Healthy Knees: Today’s Treatments and the Potential of Regenerative Medicine

Be Well Lecture Series
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David C. Ayers, M.D.
The Arthur M. Pappas Professor & Chair
Dept. of Orthopedics & Rehabilitation
University of Mass. Medical School
Orthopedist-in-Chief
UMassMemorial Healthcare System
Outline

• Introduction
• Normal Knee Joint
• Arthritic Knee Joint
• Current Non-operative Treatment
• Current Operative Treatment
• Role of Stem Cells and Regenerative Medicine
• Question and Answer Session
Orthopedic Facts

- Orthopedic disorders are the most common cause of disability in the US today; resulting in 147 million lost days of work.
- One in six Americans has an orthopedic impairment.
  
  Osteoarthritis, Osteoporosis, Back and Neck Pain

- $215 billion = cost to the US annually.
- Cost of DRG 209 is single greatest Medicare annual expense (Total Hip and Total Knee Replacement).
- Up to 70% of patients presenting to PCP office have a chief complaint that is musculoskeletal.
Arthritis Facts

• An estimated 45 million adults in the US have a form of arthritis\(^4\)

• By 2030, an estimated 67 million Americans will have doctor-diagnosed arthritis\(^6\)

\(^4\)MMWR 2006: 55(40)1089-1092 (data source 2003-2005 NHIS)
\(^5\)MMWR 2006: 55(40)1089-1092 (data source 2003-2005 NHIS)
Knee Arthritis

- Prevalence growing in parallel with the aging, overweight adult US population
- 50% over age 65 have diagnosis of arthritis
- 60% of women; making it the leading chronic condition among women
TKR Surgery

• “cost effective, reliable treatment for the pain and disability of advanced knee arthritis”
  NIH Consensus Panel 2001
• >600,000 TKR in US each year
• Is the single largest expenditure of the federal Medicare budget
Total Knee Replacement

• Projected growth; more than 600% increase by the year 2030
• Fueled by aging of the population
• Desire to remain physically active later in life
• 35% TJR patients under the age of 65 and part of the work force
Knee Surgery Most Common Surgery in USA
The Normal Joint
The Synovial Joint

- Bones provide the framework for the body that is both Rigid and Segmental
- Joints are the point of articulation between 2 or more bones
- Joints allow near frictionless movement
- And work in concert with the neuromuscular aspects of MSK system that results in a wide range of purposeful movement
Synovial Joint

• Molded ends of 2 bones shaped to permit motion of one bone upon the other
• Bones connected by sleeve of connective tissue; the joint capsule
• Joint capsule receives further support by ligaments; provide bone to bone stability
• And further support by tendons; attach muscle to bone; that provide dynamic stability
Synovial Joint

• Exposed ends of bone covered with **articular cartilage** that provides smooth glistening surface

• Ease of motion further enhanced by thin glistening lining; the synovial membrane and synovial fluid

• Synovial fluid that provides lubrication to the joint and nourishment to the cartilage
Articular Cartilage

- Unique Connective Tissue
- Ideally suited to serve as elastic shock absorber
- Wear resistant weight bearing material
Articular Cartilage

• Contains no blood vessels, no nerves and no lymphatics
• Nourished by synovial fluid
• Is 1-4 mm thick
• Contains relatively few cells, chondrocytes, dispersed in a connective tissue matrix
• Chondrocytes are metabolically active but have limited ability to replicate; obvious implications with regard to injury
Articular Cartilage

- Chondrocytes arranged in layers
- Connective tissue differs in orientation from superficial zones to deep zones
Articular Cartilage
Articular Cartilage

- Metabolically Active
- Constantly synthesizing collagen and macromolecular proteoglycans
- Type II Collagen
Articular Cartilage; PG Content

- Cartilage stained by toluidine blue
- Intense metachromasia around the chondrocytes in the deep layer
- Represents staining of the proteoglycan
Proteoglycan

• Linear protein backbone; **hyaluronic acid**
• Polysac. side chains attached to HA at right angles; called **glycosaminoglycans**
• 3 distinct components of GAG
  Chondroitin 6-sulfate
  Chondroitin 4-sulfate
  Keratin sulfate
Proteoglycans

Keratan Sulphate
Chondroitin Sulphate
Aggrecan
Hyaluronic Acid

Glycosaminoglycans
Even the best radiographic techniques are not good enough: fluoroscopically assisted semiflexed PA radiographs

Good Alignment: reproducible but insensitive to early OA

Poor Alignment: false joint space narrowing
**delayed Gadolinium-enhanced MRI of Cartilage (dGEMRIC)**

**Basic Principle:**
Unequal distribution of charged cartilage structural molecules predicts a broad range of detection in normal vs. OA cartilage

**Histologic Evaluation (ex vivo):**
Charged dye (blue) detects healthy cartilage; lack of dye (white) detects cartilage degradation

**dGEMRIC Evaluation (in vivo):**
Charged contrasts detect healthy cartilage (yellow) and focal (red) loss of cartilage
Clinical use of delayed Gadolinium-enhanced MRI of Cartilage (dGEMRIC):

Femoropatellar Joint:  
Tibiofemoral Joint:  

Normal:

Early OA:

H-12692
UMass Medical School Department of Orthopedics
IRB-approved Human Subjects Trial:

‘Efficacy of a disease-modifying osteoarthritis drug using dGEMRIC in women with osteoarthritis in a randomized, placebo-controlled, double-blind trial’

