



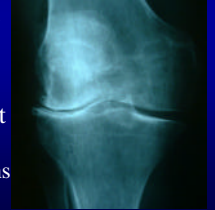
The Arthritic Knee in the Aging Athlete

Brian McKeon, MD



Osteoarthritis

- The Problem
- Arthritis affects all age groups
 - Approximately 50% of people >50 y.o. report arthritic symptoms
- Almost 40 million people/year require treatment in the United States
 - By 2020, 60 million Americans estimated to be affected by arthritis



OA

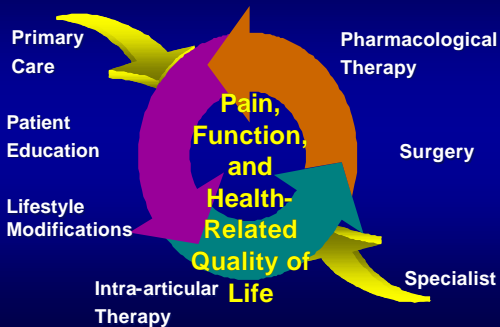
- Osteoarthritis is 2nd leading diagnosis resulting in disability expense in the United States (heart disease is 1st)
 - 315 million physician visits per year
 - 8 million hospital admissions per year
 - 17 million people with activity limitation
 - 1.5 billion days of restricted activity per year

OA

- Estimated cost of treatment for arthritis:
 - Direct medical costs: \$72.3 billion
 - Indirect costs (lost wages): \$77.1 billion
 - Total costs: **\$149.4 billion** (2.5% of GNP)

Data from 1990-1992; Yelin, Callahan. Arthritis Rheum. 1995;38:1351-1362.

An Integrated Approach to Knee OA Management



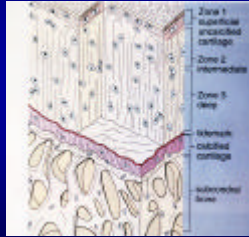
Basic Science

- Articular Cartilage
 - Simple in appearance
 - Avascular
 - Aneurial
 - Alyphatic
 - Low metabolic activity
 - One cell type



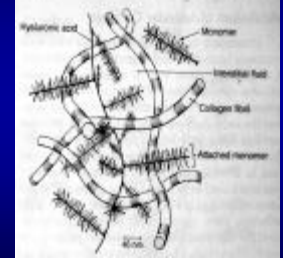
Basic Science

- Articular Cartilage
 - Composition
 - Water 60-80%
 - Moves freely in matrix
 - Imp materials properties and surface fxn
 - ECM 20-40%
 - Chondrocytes 1%
 - Zones
 - Composition varies with depth



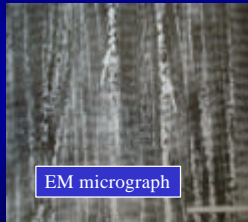
Basic Science

- Extracellular matrix
 - Collagens 60%
 - Proteoglycans 25-30%
 - Non-collagenous proteins 15-20%



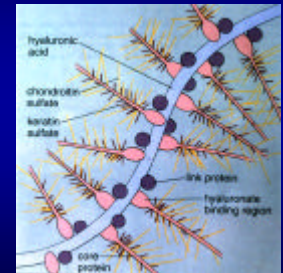
Basic Science

- Collagen "Arcade Structure"
 - Type II 90-95%
 - Form fibrils
 - Type IX, XI
 - Stabilize fibrils
 - Type VI
 - Surround chondrocytes
 - Type X
 - Calcified cartilage



Basic Science

- Aggrecan
 - Very Large 200 X 10⁶ D
 - Hyaluronic Acid backbone
 - Glycosaminoglycans
 - Protein core
 - Chondroitin sulfate
 - Keratin sulfate
 - Dermatin sulfate
 - Negative charge



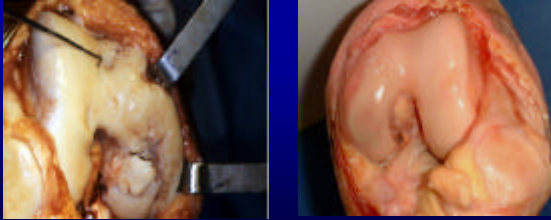
Basic Science

- Synovial Fluid
 - Volume of 1-5 mls in knee joint
 - Dialysate of blood plasma
 - No clotting factors, erythrocytes, or hemoglobin
 - Contains hyaluronan produced by synoviocytes- viscoelastic properties

Why is articular cartilage injury such a big deal?

