Molecules to Function: Osteoarthritic Changes in the Knee Joint Organ

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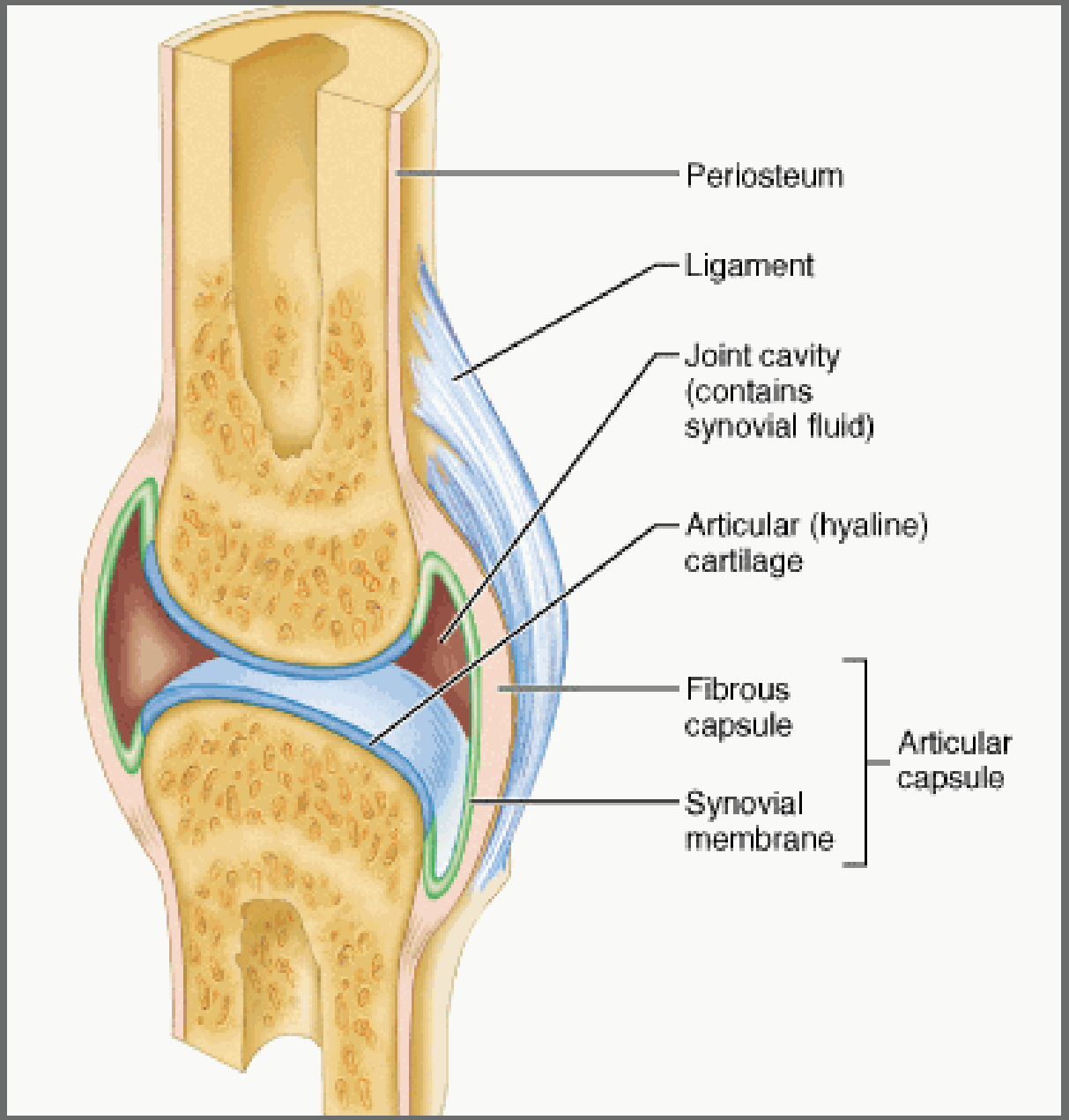
Current Concepts in the Management of Knee OA
June 12, 2009

Introduction

- Osteoarthritis (OA) affects the whole “knee joint organ” – Not just cartilage!
  (Hunter and Felson, 2009)

- OA:

  “…joint diseases characterized by repetitive response to injury with subsequent regenerative, reparative, and degenerative structural changes in all tissues of the joint…”
  (Prizker, 2003)



www.octc.kctcs.edu/gcaplan/anat/Notes/Image585.gif

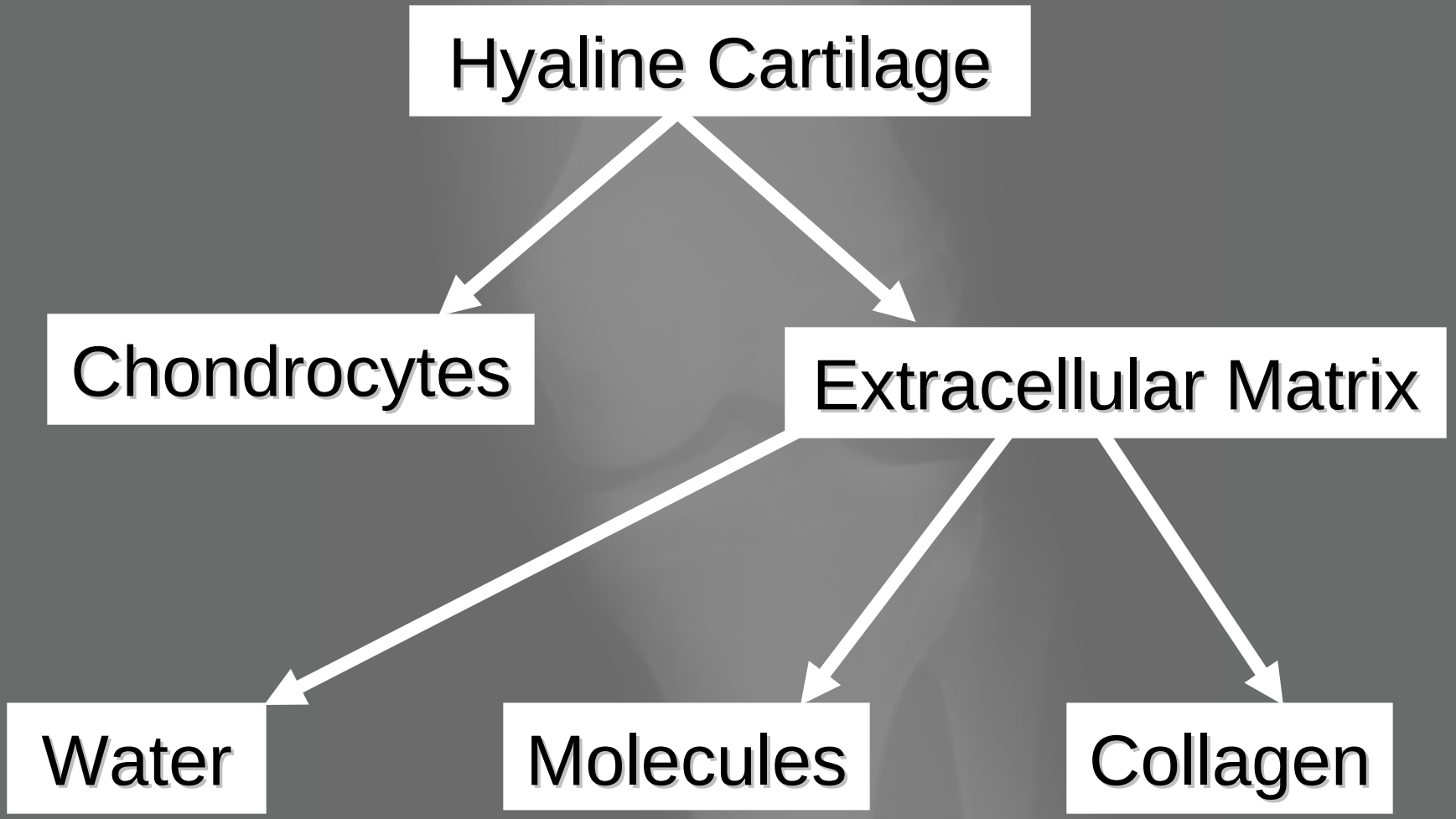
Introduction

- Examining small molecules to large concepts
- Review joint physiology and examine OA changes in body structures
  - Cartilage, bone, synovium, meniscus, joint capsule, ligaments, muscles
- Resulting effect on:
  - Range of motion, proprioception, pain, gait, function, physical activity, participation

