بسم الله الرحمن الرحيم
BIOMECHANICS ARTICULAR CARTILAGE

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• Three types of joints = fibrous, cartilaginous and synovial (diarthrodial joints)...

• **Hyaline Cartilage** (*articular cartilage*)

• **Elastic Cartilage**
  – Epiglottis, external ear, certain parts of larynx.

• **Fibro cartilage** = transitional cartilage
  – Intervertebral disk = annulus fibrosis
  – meniscus
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 sustained by contacting surfaces.

- 2:: Allow relative movement of opposing joint surfaces with minimal friction and wear.
Composition and structure of Articular 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
• **Chondrocytes** – less than 10% of the tissue volume
• Zonal distribution
  • Manufacture, secrete, organize and maintain organic components of ECM.
• Responsible for increase is ECM volume in **growing cartilage** and maintenance of the ECM in mature cartilage
• Derived from mesenchymal cells
• Respond to various stimuli (growth factors, matrix molecules, loads, hydrostatic pressures)
• No response to neural or humoral 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.
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%), however types V, VI, IX, X, and XI present in small amounts
- Provides tensile and sheer properties of the tissue and immobilizes proteoglycans in the ECM
- Tightly cross linked intra and inter-molecularly
Collagen Structure

- Alpha chain
- Triple helix
- Collagen molecule
- Collagen fibril with quarter stagger array

Fibril with repeated banding pattern seen under electron microscope

300 nm

0.1 μm
• Collagen is inhomogeneously 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
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.
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
• 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.
Zones

- Superficial tangential (10-20%)
- Middle (40-60%)
- Deep (30%)
- Calcified cartilage
- Tide mark
- Subchondral bone
- Cancellous bone

B

- STZ
- Middle zone
- Deep zone
• Anisotropic fibre orientation
• Inhomogeneous Zonal variation, highest at the surface then constant throughout the deeper zones.

• **Layering** = distribution of stresses more uniformly.

• The most important property is tensile stiffness and strength

• Single collagen fibril not tested.... so structures with highest collagen content e.g. Tendon with 80 % collagen content tested.
• **Large slenderness ratio**: Ratio of length to thickness.

• Easy for them to buckle under compressive loads.
• 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 polysaccharide 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: protein with bound side chains (glycosaminoglycans)
• **Aggrecans** consist of an approximately 200 nm long protein core to which approximately 150 GAG chains, and both O linked and N linked oligosaccharides are covalently attached.

• Aggregation promotes immobilization of PGs adding structural stability and rigidity to ECM

• **Heterogeneous distribution of GAGs.**

• Rich region in KS and oligosaccharides

• 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.
• Aggrecans are structurally non identical.
Proteoglycans

Proteoglycan Aggregate

- Second globular domain (G2)
- HA binding domain (G1)
- KS-rich region
- CS-rich region
- C-terminal domain (G3)
- Hyaluronate (HA)
- Link protein
- Keratan sulfate chains (KS)
- Chondroitin sulfate chains (CS)
- Protein core
• 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. all these early changes in AC reflect AC mturation possibly as a result of increased functional demand with increased weight bearing.
Water

- Most abundant component
- Most concentration near the articular surface = 80%
- 65% in deeper zone. (decrease in linear fashion with zones)
- Free mobile cations (Na, K, Ca)
- Essential for appropriate function of articular cartilage
- Moved through the ECM by a pressure gradient
- Frictional 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 in cartilage resides intracellularly', and approximately 30% is strongly 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 or other electrochemical motive forces are applied to the tissue.
• When loaded by a compressive force, approximately 70% of the water may be moved. This interstitial fluid movement is important in controlling cartilage mechanical behavior and joint lubrication.
Structural and physical interaction among cartilage Components.

• The chemical structure and physical interactions of PGs influence the properties of the ECM
  • The Sulphate and Carboxyl charge groups on CS and KS.
  • Inter, intra molecular charge charge repulsive forces= Donnan osmotic pressure.
  • 1 Million million (42 zeros) stronger than gravitational forces.
  • Electroneutrality for existence.
• Counter ions and Co ions.
• Na, Cl, Ca
• Formation of cloud surrounding fixed sulphate and carboxyl charges, thus shielding these charges.
• The net result is the swelling pressure
Structural and physical interaction among cartilage Components.

