OSTEOARTHRITIS – BASIC SCIENCES

Cartilage

Features

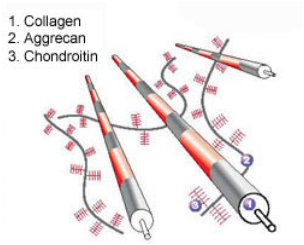
Avascular, alymphatic and aneural tissue
Smooth and resilient
Dissipates shearing and compressive forces uniformly

Constituents

70-80%	Liquid	Water
20-30%	Solid	Extracellular matrix
2%	Cellular	Chondrocyte

Extracellular matrix

Highly hydrated combination of proteoglycans and non-collagenous proteins immobilized within a type II collagen network that is anchored to bone



Glycosaminoglycans

Long unbranched polysaccharides (GAGS)

Repeating disaccharide unit either of two modified sugars N-acetylgalactosamine (GalNAc) or N-acetylglucosamine (GlcNAc) and a uronic acid such as glucuronate or iduronate.

Highly negatively charged molecules

Located primarily on the surface of cells or in ECM

High viscosity and low compressibility

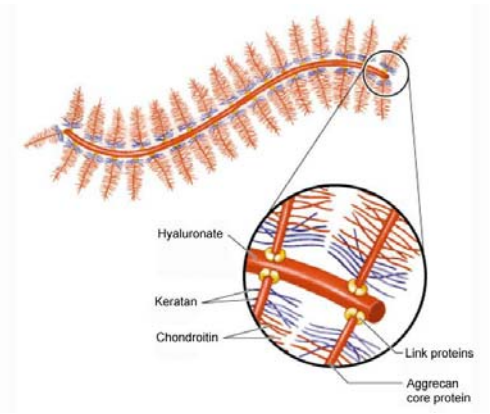
Examples are hyaluronic acid, dermatan sulfate, chondroitin sulfate, heparin, heparan sulfate, and keratan sulfate

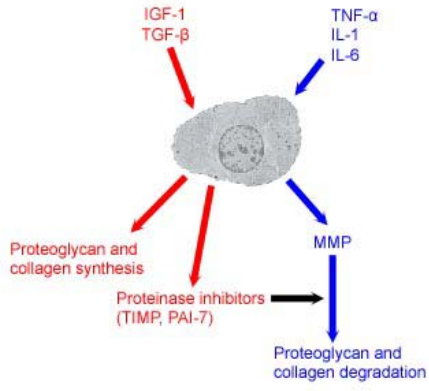
The majority are linked to core proteins, forming proteoglycans

Extend perpendicularly from the core in a brush-like structure

Proteoglycan

Aggrecan constitutes the major component in articular cartilage
Hyaluronan-binding domain near its amino terminal
[Aggrecan monomers **–** Hyaluronic acid **–** Link protein]





Collagen

Principally type II, also types IX and XI
Collagen network very stable
Stability accentuated by cross-linking that increases with age

Chondrocytes

Embedded in ECM
Dependant on diffusion for nutrients
Responsible for metabolism of ECM
Secrete degradative matrix metalloproteinases (MMP)

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Biology

Normal cartilage metabolism is a highly regulated balance between synthesis and degradation of the various matrix component

Balance is effected by a number of matrix metalloproteinases (MMP) which in turn are inhibited by tissue inhibitors of metalloproteinases (TIMP) and plasminogen activator inhibitor-7

Drivers

Synthetic	Insulin like growth factor 1
	Transforming growth factor-β
Degradative	Interleukin-1 and 6
	Tumour necrosis factor-α

Effectors

Proteases	**Inhibitors**
Collagenase (MMP-1)	TIMP-1
Gelatinases (MMP-2)	α2-Macroglobulin
Stromelysins (MMP-3)	TIMP-2
Aggrecanases	

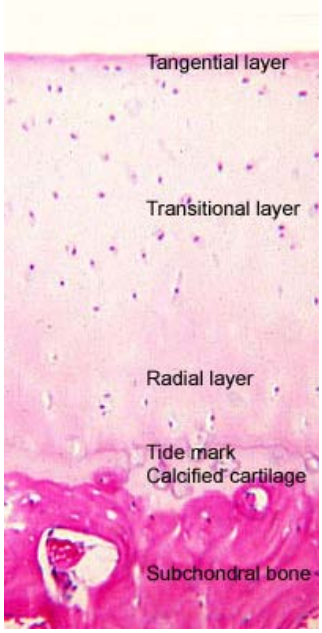
Structure

Tangential
Four morphologically distinct zones
Flattened chondrocytes
High collagen:proteoglycan ratio
High water content.
Collagen fibrils parallel to articular surface
High tensile stiffness