Cartilage

- Hyaline cartilage covers articular surface of synovial joints
- No blood/ lymphatic vessels or nerves
- Function
  - Resist compression/ shock absorber
  - Decrease friction
  - Support the body

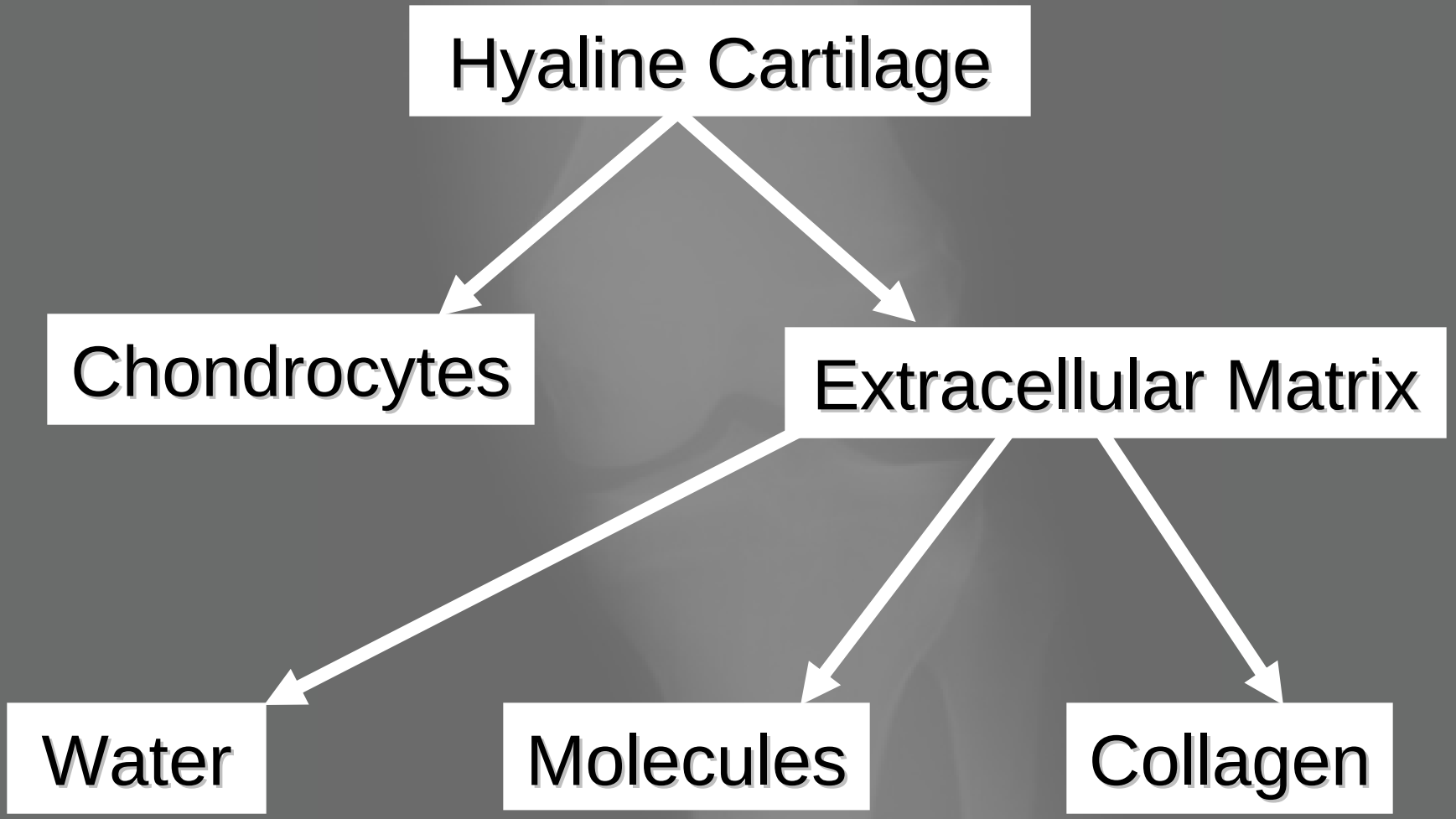
(Gartner and Hiatt, 2007)


Hyaline Cartilage
Chondrocytes
Extracellular Matrix
Water
Molecules
Collagen

Chondrocytes

- Cells
  - Large nucleus
  - Organelles for protein synthesis
- Function
  - Maintain extracellular matrix
  - Repair damaged cartilage

(Gartner and Hiatt, 2007)


Hyaline Cartilage
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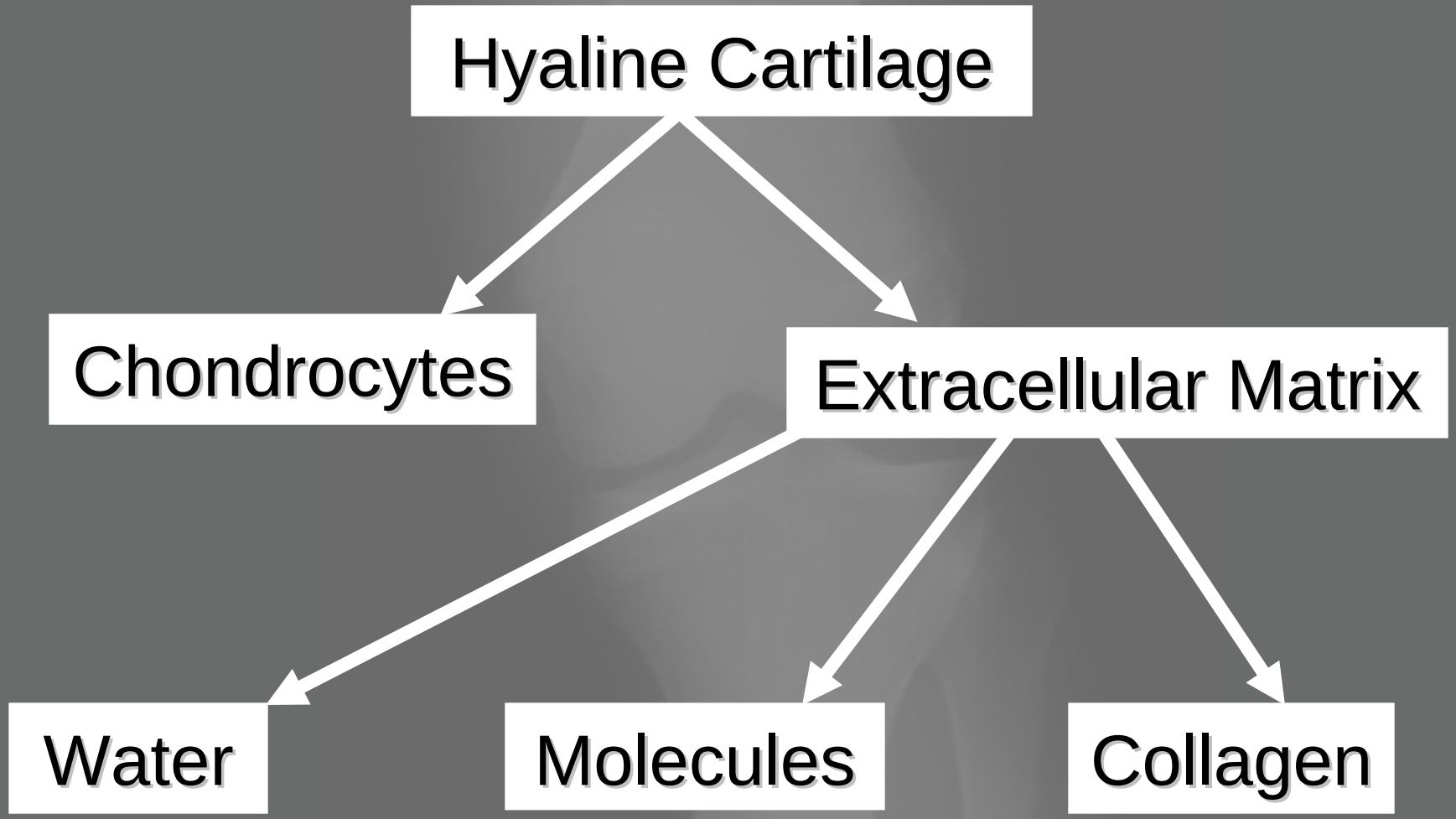
Collagen