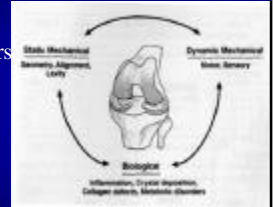


**“from Hippocrates to the present, it is universally allowed that ulcerated cartilage is a troublesome thing, and that once it is destroyed it is not repaired”
1743, Hunter**

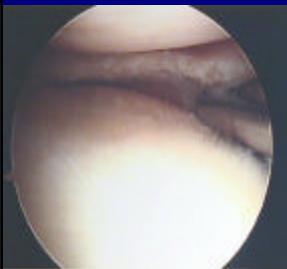


Mechanics of Knee Function

- Balanced interaction of mechanical and biologic factors
 - Mechanical
 - alignment, laxity, gait disturbance, load distribution
 - Biologic
 - State of bone/cartilage/connective tissue
 - Hereditary and Metabolic abnormalities



Meniscal Function



- 45-70% of axial load transmitted by menisci
- Peak loads post-menisectomy increased up to 235% after total or sub-total resection
- Partial meniscectomy increases load 10-65%
- Menisci primarily loaded in extension

Factors Contributing to OA

- Mechanical
 - Loss of muscle strength
 - Obesity
 - Joint structure
 - Overuse and trauma
- Endogenous
 - Heritable disorders
 - Developmental disorders
 - Diseases
 - Nutrition

Reference: Pelletier JP, Martel-Pelletier J, Howell DS. Etiopathogenesis of osteoarthritis. In: Koopman WJ, ed. *Arthritis and Allied Conditions: A Textbook of Rheumatology*. Philadelphia, PA: Lippincott Williams & Wilkins, 2001;2:2135-2215.

Osteoarthritis

- Etiology ?
 - Intrinsic factors
 - Genetics
 - “Chondropenia”, Mandelbaum
 - Extrinsic factors
 - Injury
 - Female soccer players (ACL)
 - Obesity
 - Instability
 - 50-70% ACL tears have OA at 15-20 yrs



Injury and Risk – Knee and Hip Osteoarthritis

- Conclusion
 - “Young adults with knee injuries are at considerably increased risk for OA later in life and should be targeted in the primary prevention of OA”

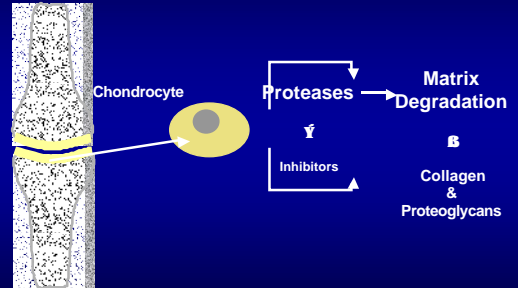
Reference: Gelber AC, Hochberg MC, Mead LA, Wang N-Y, et al. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Ann Intern Med*. 2000;133:321-326.