Transitional
Small spherical chondrocytes
Higher proteoglycan
Lower water content
Collagen fibrils bend to form arcades

Radial
Proteoglycan content highest
Collagen oriented perpendicularly
Chondrocytes are largest and most active

Calcified
Thin layer
Cartilage attached to subchondral bone



Function

Critically dependent on composition of ECM

On compression, water and solutes are expressed until repulsive forces from proteoglycans balance load applied

On unloading, proteoglycans rehydrate restoring shape of cartilage

Loading and unloading important for the exchange of proteins in extracellular matrix and thus to chondrocytes

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Osteoarthritis

Summary

Osteoarthritis is a multifactorial process in which mechanical factors have a central role and which is characterized by changes in structure and function of the whole joint organ.

Pathogenesis

The equilibrium between anabolism and catabolism altered

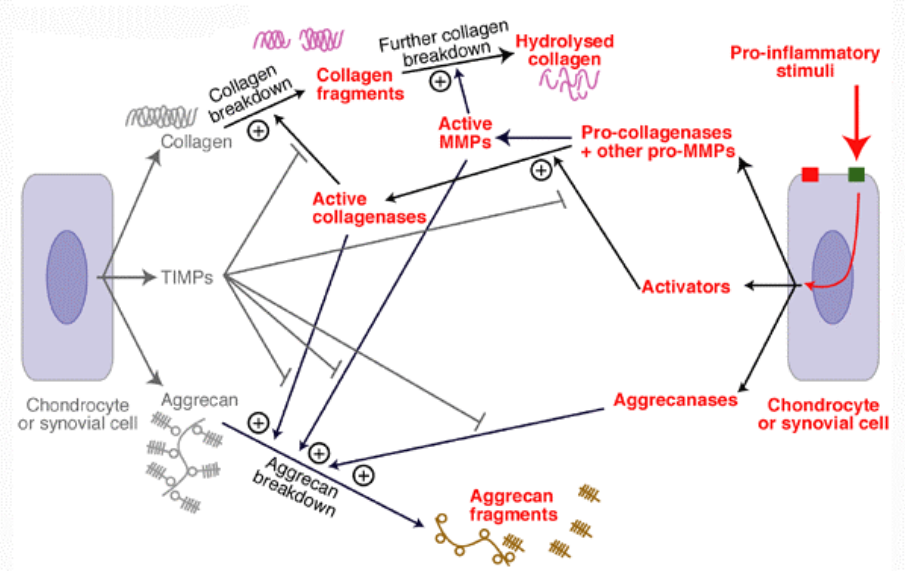
Primary lesion appears to occur in cartilage

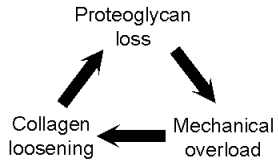
Disruption of the integrity of the collagen network allows hyperhydration and reduces stiffness of cartilage

Fibrillation, fissures, ulceration and disappearance

Leads to inflammation in synovium due to release of breakdown products

Changes in subchondral bone, capsule and periarticular muscles



Scope	Molecular Macromolecular Microscopic Macroscopic	Proteoglycan depletion Network loosening Fissuring Cartilage erosion	

Microscopic features	Irregular thickness Surface fibrillation Fissures Increased cellularity Altered matrix staining	
Causation	Multifactorial Age related	
Primary	Age Racial Sex Obesity Genetic	Non-linear increase F>M (>55yr) Hand & Knee Hip & knee
Subsets	Primary generalised (PGOA) Erosive (inflammatory) (EOA)	DIPJ, TMCJ, Hip PIPJ

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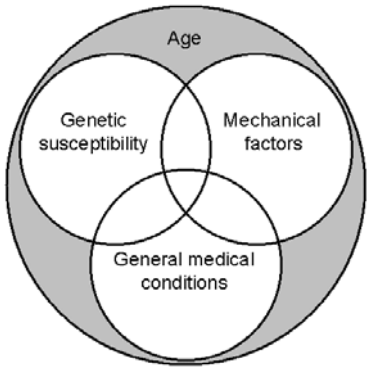
Genetics

Up to 65% of the variance in osteoarthritis of the hand and knee in women in twins being explained by genetic factors.