- The chemical structure and physical interactions of the PG aggregates influence the properties of the ECM.
- The closely spaced sulfate and carboxyl charge groups on the CS and KS chains dissociate in solution at physiological pH, leaving a high concentration of fixed negative charges that create strong intramolecular and intermolecular charge-charge repulsive forces;
- the colligative sum of these forces is equivalent to the Donnan osmotic pressure
• these charge-charge repulsive forces tend to extend and stiffen the PG macromolecules into the interfibrillar space formed by the surrounding collagen network,

• magnitude this electrical repulsion is one million, million, million, million, million, million, million, million times ---- greater than gravitational forces.
• charged body cannot persist \(\rightarrow\) discharging or attracting counter-ions to maintain electroneutrality,
• charged sulfate and carboxyl groups **attract** various counter-ions and co-ions (mainly Na', Ca', and Cl') 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 co-ions **form a cloud** surrounding the fixed sulfate and carboxyl charges, thus shielding these charges from each other--\(\rightarrow\) diminish large electrical repulsive forces.
• **Swelling pressure:**

• The Donnan osmotic pressure theory' has been extensively used to calculate the swelling pressures of articular cartilage and the intervertebral disc.,

• **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
• When a compressive stress is applied to the cartilage surface, deformation caused primarily by a change in the PG molecular domain,
• 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.
How Cartilage Acts as a Shock Absorber

- Collagen Fibrils
- Proteoglycan
- Glycosaminoglycan
- Core Protein

Load-Induced Compression (Reversible)

Electrical Field Streaming Potential Currents

Fluid Flow

Water

Core Protein
• **This mechanism complements** the role placed by collagen that, is strong in tension but week in compression.

• **PGs in collagen interactions serve as a bonding agent between the collagen fibrils to play an important role in maintaining the ordered structure and mechanical properties of the collagen fibril to form networks of significant strength**

• **the density and strength of the interaction sites also depend on LP between aggregcans and aggregates, as well as collagen.**
• There are fewer aggregcanes, 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.
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**
• To determine intrinsic mechanical response of collagen solid matrix in tension, it is necessary to negate the biphasic fluid flow effects.
  • Perform slow low strain experiment incremental 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.
• The equilibrium stress strain curve
Young's Modulus = $\frac{\sigma}{\varepsilon}$

- **TENSILE STRESS, $\sigma$ (F/A)**
- **STRAIN, $\varepsilon$ ($\Delta l/l_0$)**

### Graph

- **Tensile modulus (MPa)**
- **OA**
- **Fibrillated**
- **Normal**

- **Linear Region**
- **Failure**
- **Toe Region**
• **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 fluid will flow.
- Steady dynamic pure shear experiment can be used to determine intrinsic VE (visco-elastic) properties of the collagen-PG solid matrix.
In experiment Thin circular wafer of tissue to a steady sinusoidal torsional shear, compression within 2 rough porous platens.

The lower platen is attached to a sensitive torque transducer and upper platen to precision 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 $\epsilon_d$ and frequency $f$. 

![Graph showing strain over time with a sinusoidal wave and marked values $\epsilon_0$ and $\epsilon_d$.](image-url)
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 modulus**.

• **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 is the ability of a tissue to gain or lose size or weight when soaked in a solution.

AC swelling is physiochemical in that it results from the charged nature of the proteoglycans. These negative charges require counter ions (Na+, Ca++) for electro neutrality.

This results in a 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

- Sophisticated lubrication mechanism - minimal wear under maximum and variety of loading conditions.
- Characteristic of synovial joint.
- Within the joint as well as within and on the surface of the tissues.
- A number of lubrication mechanisms
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.
- Both occurring under varying circumstances.
• Extremely low frictional coefficient 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

- Thin film of lubricant that causes separation of the bearing surfaces.
- Load supported by the pressure generated within the fluid film.
- Engineering bearings = fluid film thickness less than 20µm – exceeds three times the roughness on the AC.
- If heavy & prolonged loading, incongruent gap geometry, slow reciprocating grinding motion, low synovial fluid viscosity then boundary lubrication takes over.
• Two classical modes applicable to rigid bearing, relatively undeformable.

• **Hydrodynamic lubrication** = non parallel bearing surfaces move tangentially to each other-(Slide over each other).- converging wedge of the fluid, fluid dragged into the wedge, lifting pressure.

• **Squeeze film lubrication** = when bearing surfaces move perpendicular to each other-pressure generated within the fluid film as a result of viscous resistance.
• Sufficient to carry high loads for shorter durations.
• Eventually resulting in thinning of the fluid film - contact of the peak surfaces.
• Surface roughness and relative thickness of the fluid film = existence of hydrodynamic lubrication.
• Independent of bearing surface material
• Dependent upon lubricants properties.
• Cartilage = unique frictionless.
• A variation of the hydrodynamic and squeeze film
• Elastohydrodynamic mode = operates when relatively soft bearing surfaces undergo either sliding or squeeze film action= pressure generation= substantial deformation of the surfaces.
• Alteration of film geometry.
• Longer lasting lubricant film
• Enhancement of load carrying capacity
• Hyaluridase treatment= decreased viscosity= little effect on lubrication= indicative of alternative modes.
Boundary lubrication

• Surfaces are protected by adsorbed layer of boundary lubricant preventing surface to surface contact, elimination of wear.

• Independent of physical properties of either 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.
Two layers ranging in combined thickness from 1 to 100nm, able to carry load and effective in reducing friction.

Recent investigations suggest boundary lubricant as phospholipid named DIPALMITOYL PHOPHATADYLCHOLINE.