- Protein
- Hyaline cartilage mainly consists of collagen II, IX and XI
- Function
  - Resist tensile forces
  - Provides meshwork for other molecules

(Gartner and Hiatt, 2007)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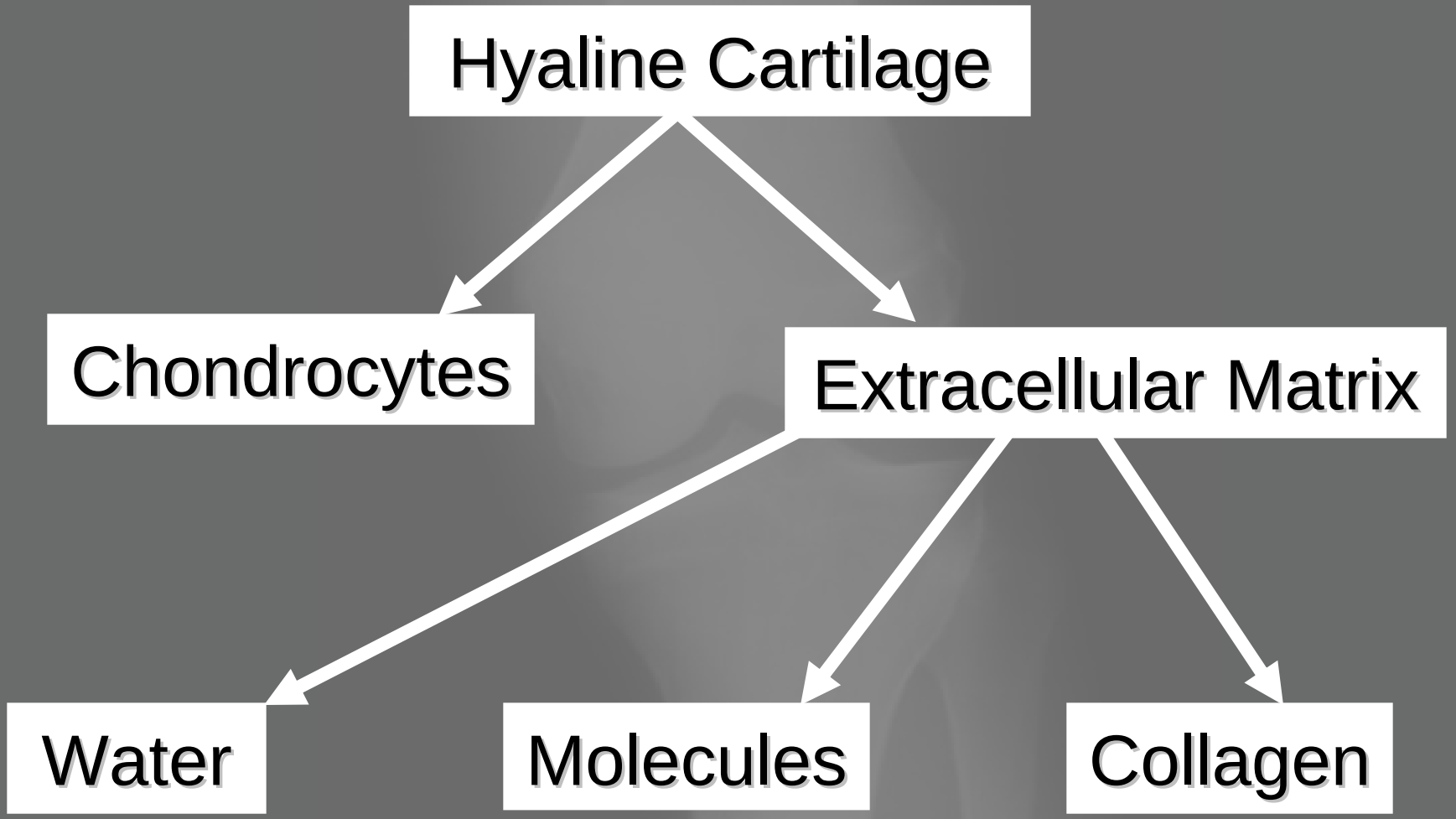
Molecules

- Proteoglycans (PG)
  - Resist compression, retard movement, bind molecules
  - e.g. aggrecan
- Glycosaminoglycans (GAG)
  - Resist compression
  - e.g. hyaluronic acid, chondroitin sulphate
- Glycoproteins
  - Assist cells in adhering to matrix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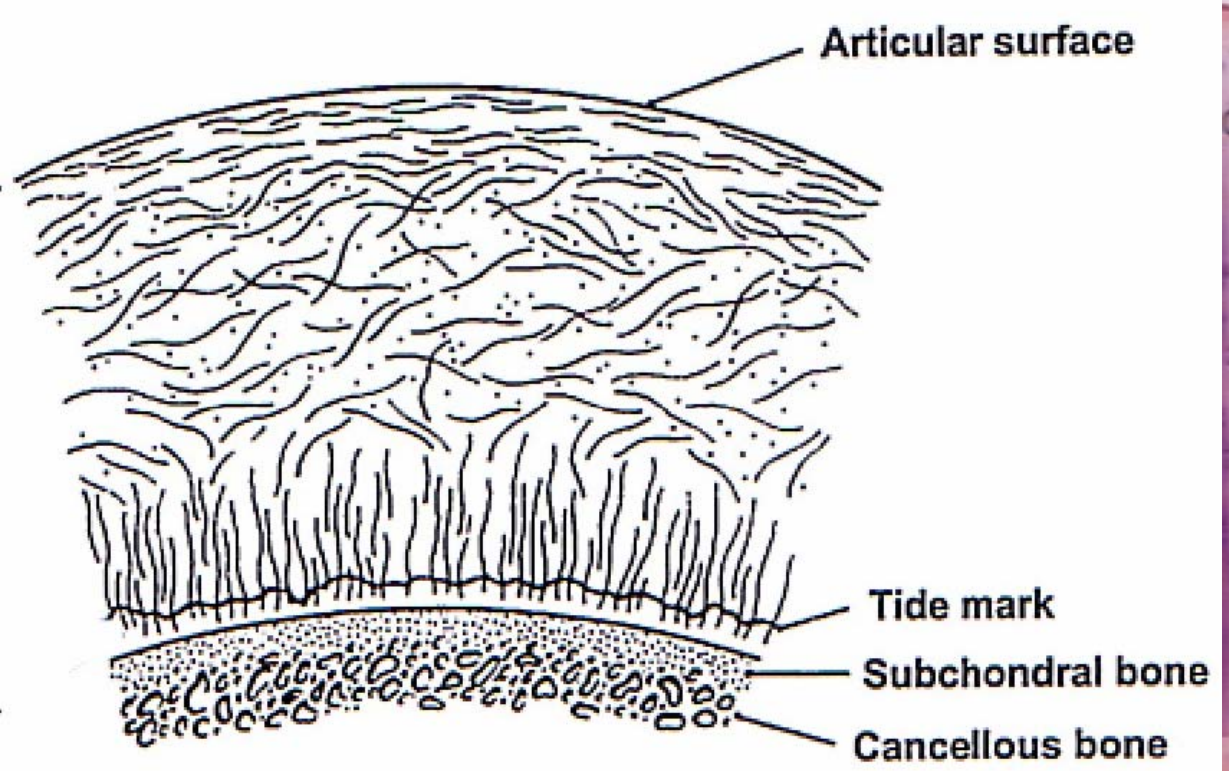
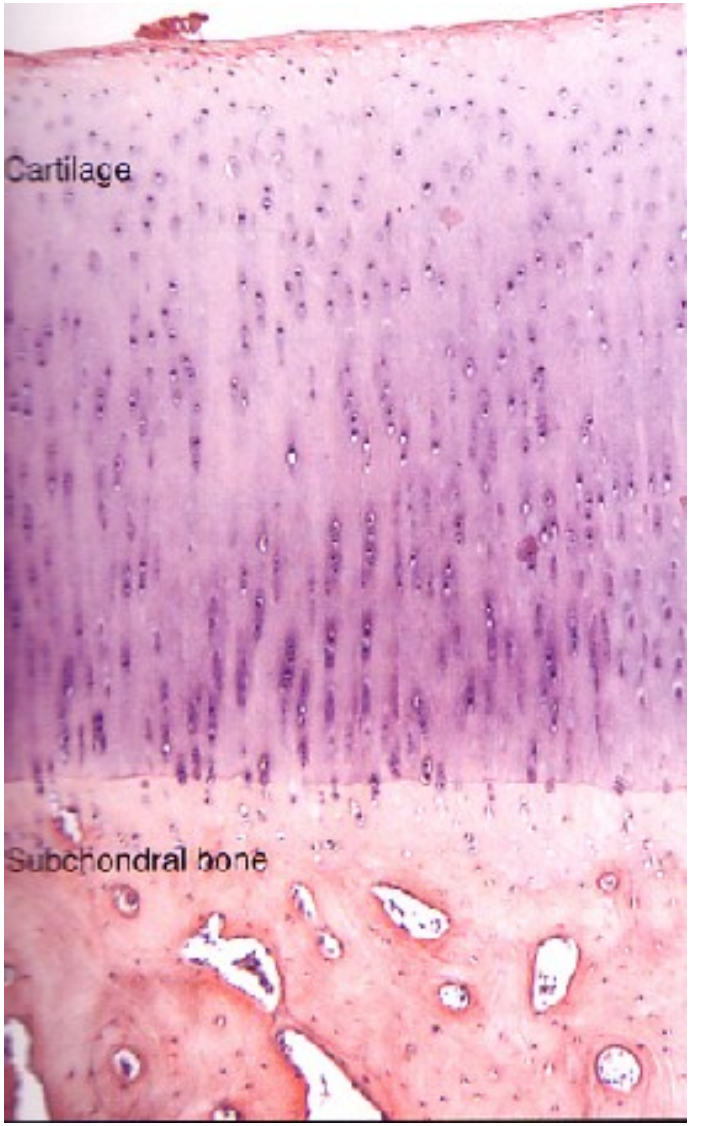
Water