Osteoarthritis vs. Normal Aging

	Aging	OA
Water content	↓	↑
Chondroitin sulfate concentration	↓	↑
Keratin sulfate concentration	↑	↓
Modulus of elasticity	↑	↓
Proteoglycan synthesis		↑
Proteoglycan degradation	↓	↑↑

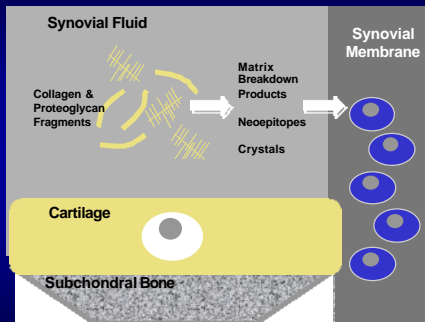
➡ Very different processes

OA Disease Evolution – Stage I



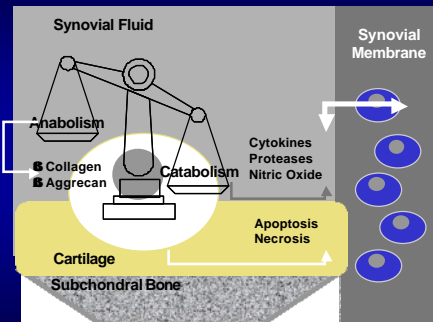
Reference: Pelletier JP, Martel-Pelletier J, Howell DS. Etiopathogenesis of osteoarthritis. In: Koopman WJ, ed. *Arthritis and Allied Conditions: A Textbook of Rheumatology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2001;2:2195-2215.

OA Disease Evolution – Stage II



Reference: Pelletier JP, Martel-Pelletier J, Howell DS. Etiopathogenesis of osteoarthritis. In: Koopman WJ, ed. *Arthritis and Allied Conditions: A Textbook of Rheumatology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2001;2:2195-2215.

OA Disease Evolution – Stage III



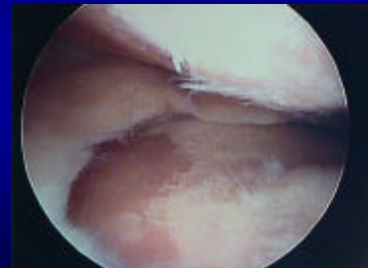
Reference: Pelletier JP, Martel-Pelletier J, Howell DS. Etiopathogenesis of osteoarthritis. In: Koopman WJ, ed. *Arthritis and Allied Conditions: A Textbook of Rheumatology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2001;2:2195-2215.

OA-History

- Employment
- Activity level
 - Sports
- Symptoms (swelling, pain)
- Instability

Osteoarthritis

- Pain- WB
- Stiffness
- Deformity
- Crepitus



OA-Pain

- Synovial tissue- sensitive nociceptors
- Capsule, ligament, muscle
- Cartilage
 - aneural
 - wear: enzymatic release
- Late subchondral pain

OA-Physical Exam

- Body Habitus
- Gait
 - dynamic compensatory patterns
- Alignment
 - Varus- ACL
 - Valgus- renal rickets
 - Internal squinting patella
- ROM

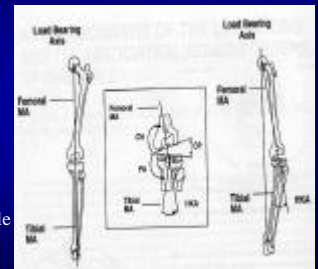


OA-Physical Exam

- Laxity
- Meniscus
- Back and Ipsilateral hip and ankle
- Vascular Status

Alignment

- Hip-Knee-Ankle xrays
- Variable in population
- LBA- Load bearing axis
- HKA- hip-knee-ankle
 - (CH) condylar hip angle
 - (PA) plateau-angle
 - (CP) condylar plateau angle
- Normal HKA 1° varus



Sagittal Alignment

- Normal “set back” femoral condyle and tib plateau
- Places center of knee behind load bearing axis
 - Passive extension during stance
- Allows tibia to rotate full 160° in F/E



Knee angular variations

- Ground reaction force should pass through the center of the knee
- OA related to angular abnormalities

TABLE 1. Knee Geometry Parameters (Means \pm SD) in Healthy Adult Volunteers and Osteoarthritic Patients