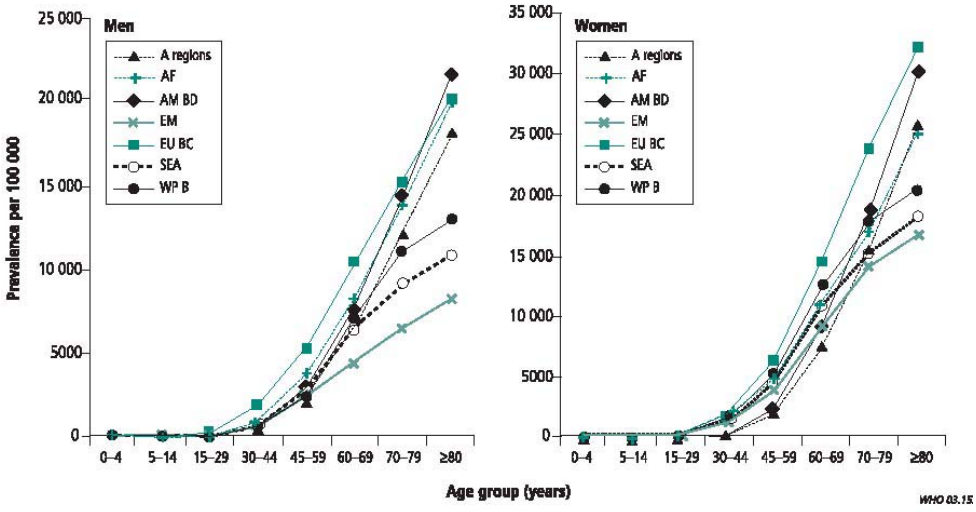
Secondary



Metabolic	Chondrocalcinosis Gout Hemochromatosis Amyloidosis Acromegaly Hyperparathyroidism Ochronosis (alkaptonuria) Wilson's disease
Anatomical	Congenital anomaly, dysplasia Joint instability Muscle weakness Paget's disease
Traumatic	Joint injury or surgery Osteonecrosis Overuse (occupational) Osteochondritis
Inflammatory	Rheumatoid and sero-negative arthropathy Septic arthritis
Other	Neuropathy Hemophilia Diabetes Hyperlaxity syndromes Ehlers-Danlos disease

Incidence

A=Developed countries, AF=Sub-Saharan Africa, AMBD=Developing counties in Americas, EM=Eastern Mediterranean, EUBC= Developing counties in Europe, SEA=South East Asia, WPB=Western Pacific



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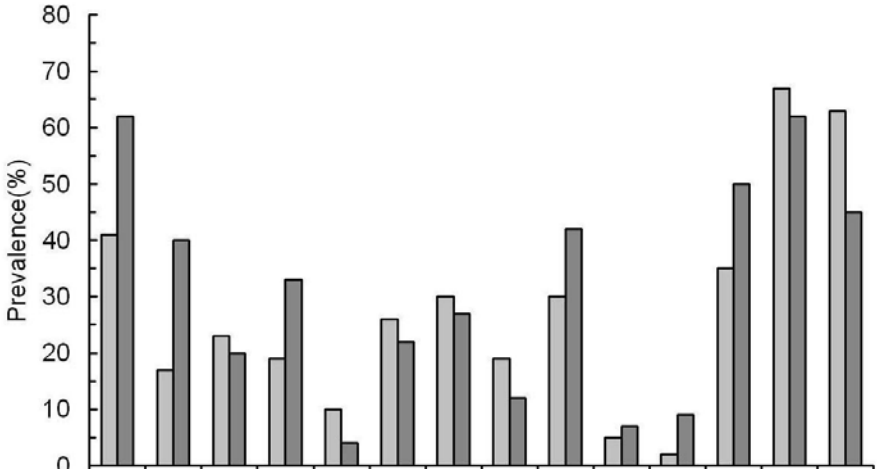
Distribution