- 65 to 80% weight of hyaline cartilage

- Function
  - Nutrient transport
  - Resist compression

(Gartner and Hiatt, 2007)

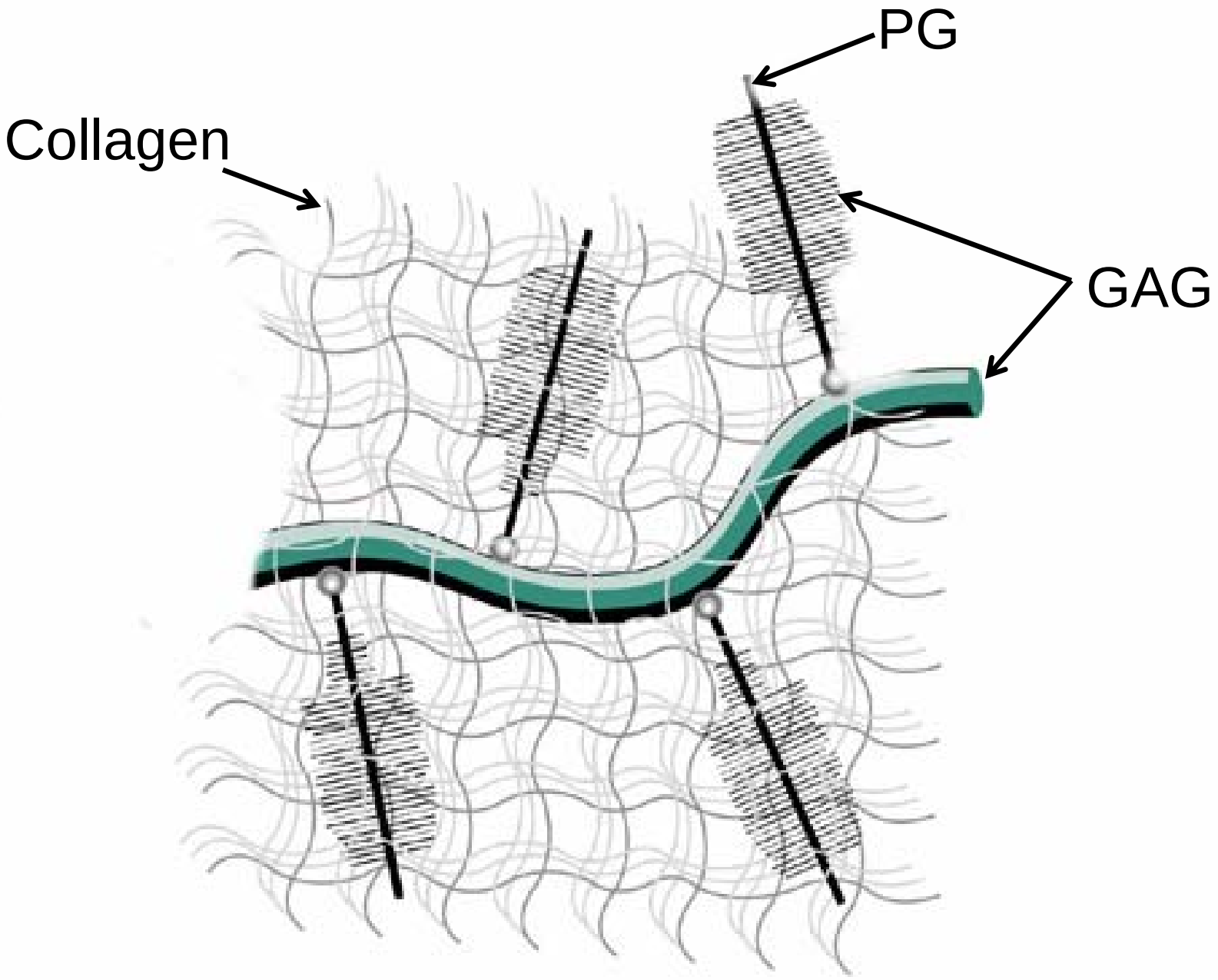




(Flik et al., 2007; Sharma and Berenbaum, 2007)

Cartilage

- How does it work?