**Goals:**
Longitudinal study in a small female OA patient cohort (n=40) to:

- Map unilateral knee OA cartilage lesions (ROIs) at baseline (MRI)
- Randomize 20/40 OA subjects to potential DMOAD (FDA-approved) group
  - Randomize 20/40 OA subjects to placebo control group
- Observe changes in GAG concentrations over time (2 & 4 months) in both control and treatment groups
- Calculate & report effects for larger-scale trial(s)/funding
Step 1: Remember the Anatomy

- FEMUR
- PATELLA
- FIBULA
- TIBIA
ANATOMY: Cartilage

ARTICULAR CARTILAGE

MEDIAL MENISCUS

ARTICULAR CARTILAGE

LATERAL MENISCUS

Femur

Patella

Tibia
Arthroscopic Knee Surgery

- Out-Patient
- Small portals
- Correction of meniscus tears, loose bodies
- Does not change arthritis
MENISCAL TEARS:

- **Characteristics of the Pain**
  - PAIN USUALLY LOCATED OVER SIDE OR BACK OF KNEE
  - PAIN WORSE WITH MOVEMENT, BETTER AT REST

- **LOCKING** - KNEE GETS STUCK IN ONE POSITION or unable to fully extend knee

- **Age Specific features:**
  - IN PEOPLE < 40 yo SUDDEN ONSET & ASSOCIATED WITH TWISTING INJURY
  - PEOPLE > 50 yo MAY NOT HAVE INJURY
MENISCAL TEAR

ARTHROSCOPIC VIEW
MENISCUS

Normal Meniscus

MENISCAL TEAR
Treatment of Degenerative MENISCAL TEARS

TEAR

TORN SEGMENT REMOVED
MENISCAL REPAIR IN YOUNG and Rim Tears
Treatment of Arthritis

• Conservative options; first line of treatment
  – Physical therapy for ROM and strengthening
  – Weight Reduction
  – Glucosamine and Chondroitin Sulfate
  – Tylenol and anti-inflammatory drugs
  – Steroid (cortisone) injection
  – Synvisc injections
Unicompartmental Knee Replacement
Compartments of The Knee

Medial: NARROWED SPACE

Lateral: NORMAL SPACE
TJR OUTCOME STUDIES SHOW:

• Successful Surgical Procedure
• Sustained Pain Relief
• Improved Physical Function
• Best QUALY Analysis for ANY surgical procedure
UMASS Excellence in TKR

- Gender TKR; made specifically for women
- High Flexion TKR
- Ranawat Award from the Knee Society
Younger Patients

• More reasonable to do joint replacement with current options available
• Often an option for patients in 50’s
• Any age in Inflammatory Arthritis
• Patients must limit their activities to maximize the longevity of their implants
  – no high impact activities
Treatment of Arthritis

- Arthroscopy
  - Not indicated for Arthritis
  - Indicated for meniscal tear or mechanical symptoms

- Joint replacement surgery
  - Elective surgical procedure
  - Never an emergency
  - Indication is PAIN RELIEF
  - One of the most successful operative treatments in all of medicine today; a Miracle of Modern Medicine
Cartilage Repair and Regeneration
OAT Procedure
ARTICULAR CARTILAGE INJURY
AUTOLOGOUS CARTILAGE CELL TRANSPLANTATION

CARTILAGE DEFECT

PATCH & CELLS
The “New Patient”

- Younger
- More Active
- More Educated
- More Informed
- Heavier
- More #'s
Thank You
For Your Attention
Joint Stability

- Congruity of opposing bone surfaces
- Support provided by fibrous capsule, ligaments and in some cases menisci
- Muscular contraction provides dynamic stabilization of the joint, an important stabilizer
- Synovial fluid contributes some by inhibiting distraction of the bones, acting as an adhesive
Minimally Invasive Joint Replacement:

• Definition- What is it?
• Mini-incision vs. MIS
• Advantages
• Disadvantages
• Future
ANATOMY: Ligaments

LIGAMENTS

MCL

LCL

ACL

PCL

Femur

Patella

Tibia
ANATOMY; Musculotendinous

QUADRICEPS MUSCLE

QUADRICEPS TENDON

PATELLA TENDON
Hinge Joint
Knee and Elbow

• Acts similar to door hinge
• Allows flexion and extension in 1 plane
GAG

Have negative charged side chain

- Produces a spatial lattice structure
- Lattice is hyper hydrated
- 80% water; water molecules assist in keeping the negatively charged groups in GAG apart
Cartilage Matrix
Cartilage under compression

• Under compressive force, some water is expelled from the matrix
• Water returns into the cartilage with release of the compressive force
• Allows cartilage to maximize elasticity and permit it to sustain cumulative trauma of life so effectively
Cartilage Matrix
Osteoarthritis
The Options

♦ Non-medical Therapy Options
  • Pacing activities
  • Joint protection
  • Exercise/Physical activity
  • Application of heat and cold
  • Self-care skills

♦ Medications

♦ Therapy
Arthritis Warning Signs:
YOUR Signs to See Your Doctor

♦ Pain
♦ Stiffness
♦ Difficulty moving
♦ Swelling
Three Key Steps

♦ A history (questions about your symptoms)
♦ A physical examination
♦ X-rays and other tests
Synovial Membrane

- Derived from mesenchymal cells
- Functionally comprised of two cell types
- Phagocytic cells; similar to macrophage, activated by degradation of matrix
- Secretory cells; secrete synovial fluid
The Normal Joint
Orthopedic Surgery
Biology and Biomechanics

Thank you!
MENISCAL TEARS

• TWISTING INJURY CAUSES TEARING OF MENISCUS

• DEGENERATIVE TEARS ASSOCIATED WITH MILD ARTHRITIS not amenable to repair
  – OCCUR WITHOUT KNOWN TRAUMA