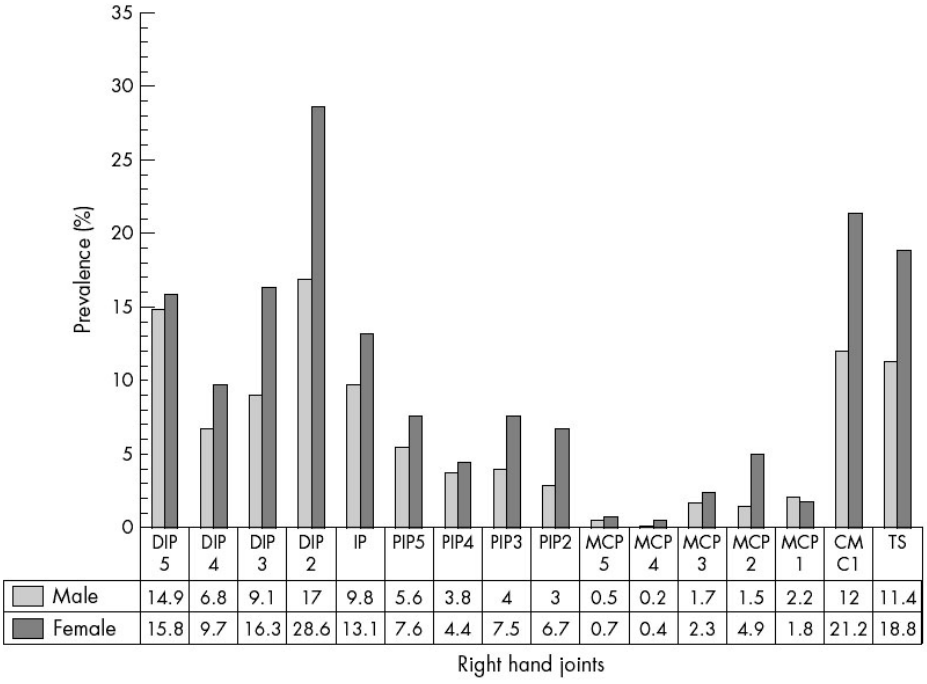
UK radiological survey, 55-64 age group, 204 males & 277 females
Involvement at one or more joints in 83%M and 87%F (ns)
Involvement of more than three joints 29%M and 47%F (p<0.001)



	DIPJ	PIPJ	MCPJ	TMCJ	Wrist	Cervical spine	Lumbar spine	Hip	Knee	Tarsi	MTPJ (2-5)	MTPJ (1)	Cervical disk	Lumbar disk
Male	41	17	23	19	10	26	30	19	30	5	2	35	67	63
Female	62	40	20	33	4	22	27	12	42	7	9	50	62	45

Hand distribution

Prevalence of radiographic osteoarthritis (K-L grade≥2) in the hand joints of men and women ≥50yrs (mean=67, n=3906).



	DIP 5	DIP 4	DIP 3	DIP 2	IP	PIP5	PIP4	PIP3	PIP2	MCP 5	MCP 4	MCP 3	MCP 2	MCP 1	CM C1	TS
Male	14.9	6.8	9.1	17	9.8	5.6	3.8	4	3	0.5	0.2	1.7	1.5	2.2	12	11.4
Female	15.8	9.7	16.3	28.6	13.1	7.6	4.4	7.5	6.7	0.7	0.4	2.3	4.9	1.8	21.2	18.8

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Presentation

Swelling
Nodules & cyst formation
Tenderness
Pain
Stiffness
Deformity
Crepitus
Tendon rupture

Diagnosis

Clinical examination
Radiograph
Bone scan
Arthroscopy

Diagnosis

American College of Rheumatology Diagnostic Criteria for OA

Hand pain, aching, or stiffness and 3 or 4 of the following features:

- Hard tissue enlargement of 2 or more of 10 selected joints*
- Hard tissue enlargement of 2 or more DIP joints
- Fewer than 3 swollen MCP joints
- Deformity of at least 1 of 10 selected joints

* The 10 selected joints are the second and third DIPJ, the second and third PIPJ, and the first CMCJ of both hands. This classification method yields a sensitivity of 94% and a specificity of 87%.

Radiology

Osteophytes on the joint margins
Periarticular ossicles
Narrowing of joint cartilage
Sclerosis of subchondral bone
Pseudocysts with sclerotic wall
Altered shape of bone ends

Grading (K&L)

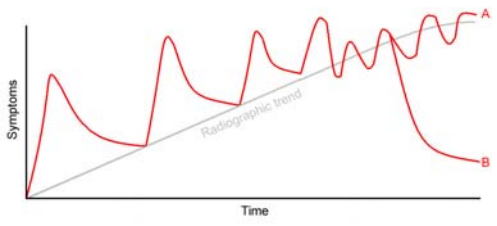
0	None
1	Doubtful
2	Minimal
3	Moderate
4	Severe

Progress

Symptomatic progress unpredictable and non-linear
Exacerbations due to microtrauma?
Symptoms not necessarily equivalent to radiographic signs
A: Continued severe symptoms
B: Symptomatic resolution due to ankylosis

Joints affected

DIPJ
PIPJ
MCPJ
TMCJ
STT
Radio-carpal
Distal radio-ulnar
Piso-triquetral
Other



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Treatment

Activity modification
Splint
Aids
Physiotherapy
Glucosamine
Analgesic and NSAID
Steroid injection
Hyaluronic acid injection
Surgery

Indications

Pain
Deformity
Stiffness
Appearance

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