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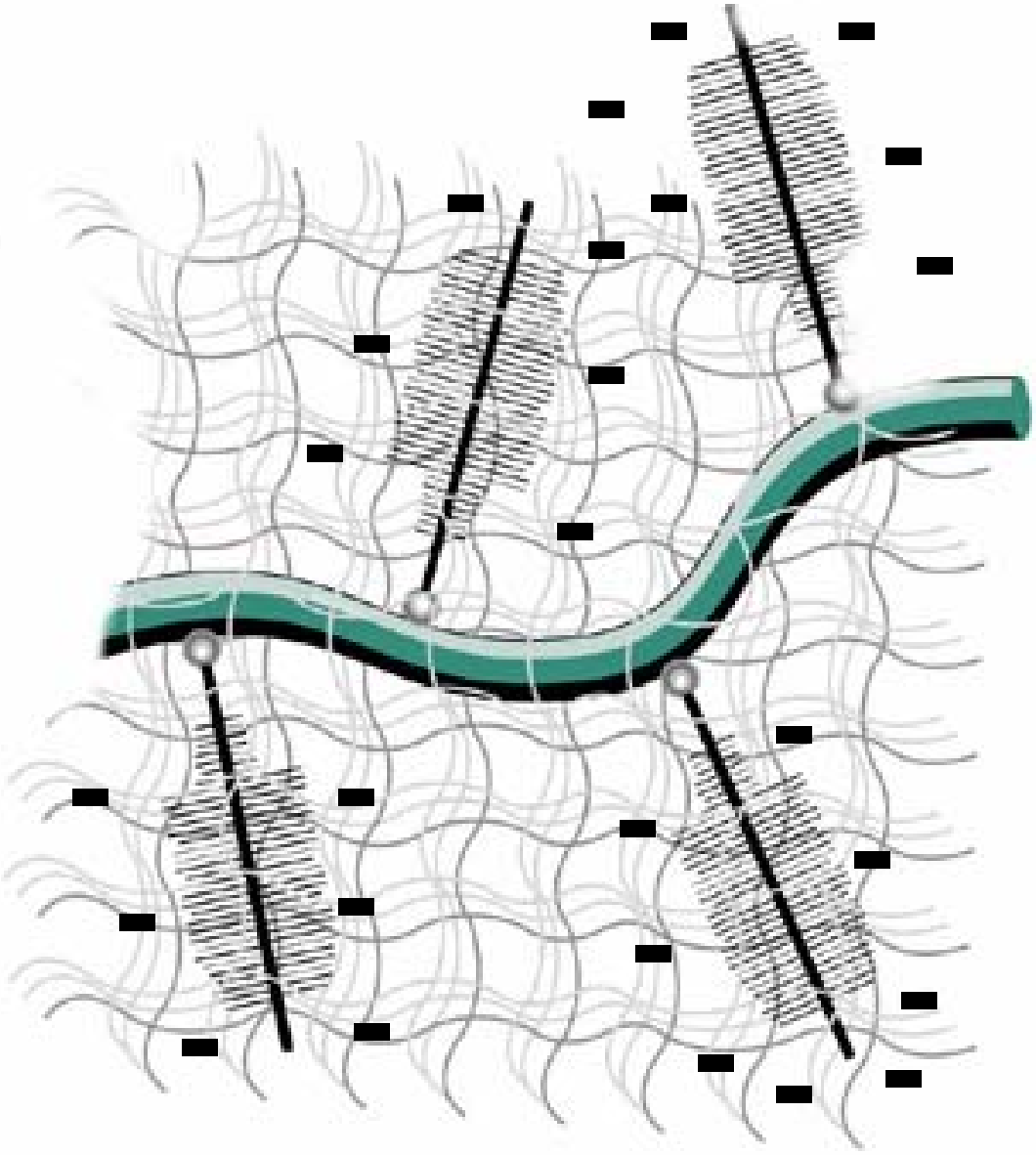
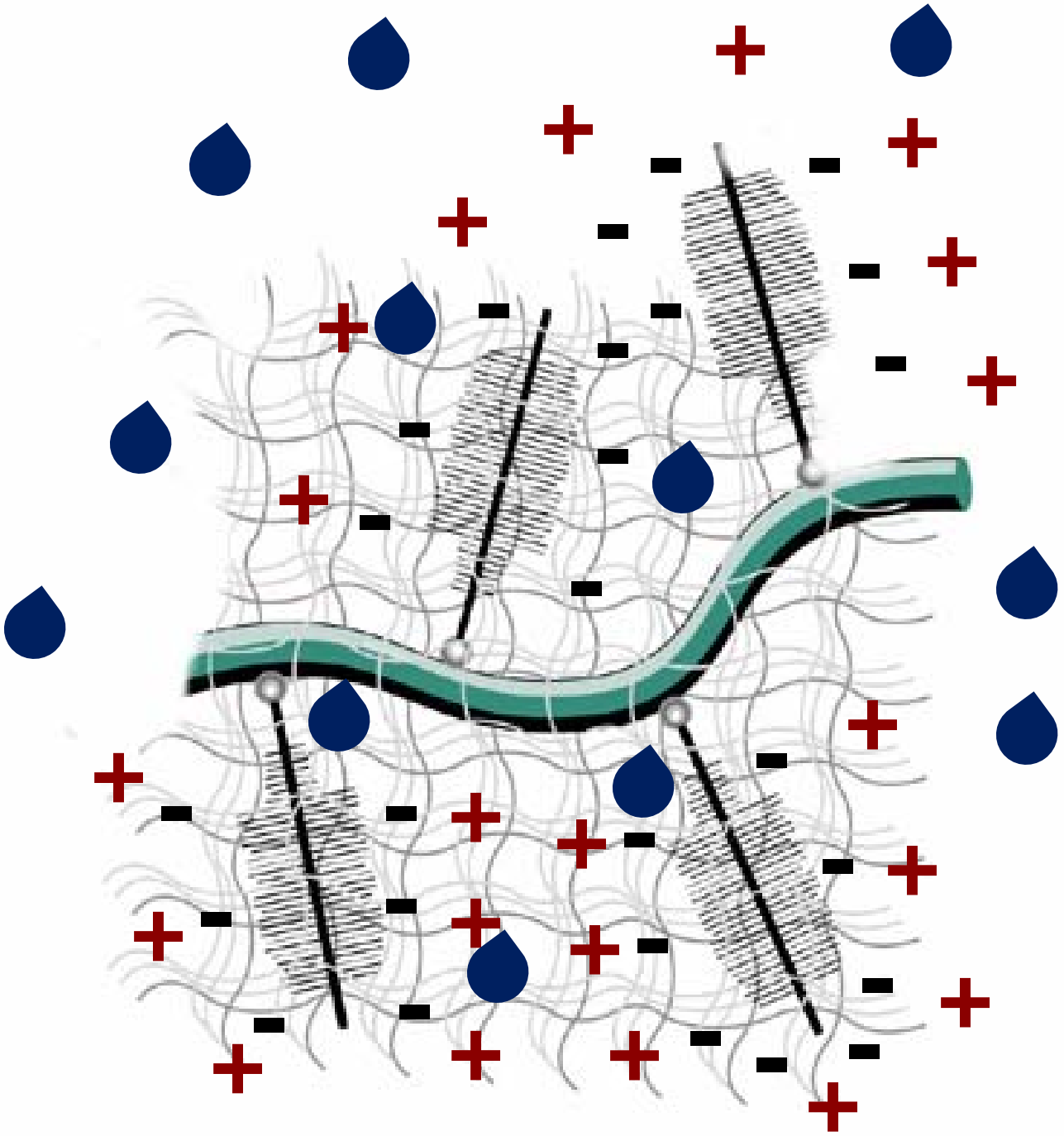
