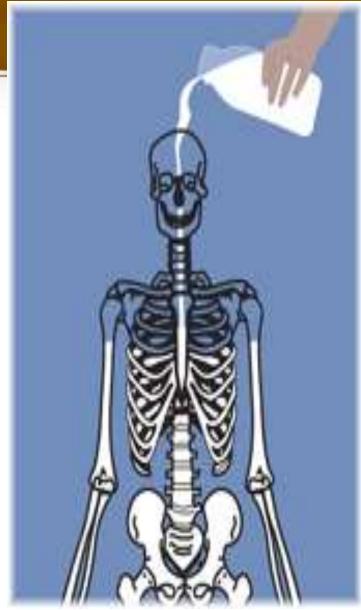




ACHIEVE LONG TERM HAPPINESS IN WORK











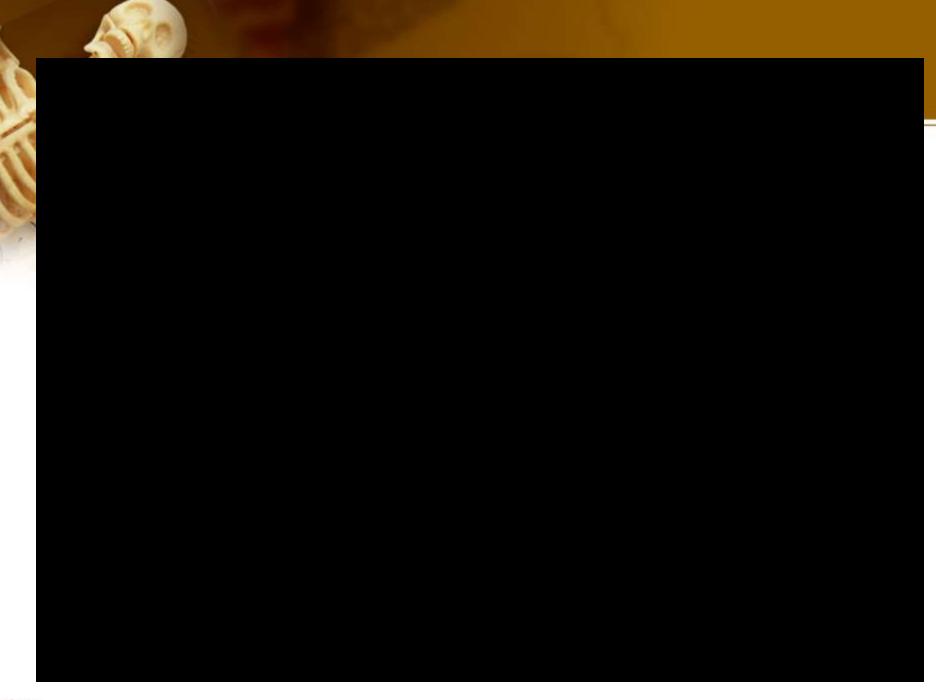
- Articular cartilage surface like other surfaces is not perfectly smooth.
- Projection of Asperities (Peaks).
- When fluid film thickness is of same order as AC surface = boundary lubrication occurs.
- Mixed mode operates = loads sustained by both fluid film in area of noncontact and boundary lubrication at the area of contact.

- Boosted lubrication = movement of fluid from the gap between the approaching articulating surface and AC.
- Filtration of synovial fluid through the PG matrix.
- Solvent components move into AC leaving behind conc. Gel of HA protein complex.
- Purified HA poor lubricant.
- Hyaluronidase treatment of synovial fluid viscosity but little effect on lubrication..



سلمانول يرباته أشاياء ووالم يتل سلمان كوكالي دينا (فسق) كناه باوراسكول كرنا (7070 / 7076_6年)

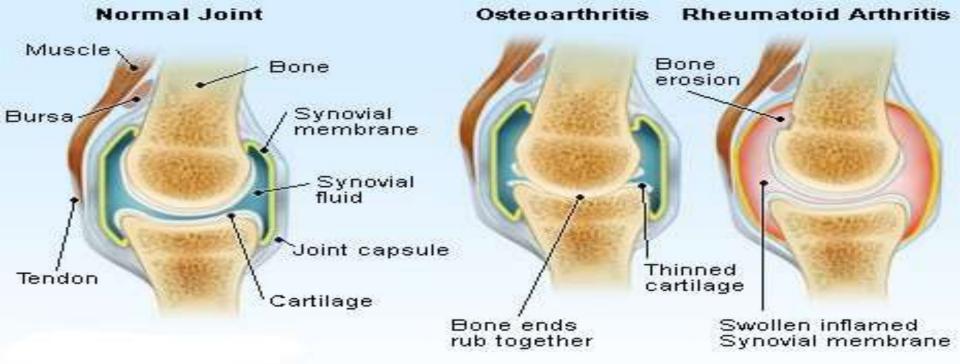
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Wear of Articular Cartilage

- UNWANTED removal of material from the solid surfaces by mechanical action.
- Two components-
- 1::FATIGUE WEAR: Accumulation of microscopic damage bearing deformation under load.
- 2:;;;Interfacial wear: when bearing surfaces come into direct contact with no lubricant film separating them.
 Adhesions and Abrasions.
- --- Adhesive wear= bearings on surface fragments adhere with each other and torn off during surface sliding.

- ---Abrasive wear: soft material scrapped by a harder one, harder material can either be opposing bearing or loose particle inside the joint.
- structural defects or decrease in mass of AC resulting in more softer and permeable AC, fluid leaks away more easily, greater chance of surface to surface contact.
- Repeated Application of high loads over short time or smaller loads over extended period of time.



Normal and Arthritic Joints







- First mechanism- hypothesis- tensile failure of collagen fibres- Age related degenerative changes, disease processes.
- Result in lower PG-collagen/PG-PG interactions and lower network strength.
- Secondly repetitive, mass exudation and imbibition of interstitial fluid causes degraded PGs to wash out from ECM.
- Decreased stiffness= increased permeability = reduced stress shielding- Cycle of Cartilage degeneration.

- Third mechanism = synovial joint impact loading i.e. rapid application of high load.
- Compaction during loading and lubrication through exudation, stress relieved during fluid redistribution over time. (normal mechanism)
- If High loads applied quickly-→ insufficient time for fluid redistribution -→high stresses in PG Collagen matrix--→Damage--→Splitting of cartilage surface
- Vertical sections called fibrillations extend throughout the full depth of AC.



- Once collagen- PG matrix of AC is disrupted, further damage by 3 wear mechanisms.
- 1-Further disruption of collagen –PG matrix
- 2-increased washing out of PGs
- 3-gross alteration of normal load carriage mechanism
- These mechanisms accelerate the rate of interfacial and fatigue wear of already disrupted AC.

- loosening of the collagen network= abnormal PG expansion, swelling, increased permeability, decreased stiffness.
- Magnitude of stress= total load on joint, mode of distribution.

potheses on Biomechanics of Cartilage Degeneration

- AC has limited capacity of repair and regeneration.
- Quick total failure progression due to
- 1- magnitude of imposed stresses
- 2- total number of sustained stress peaks
- 3- changes in intrinsic molecular and microscopic structure of the collagen- PG matrix
- 4- changes in intrinsic mechanical property of the tissue

- High contact pressures decreases the fluid film lubrication
- Certain occupations, football player knees,
 ballet dancer ankles-- cartilage degeneration
- Osteoarthritis:. Due to deficiency in stress regulating mechanisms = deficiency active processes of joint flexion, passive absorption of shocks by subchondral bones and meniscus, muscle lengthening(weakness)