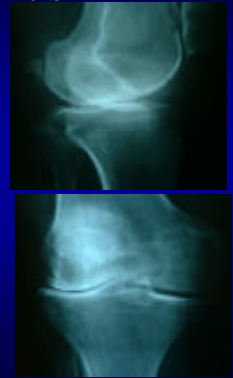
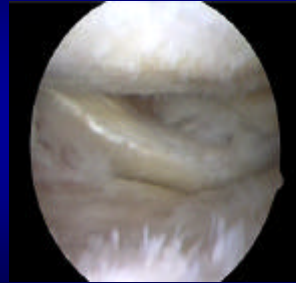
Angle	Healthy Adult Volunteers (n = 119)	t-Test	Symptomatic Osteoarthritic Patients (n = 167)
HKA	-0.97 \pm 2.86	P < .001	-3.95 \pm 7.75
CH	3.96 \pm 2.33	P < .001	1.92 \pm 3.26
PA	-3.08 \pm 2.33	NS	-2.32 \pm 4.10
CP	-1.85 \pm 1.81	P < .001	-3.55 \pm 4.27

Data from Cooke et al. Osteoarthritis Cartilage 5:39-47, 1977.

OA- Imaging

- 45° standing PA flexion
 - earliest loss of cartilage 30-60° range
- Hip-knee-ankle WB X-rays
 - mechanical alignment
- MRI
- Bone Scan

Osteoarthritis

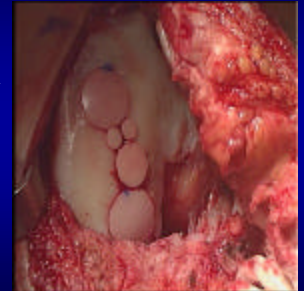


OA-Treatment Options

- Nonsurgical
 - Activity modification, weight loss
 - Bracing, orthotics
 - NSAIDS, Acetaminophen, Steroids
 - COX-2 inhibitors
 - Glucosamine/Chondroitin Sulfate
 - Intraarticular steroids
 - Viscosupplementation

OA-Treatment Options

- Surgical
 - Cartilage restoration procedures
 - Mosaicplasty
 - Cartilage transplantation
 - Allograft
 - Arthroscopy
 - Osteotomy
 - Arthroplasty



Caveat-Positive Results in 94% OA articles !!

- Published articles 1950-1998
 - 930 scientific articles
 - 59% drugs, 25.6% surgery, 6.5% PT, 8.9% alternative
 - Positive findings highest in pharmacological studies
 - Commercially funded results significantly higher than non-commercially funded research
 - Very challenging to document progression of OA with current imaging techniques

Chard JA et al. Annals of Rheumatic Diseases, 2000

OA- Lifestyle Modification

- High stools instead of standing
- Decrease weight (Felson et al, Ann Intern Med 1992)
- Low impact exercises (swimming/bicycle)
- Modify employment



OA- Rehabilitation

- Limit progressive shear loads
- ROM (esp. Hamstrings)
- Strengthening of periarticular tissues stabilizes knee
- Modalities
 - via reflex mediated pathways involving free nerve endings
 - Vasodilation
- PT delayed/prevented TKA compared to control

Deyle, et al. Annals Internal Med, 2000

OA- Exercise

- 179 pts with OA
- Randomized
 - Home exercise program
- Changes in functional ability/proprioception sig. better

Petrella et al. J of Rheum 2000

OA- Aquatic exercise

- Ten patients with OA
- 8 week aquatic intervention
 - Sig. improvements in isometric hip abduction and 11% improvement in functional balance test

Suomo and Kocaja, 2000

Knee OA and Proprioception

- Control group detect passive motion one degree sooner than scheduled TKA pts
- OA loss of proprioception affected contralateral (nl xray) knees
- This is due to lack of exercise

Collier, et al. JBJS 2000

OA and Neoprene sleeves

- Mechanoreceptors in synovium, tendons, joint capsule, ligaments deteriorate with age/OA process
- Braces compress mechanoreceptors, “sensitize”
- Bracing improved tracking of the knee joints position by 11%