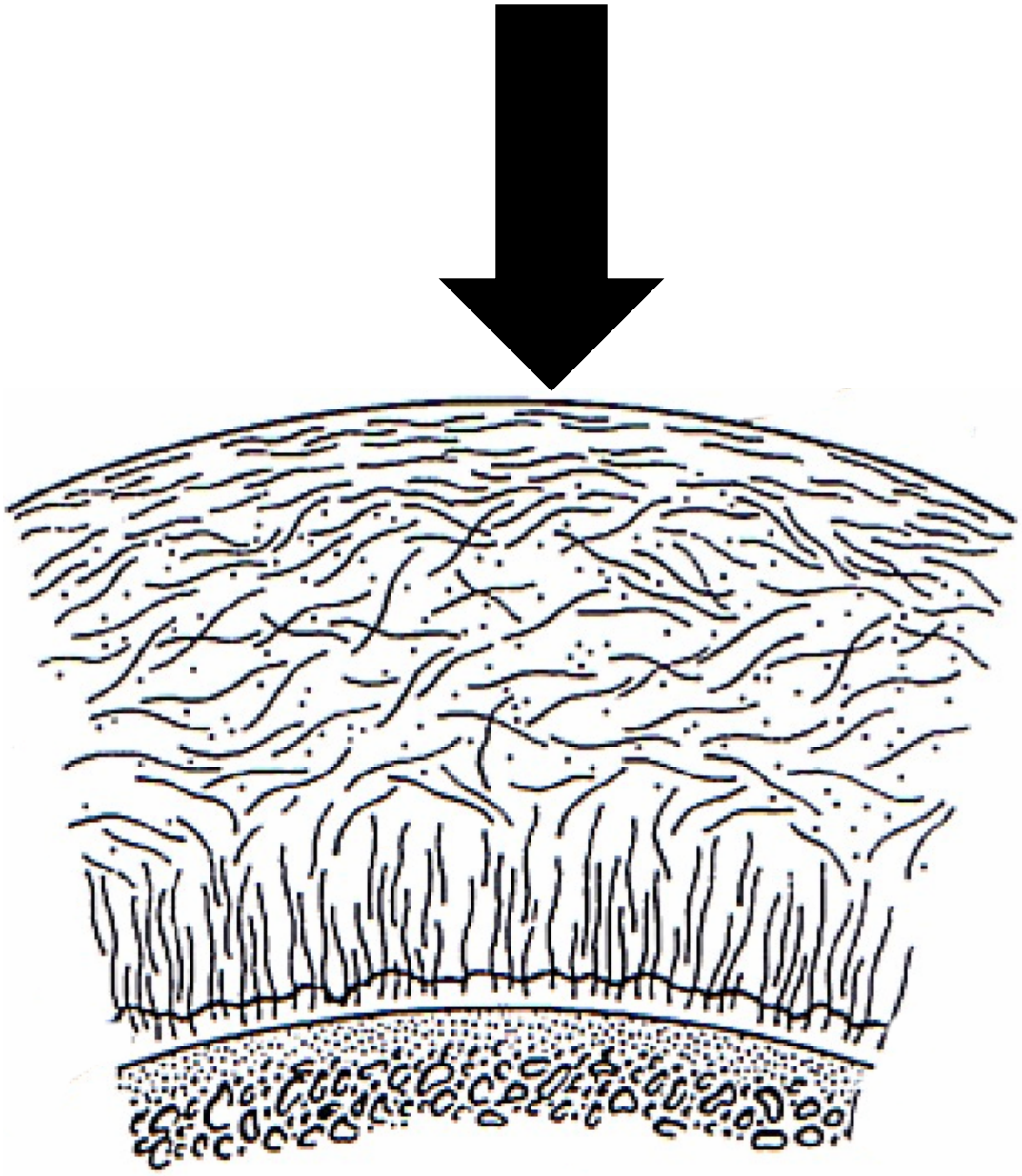
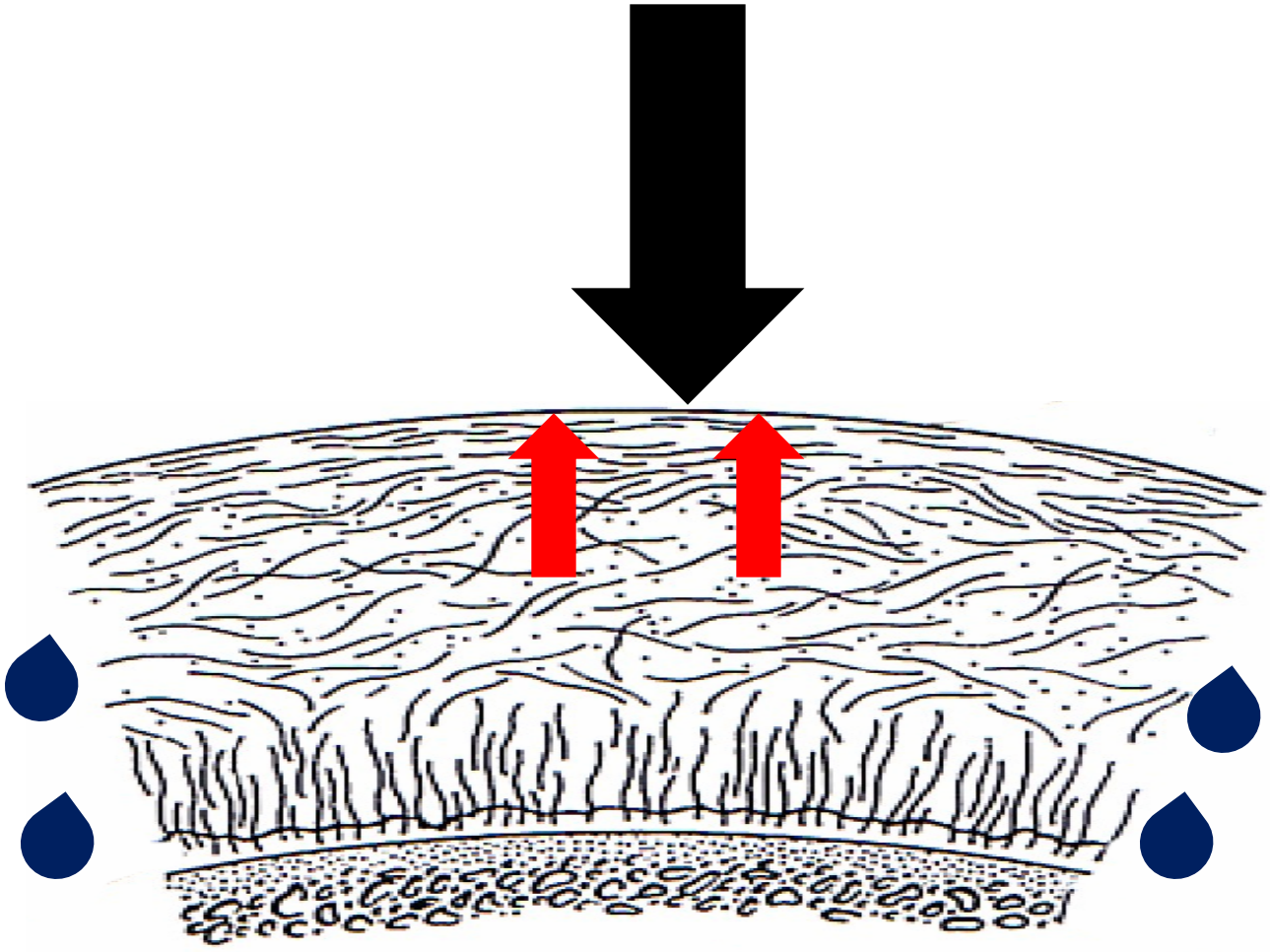
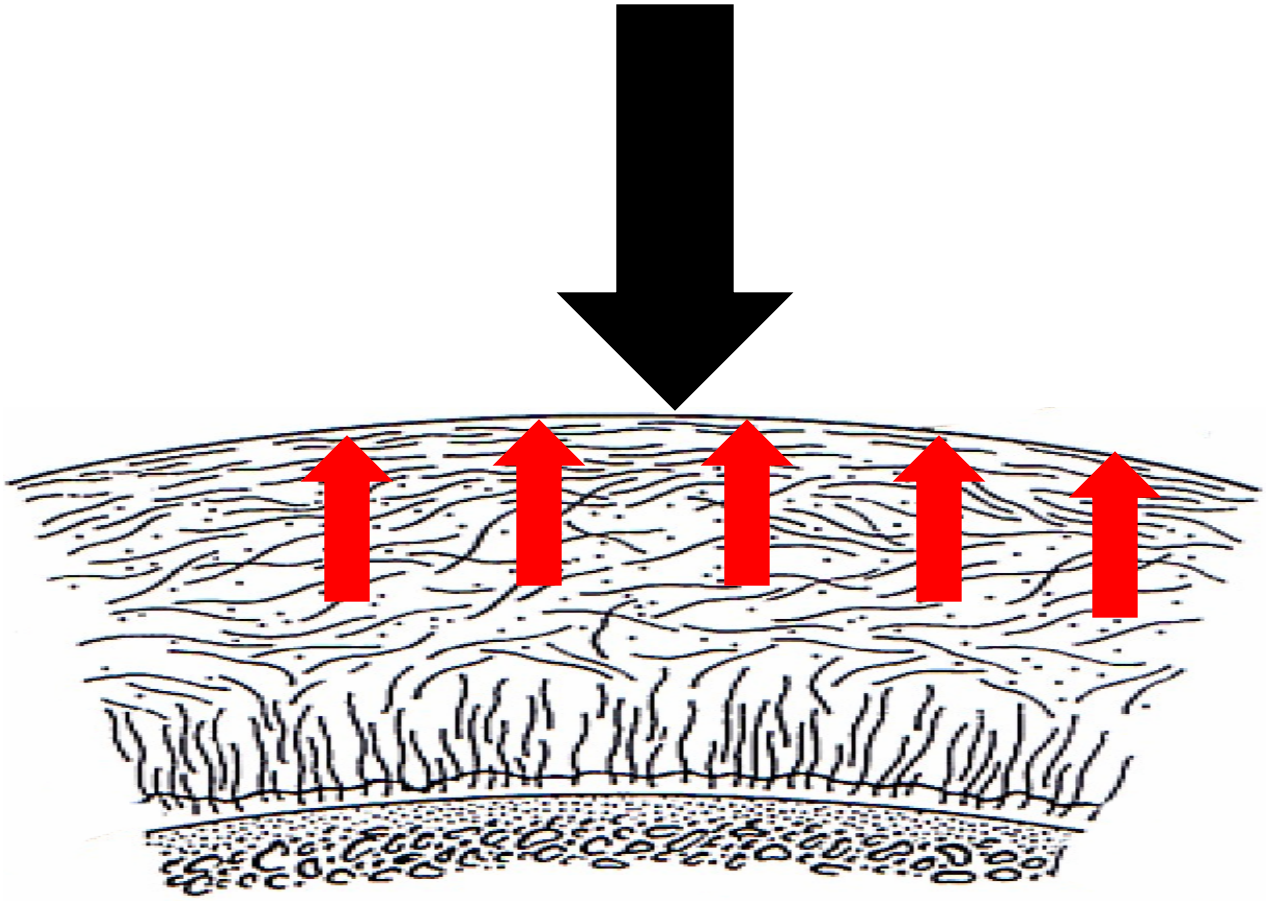
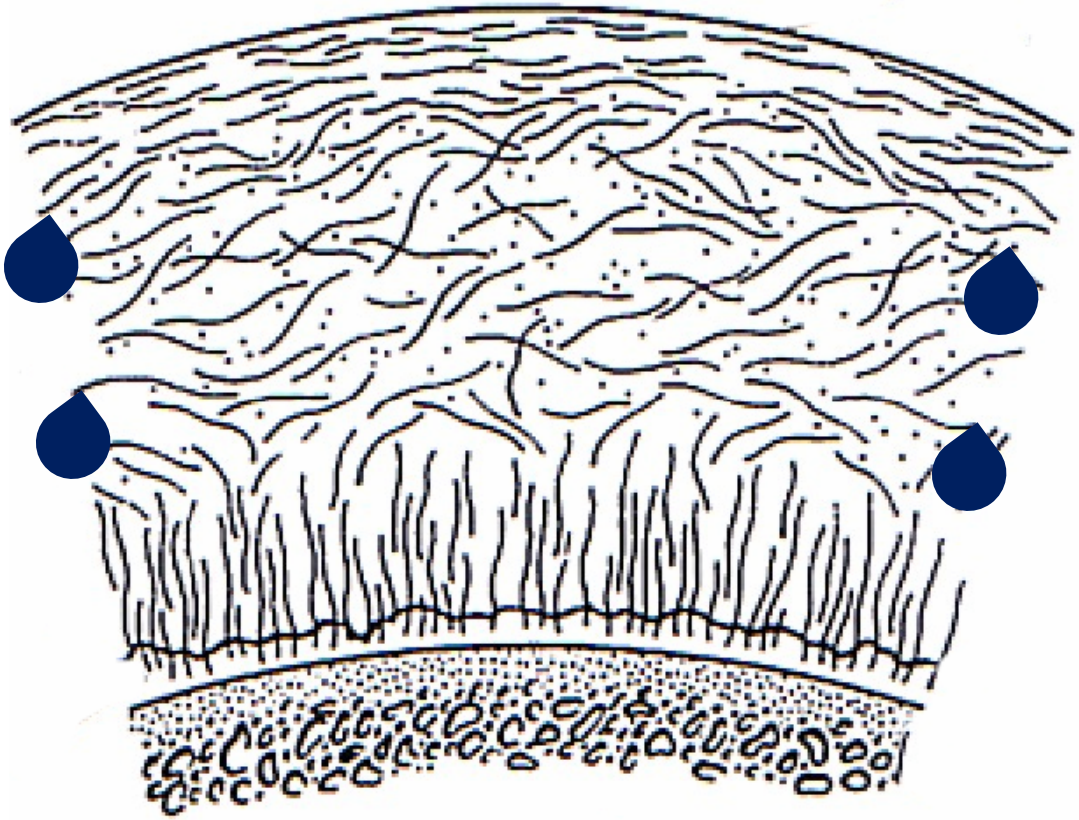