Reduction of friction coefficient by a fraction of three to 6 folds quite modest as compared to earlier suggestive findings (60 folds).

So existence as a complementary mode
Mixed lubrication

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

• 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.
• Friction in boundary lubricated and load sustained by the fluid film.
• Boosted lubrication = movement of fluid from the gap between the approaching articulating surface and AC.

• Ultra filtration of synovial fluid through the PG matrix.

• Solvent components move into AC leaving conc. Gel of HA protein complex behind.

• Purified HA poor lubricant.
Figure 1: Boundary Lubrication
Figure 3: Mixed Film Lubrication
Wear of Articular Cartilage

• Wear is the UNWANTED removal of material from the solid surfaces by mechanical action.

• Two components - interfacial wear = interaction of the bearing surfaces

  Fatigue wear = bearing deformation under load.

• **Interfacial wear** when bearing surfaces come into direct contact with no lubricant film separating them. Adhesions and Abrasions.

  --- Adhesive wear = bearings come into contact surface fragments adhere with each other and torn off during surface sliding.
Abrasive wear: soft material scraped by a harder one, harder material can either be opposing bearing or loose particle inside the joint.

- Multiple modes of lubrication result in unlikely interfacial wear.
- Occurrence in degenerated or impaired joints.
- Ultra 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.

- **FATIGUE WEAR:** Accumulation of microscopic damage
• Repeated Application of high loads over short time or smaller loads over extended period of time.
• Rotation and sliding = specific AC regions contact areas moves in and out.
• Repeated stressing of ECM matrix and exudation of interstitial fluid.
• Two mechanism = disruption of the collagen and PG solid matrix, PG wash out.
• First mechanism- hypothesis- tensile failure of collagen fibres- Age related degenerative changes, disease states.
• Molecular, structural changes result in lower 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 mechanism, Vicious 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.

• Stress relaxation takes place quickly, 63% reduction may take place within 2-5 sec.

• If high loads applied quickly = insufficient time for fluid redistribution to relieve the compacted region = high stresses in PG-Collagen matrix = Damage
• Variety of structural defects seen as a result of these mechanisms.

• Splitting of cartilage surface
• Vertical sections called **fibrillations**. Eventually may extend throughout the full depth of AC.
• Cartilage surface erosion called as smooth surface destructive thinning.
• Variety of defects suggest not a single wear mechanism is responsible.
• Little experimental information on type of defect and wear mechanism.
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 microstructure.
Hypotheses 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
• Most important is loosening of the collagen network =
  abnormal PG expansion, swelling, increased
  permeability, decreased stiffness.
• Magnitude of stress = total load on joint, mode of
  distribution.
• Intense stress concentration in contact area, e.g.
  surface incongruity leading to O.A. like congenital
  acetabular dysplasia, slipped capital femoral
  epiphysis, intra articular fractures.
• Knee joint menisectomy, Ligament rupture.
• High contact pressures decreases the fluid film lubrication
• Certain occupations, football player knees, ballet dancer ankles.
• O.A. Due to deficiency in stress regulating mechanisms = active processes of joint flexion, passive absorption of shocks by subchondral bones and meniscus, muscle lengthening
• Breakdown in matrix integrity e.g. R.A, Haemophilia, collagen metabolism disorders, tissue degradation by proteolytic enzymes, cytokines, growth factors.
• Age related changes in chondrocytes.
Implications on chondrocyte functions

• Responsible for increase in ECM volume in growing cartilage and maintenance of the ECM in mature cartilage
  • Derived from mesenchymal cells
  • Respond to various stimuli (growth factors, IL’s, matrix molecules, loads, hydrostatic pressures)
  • No response to neural or humoral systems
• ECM modulates the joint loads to the chondrocytes.
• Normal healthy AC, from joint movements= MECHANO-ELECTROCHEMICAL stimuli are produced .i.e. hydrostatic pressure, stress and strain fields, streaming potentials.
• Result= normal cartilage maintenance, normal tissue function.
• In case of compromised integrity of collagen, PG network= abnormal stimuli= abnormal ECM remodelling by chondrocytes, and debilitating joint functions.
• In absence of joint loading, pre stress established by balance between tension in collagen fibres and Donnan osmotic pressure.
• In case of joint loading, unbound water movement= streaming potential,
• Considerable resistance to fluid flow through pores gives fluid induced matrix compaction.
In OA, increased tissue permeability ==> diminished AC fluid pressure support mechanism ==> shift of load support onto the solid ECM ==> supra normal stresses on the chondrocyte functions ==> Imbalance between chondrocyte Anabolic and catabolic activities ==> vicious cycle of cartilage degeneration.
The ECM also arranged into pericellular, territorial, and interterritorial regions based upon the chondrocyte proximity

**Pericellular** just adjacent to cell membrane and contains proteoglycans and no collagen

**Territorial matrix** surrounds pericellular and has a fibrillar network of thin collagen fibers

**Interterritorial matrix** is largest and has most contribution to function. Consists of combination of proteoglycans and collagen