Lephart, et al. Isokinetics and Exercise, 1997
Arch Phys Med Rehabil, 1996

OA- Bracing

- Unload affected compartment
- Horick & Loomer: Clin J of Sp Med, 1993
 - sig improvement
- Hewett et al: Orthopedics, 1998
 - prospective analysis of valgus bracing
 - 50% deer in pts c/o pain with ADL
 - 7 hrs/day, 5d/wk



OA- Bracing

- Pollo FE: Am J of Knee Surg, 1998
 - \$800-\$1000
 - cumbersome
 - many pts don't use them
- Young patients
- Avoid surgery



OA- Footwear

- Energy absorbing shoes or inserts
- Yasuka et al: CORR 1987
 - Wedge inserts can correct pronation or supination deformities leading to realignment and decrease medial comp load
- Keating et al: Orthop Review, 1993
 - 75% of 80 pts with medial OA tx'd w/ lat wedge had HSS statistical improvement at 12 mos
- No change in mechanical axis, Subtalar joint only



OA- Acetaminophen

- Pain relief is goal
- Favorable side effect profile, coumadin rxn
- Bradley et al: NEJM 1991
 - Equivalent to ibuprofen in pain control
- Max 4000 mg/day
- #1 ACR since 1995



Conservative Treatments: Anti-inflammatory Medications

- Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly prescribed drugs for degenerative joint disease



- Corticosteroids also function as anti-inflammatory agents by blocking the action of Phospholipase A2

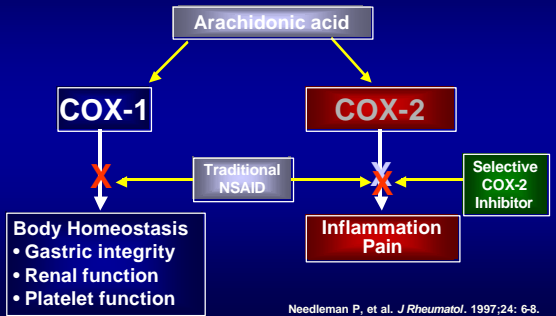
NSAIDs

- Mechanism
 - Inhibits cyclooxygenase thereby preventing the first two steps in conversion of arachadonic acid
 - Blocks PG production
 - But... NSAID's have NOT been shown to:
 - alter the progression of the disease OR
 - enhance cartilage repair

NSAIDs

- Two primary forms of cyclooxygenase have been identified:
 - COX-1
 - primarily provides a physiologic maintenance role, particularly in the GI tract
 - COX-2
 - the inducible form, much more significantly involved in the inflammatory pathway

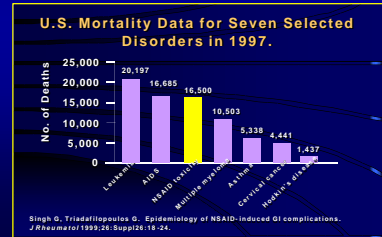
The Arachidonic Acid Cascade and COX-1 and COX-2 Inhibition



Needleman P, et al. *J Rheumatol*. 1997;24: 6-8.
Simon LS, et al. *J Clin Rheumatol*. 1996;2:135-40.

NSAIDs

- 25% of treatment actually goes to treat adverse effects of NSAIDs
 - 100,000 hospitalizations/yr in the U.S.
 - 16,500 deaths/yr in the U.S.
 - 33% of cost of treatment is to treat adverse events



Singh G, Triandafillopoulos G. Epidemiology of NSAID-induced GI complications. *J Rheumatol* 1999;26(Suppl2):18-24.

NSAID Safety Overall Cost

Estimated Annual Costs of Toxicities*

Acetaminophen	51.5 million
Aspirin	458.6 million
NSAIDs	1.35 billion†

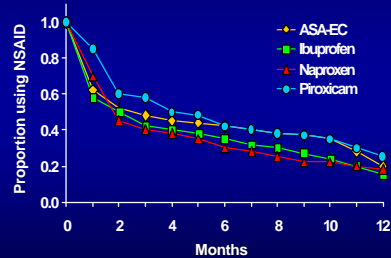
*US\$, 1997

†\$1.16 billion attributed to renal disorders

‡\$150 million due to GI complications

Reference: McGoldrick MD, Baillie GR. Nonnarcotic analgesics: prevalence and estimated economic impact of toxicities. *Ann Pharmacother*. 1997;31:221-227.