Bone

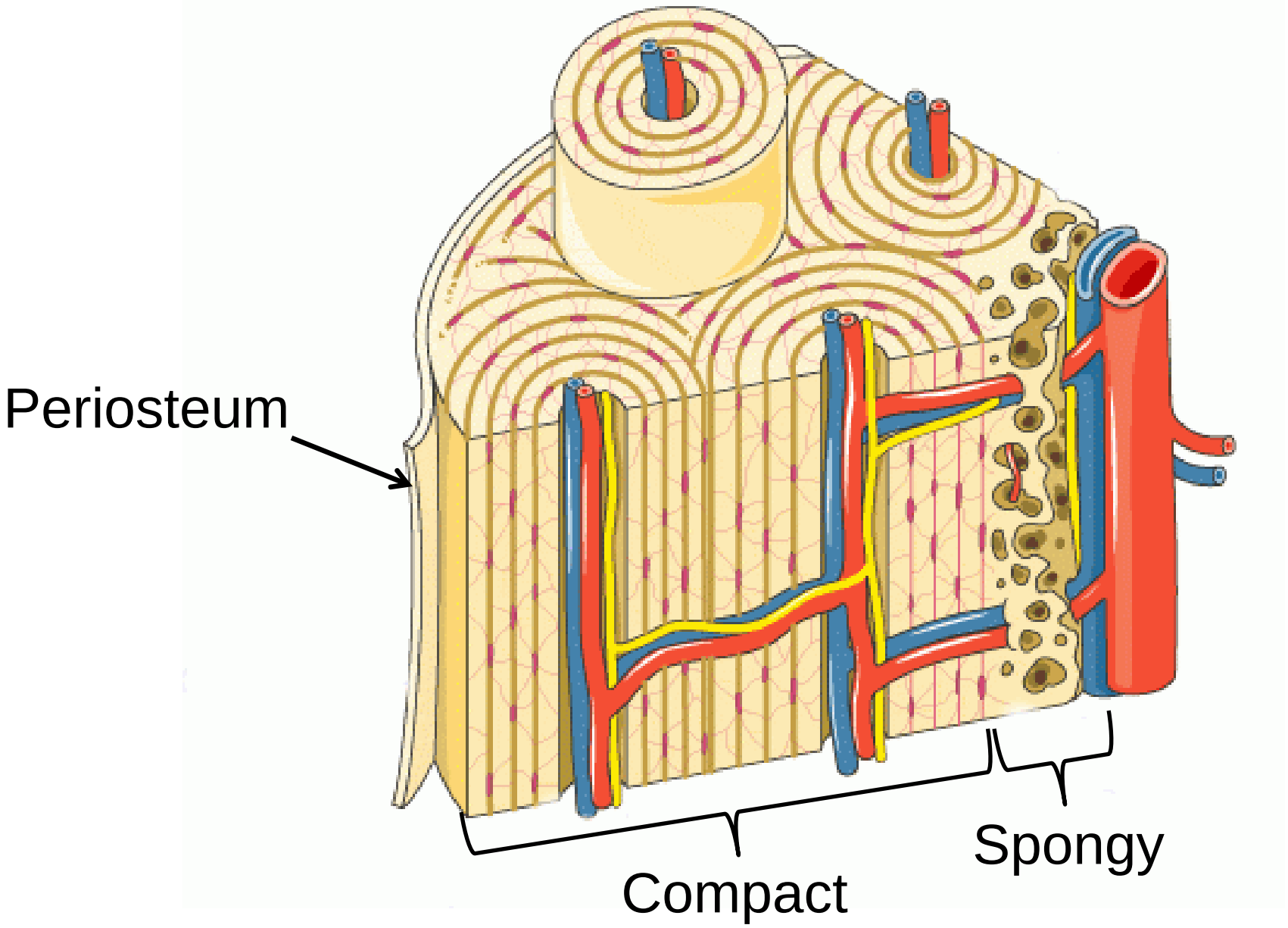
- Cells: osteoblasts, osteocytes, osteoclasts
  - Maintain and turnover bone
- Inorganic component
  - Calcium and phosphorous crystals
- Organic component
  - Collagen I, GAG, PG, glycoproteins