Discontinuation of NSAID Use by Drug



Reference: Scholes D, Stergachis A, Penna PM, Normand EH, et al. Nonsteroidal anti-inflammatory drug discontinuation in patients with osteoarthritis. *J Rheumatol*. 1995;22:708-12.

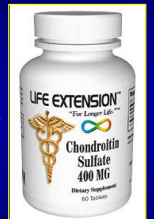
Chondrosupplements

- Very poorly regulated industry
- Very few “scientific studies” of their potential benefits and risks



Chondroprotective Supplements

- Chondroitin Sulfate/Glucosamine
 - inhibits degradative enzymes
 - prevent thrombi in periarticular tissues
 - stimulates chondrocyte/synoviocyte metabolism
- Nontoxic, OTC, No Rx needed
- Purity is issue
- Funding issues



McKeon, Gillis, Burstein et al, 2002

- Pilot study in progress
- 6 pts with arthroscopic documented discrete cartilage softening (Grade I)
- Baseline dGEMRIC, quantify PG content
- Cosamine DS x 1yr
- Serial MRI's to assess PG content

Intra-Articular Steroid

- Block action of Phospholipase A2 which prevents conversion of phospholipid to arachadonic acid
- Inhibit vasodilation thereby decreasing edema and pain
- Ideally should be given at most every three months ?

Corticosteroid injection

- Pros
 - Effective short-term pain relief¹
 - Effective short-term increase of joint strength¹
 - Local anti-inflammatory¹
- Cons
 - Mild flare of synovitis¹
 - Low risk of infection¹
 - Short-term option¹
 - Risk of cartilage damage with repeated use²

1. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum.* 2000;43:1905-1915

2. Robion FC, Doize B, Bourne L, Marcoux M, et al. Use of synovial fluid markers of cartilage synthesis and turnover to study effects of repeated intra-articular administration of methylprednisolone acetate on articular cartilage in vivo. *J Ortho Res.* 2001;19:230-236.

What is Viscosupplementation?

- Viscosupplementation is the introduction of purified or synthesized hyaluronic acid or one of its polymers into a joint to replace the native hyaluronic acid that has degraded secondary to osteoarthritis.

Functions of HA in the Normal Joint

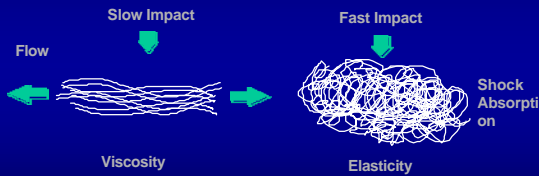
- HA plays a key role in homeostasis of the normal joint
 - Macro-homeostasis – the rheological environment
 - Mini-homeostasis – the fluid environment
 - Micro-homeostasis – the chemical environment

Reference: Adams, ME. Viscosupplementation as articular therapy. In: Laurent TC, ed. *The Chemistry, Biology, and Medical Applications of Hyaluronan and its Derivatives*. London, England: Portland Press, Ltd; 1998:243-253.

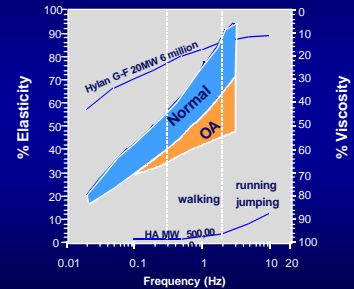
Basic Structure of Hyaluronic Acid

- Repeating disaccharide unit
 - MW 4-6 million
 - N-acetylglucosamine – glucuronic acid
 - Negatively charged random coil
 - Occupies 1000x the space of unhydrated molecule

Synovial Fluid Response to Movement



Viscosupplementation Basic Principle



Reference: Weiss C, Bond P. Basic principles underlying the development of viscosupplementation for the treatment of osteoarthritis. *J Clin Rheumatol*, 1999;5:S2-S11.