(Gartner and Hiatt, 2007)

Bone Layers

- Periosteum
  - Outside of bone, noncalcified collagen
  - Not present at articular ends
- Compact bone
  - Dense, composed of lamellae
  - Thin layer at articular ends
- Spongy/ cancellous
  - Porous, lines marrow cavity

(Gartner and Hiatt, 2007)



http://www.iofbonehealth.org/osteofound/cache/img

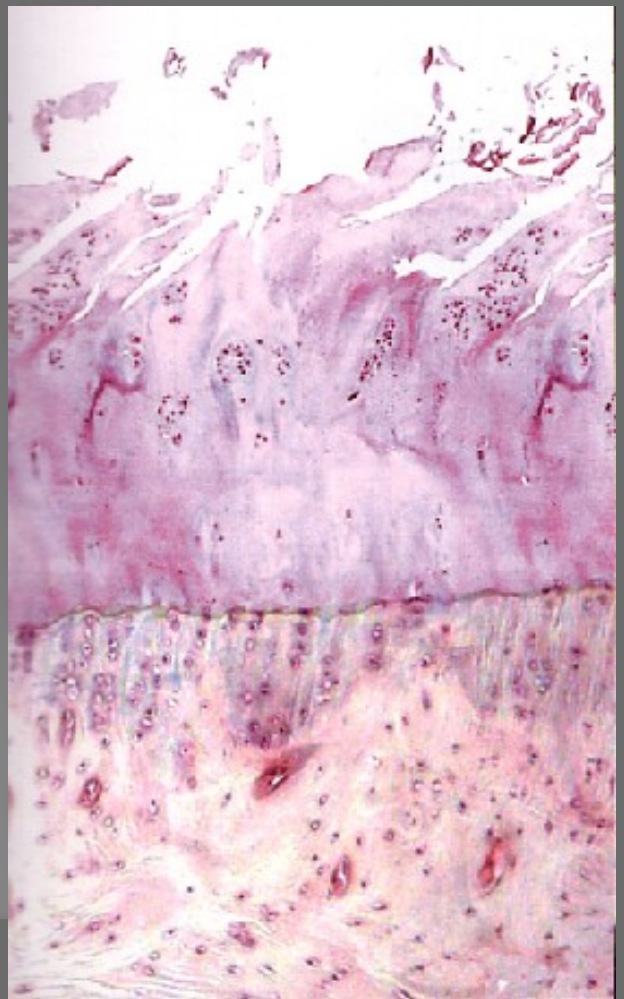
Subchondral Bone

- Subchondral plate 0.1 to 3.0 mm thick
- Extends from tidemark to marrow
- Consists of calcified cartilage and compact bone
- Highly vascular
- Nerve fibers
- Functions as shock absorber

(Brandt et al., 2003)

OA

- What happens in OA?



Early OA- Cartilage

- Fibrillation of superficial cartilage
- Advancement of blood vessels
- Increase in water- increase permeability and decrease stiffness
- Weakening of matrix

(Lorenz and Richter, 2006)

Early OA- Cartilage

- Chondrocytes- cluster, hypertrophic, change in gene expression
- Change in collagen content
- Loss of PG and decrease in size
- Decrease GAG size
- Increase in “breakdown” enzymes
- Imbalance of repair/breakdown

(Appleton et al., 2006; Lorenz and Richter, 2006)

Late OA- Cartilage

- Deep fissures to bone
- Invasion of blood vessels
- Hyaline cartilage replaced by bone, fibrocartilage
- Unclear tidemark
- Decrease in water

(Lorenz and Richter, 2006)

Late OA- Cartilage

- Chondrocytes disappear
- Change in collagen content
- Loss of PG, GAG
- Replace by smaller PG
- Increase in “breakdown” enzymes

(Lorenz and Richter, 2006)

OA- Cartilage

- Microscopic changes (Sharma and Berenbaum, 2007) :

OA- Bone

- Increase vascularity
- Initial increase in bone formation rate followed by decrease
- Imbalance of bone formation/ resorption
- Increase thickness and density
- Increase stiffness, decrease shock absorption

(Brandt et al., 2003)

OA- Bone

- Joint space narrowing
  - Cartilage loss
- Subchondral sclerosis
  - Increase bone density
- Subchondral cyst
  - Cavity
- Osteophytes
  - Bony outgrowths

(Brandt et al., 2003)

www.yorkshirekneeclinic.co.uk/knee-arthritis-treatment.htm

Synovium

- Lines the articular joint
- Cells- Fibroblasts and macrophages
- Secretes synovial fluid
- Molecules- lubricin, hyaluronic acid
- Lubricates joint, decrease friction
- Hydrodynamic lubrication

(Brandt et al., 2003)

OA- Synovium

- Hyperplasia, thickening and fibrosis of synovium
- Edema
- Increase in hyaluronic acid
- Bone and cartilage fragments
- Increase in chemical mediators
- Imbalance of destructive and inhibitor molecules

(Brandt et al., 2003; Lorenz and Richter, 2006)

OA- Meniscus

- Meniscus- fibrocartilage
- Disruption of collagen fibers
- Degenerative tears
- Increase in cells next to tear
- Synthesis of collagen
- Vascularization at margins

(Brandt et al., 2003)

OA- Joint Capsule/ Ligaments

- Capsule and ligaments
  - Collagen I and fibroblasts
- Capsule
  - Edema, increase PG, fibrosis
  - Laxity or stiff
- Ligaments
  - Laxity or stiff

(Brandt et al., 2003; vander Esch et al., 2006)

OA- Muscle

- Muscle atrophy and lower cross-sectional area
- Quadriceps and hamstring weakness
- ? Weakness leads to disease progression
- Decrease voluntary muscle activation
- Increased co-activation of quadriceps and hamstring

(Diracogul et al., 2009; Fink et al., 2007; Gartner and Hiatt, 2007; Hortobagyi et al., 2005; Hubley-Kozey et al., 2009; Petterson et al., 2008; Slemenda et al., 1997)

But.....what do we see?

OA- ROM

- Decrease in range of motion (ROM) in OA
- ROM related to disease severity and self-report disability

(Arokoski et al., 2004; Ersoz and Ergun, 2003; Steultjens et al., 2000)

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OA- Proprioception

- Proprioception = joint position sense
- Sensory signals from receptors in muscles, tendons, joint capsule, ligaments, skin
- Impaired proprioception in OA
- Proprioception defects influences OA?

(Lund et al., 2008; Sharma, 2003)

OA- Pain

- Higher self-report pain levels
- Radiological OA not related to pain
- Innervated structures: synovium, capsule, bone, tendons, ligaments
- Sensitization of pain fibres by chemical mediators
- Psychogenic pain

(Hubley-Kozey et al., 2009; Kidd, 2003)

OA- Gait

- Decreased gait speed
- Decreased step length
- Increase loading in medial knee compartment
  - Related to progression of OA
- Compensations to reduce loading
  - Toe-out, trunk lean

(Hubley-Kozey et al., 2009; Hunt et al., 2008; Miyazaki et al., 2002; Thorp et al., 2006)

OA- Function/ Physical Activity

- Decreased self-report function
- Lower average and peak physical activity
- Decrease time spent in vigorous activity
- Do not achieve recommended level of physical activity

(Farr et al., 2008; Hubley-Kozey et al., 2009; Murphy et al., 2008; Vignon et al. 2006)

OA- Participation

- Individuals with OA not satisfied with time spent participating in “social roles”
  - Physical leisure, travel, social events

(Gignac et al., 2008; Machado et al., 2008)

Conclusion

- Osteoarthritis (OA) affects the whole “knee joint organ” – Not just cartilage!
  (Hunter and Felson, 2009)

- OA:

  “…joint diseases characterized by repetitive response to injury with subsequent regenerative, reparative, and degenerative structural changes in all tissues of the joint…”
  (Prizker, 2003)

Conclusion

Cartilage

Synovium

Joint Capsule

Ligaments

Muscle

Bone

Meniscus

?

Function

ROM

Gait

Participation

Proprioception

Pain

Strength

Physical Activity

Questions