Synovial Fluid Elastoviscosity

Dynamic Moduli at 2.5 Hz

	Elasticity (Pa)	Viscosity (Pa)
Normal (18- to 27-year-olds; n=16)	117 ± 13	45 ± 8
Osteoarthritic (n=11)	8 ± 5	5 ± 3

Reference: Balazs EA. The physical properties of synovial fluid and the special role of hyaluronic acid. In: Helfet AJ. *Disorders of the Knee*. 2nd ed. Philadelphia, Pa: JB Lippincott Company; 1983:61-74.

Viscosupplementation

- Hyaluronic Acid
 - Indirect anti-nociceptive effect
 - Increased production of hyaluronic acid by synoviocytes
 - Chondroprotection by stimulating production of tissue inhibitors of metalloproteinases (TIMP-1) by chondrocytes
 - Inhibits neutrophil-mediated cartilage degradation by increased viscosity



A Randomized Prospective Evaluation of the Efficacy of Hylan G-F 20 Versus Methylprednisolone in the Treatment of Osteoarthritis of the Knee

Brian McKeon, MD
 Doug Goumas, MD
 Arnold Scheller, MD
 Lampros Minos, PAC
 Fred Gibney

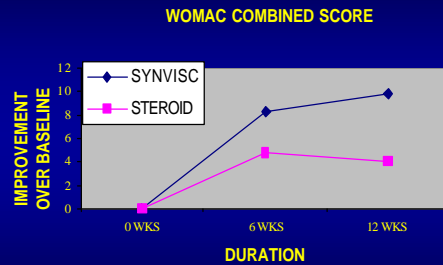
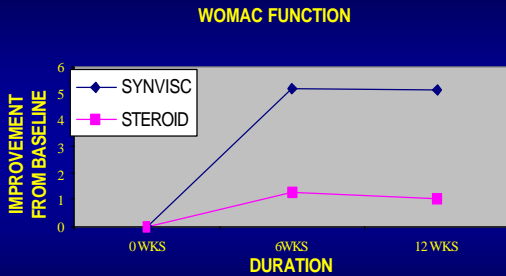
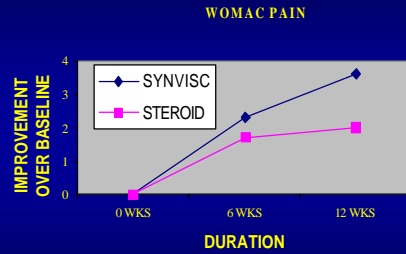
The WOMAC Osteoarthritis Scale

- Three primary areas of assessment
 - Pain
 - Stiffness
 - Physical function

Table 1A
Patient Disposition by Treatment Cohort

	Methylprednisolone	Hylan G-F20	Total
Completed	13 (34.21%)	34 (80.95%)	47
Discontinued for Lack of Efficacy	21 (55.26%)	5 (11.90%)	26
Intercurrent Illness	2 (5.26%)	0	2
Lost to Follow-Up	2 (5.26%)	3 (7.14%)	5
Total	38	42	80

Fisher's Exact Test
 $p < 0.001$



Patient Disposition

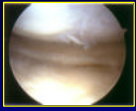
Patient disposition appears to be highly dependent upon treatment group ($p < .001$). Kaplan-Meier survival functions were constructed for each treatment to further examine this relationship. Heterogeneity of the two functions was demonstrated using the log-rank test ($p = 0.0002$).

Methylprednisolone group median survival 95.5 days, were more likely to experience treatment failure sooner compared with those patients in the hylan G-F 20 group (151.2 days)

Viscosupplementation

- Hyaluronic Acid supplementation doesn't always work...
...even in horses





Operative Treatment: Arthroscopy

- Provides short-term symptomatic relief in many, but likely doesn't affect natural history of disease
- Multiple studies demonstrate overall 60-65% symptomatic relief at 3 years
 - Hubbard MJS, JBJS 78B: 217-219, 1996.
 - Rand JA. Arthroscopy 7: 358-363, 1991.
- Moseley, NEJM July 2002. Controversial
- Excellent when “mechanical symptoms” are present

OA-Arthroscopy

- Check for malalignment and instability
- If mechanical symptoms, then reliable results !!!!



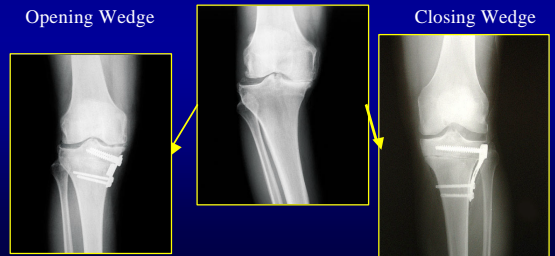
OA-Cartilage Resurfacing

- Marrow stimulating techniques
 - Provide source of pluripotential stem cells (“reparative cells”)
- Cartilage transplantation
 - Autologous
 - Allograft
- **I WOULD NOT RECOMMEND !!!!**



Operative Treatment: Osteotomy

- Addresses unicompartmental disease
 - unload the involved compartment
- Tibial vs. Femoral



Operative Treatment: “Unispacer”

- Restore axial alignment
- No bone cuts or fixation
- Easy to convert to reconstructive procedure

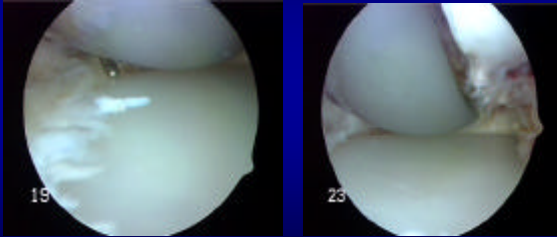


Operative Treatment: Reconstructive

- Unicompartmental Arthroplasty

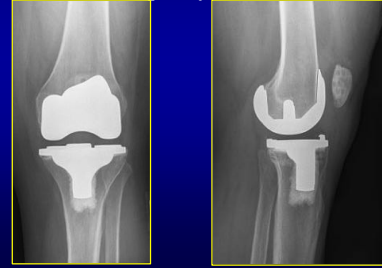


Unicompartmental Replacement



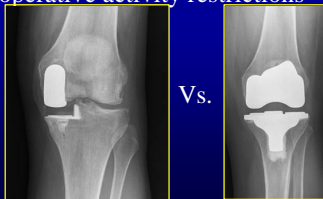
Operative Treatment: Reconstructive

- Total Knee Arthroplasty

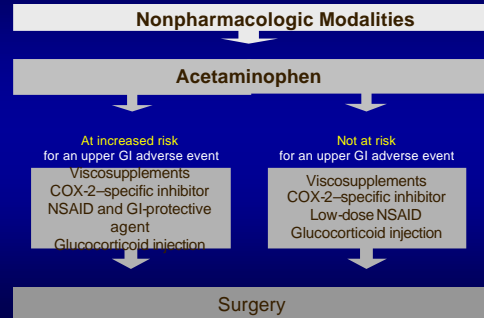


OA-Reconstructive

- Unicompartmental Arthroplasty
- Total Knee Arthroplasty
- Post-operative activity restrictions



American College of Rheumatology 2000 Guidelines for OA of the Knee



OA Nonsurgical Future

- Biotech
 - Synvisc..... 2,3 and beyond !!
 - Other HA composites (High MW)
 - Biochemical markers
 - Chondrosupplements
 - MRI
 - Gadolinium and PG content
 - Metalloproteinase inhibitors... after injury?
 - Matrix stimulation w/ genetic engineering
 - TGF, IGF, BMP's... others?
- Prevention
 - ACL injury