

Dr John Best

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Dr John Best
Sport & Exercise Medicine Physician

The Non-Operative Management of Knee Joint Osteoarthritis (KJOA)



KJOA - Prevalence and burden

- Chronic disease – joint pain, swelling, altered qOL
- OA sufferers report fair to poor health
 - National Orthopaedic Registry 2016
- 45% lifetime risk; increases >55years
- 65% prevalence with obesity
- X-ray changes in 25% 50yo; 85% >65 yo
- **The aim of good non-operative care is to improve qOL and delay arthroplasty**



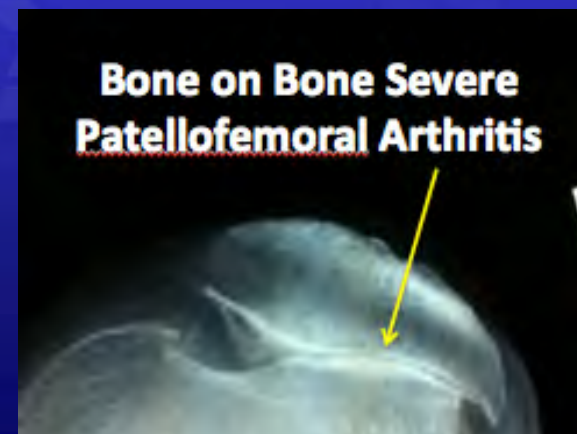
Pathogenesis of KJOA

- Genetics, trauma, malalignment, other.....
- Imbalance between anabolism and catabolism
- Not simply the “wear and tear” of ageing
- Chronic inflammatory changes including the upregulation of substances such as matrix metalloproteinases (MMPs), proliferation of cytokines and inflammatory mediators
- Volume of KJ articular cartilage degenerates by 4-5% / decade; more rapidly with obesity



Load and Knee Joint Mechanics

- Altered load with:
 - Varus / valgus
 - Patella tilting
 - Meniscectomy
- Normal Walking
 - 150% TBW through knees
- Stairs
 - 250% TBW through knees
- Squat
 - 500% TBW through knees



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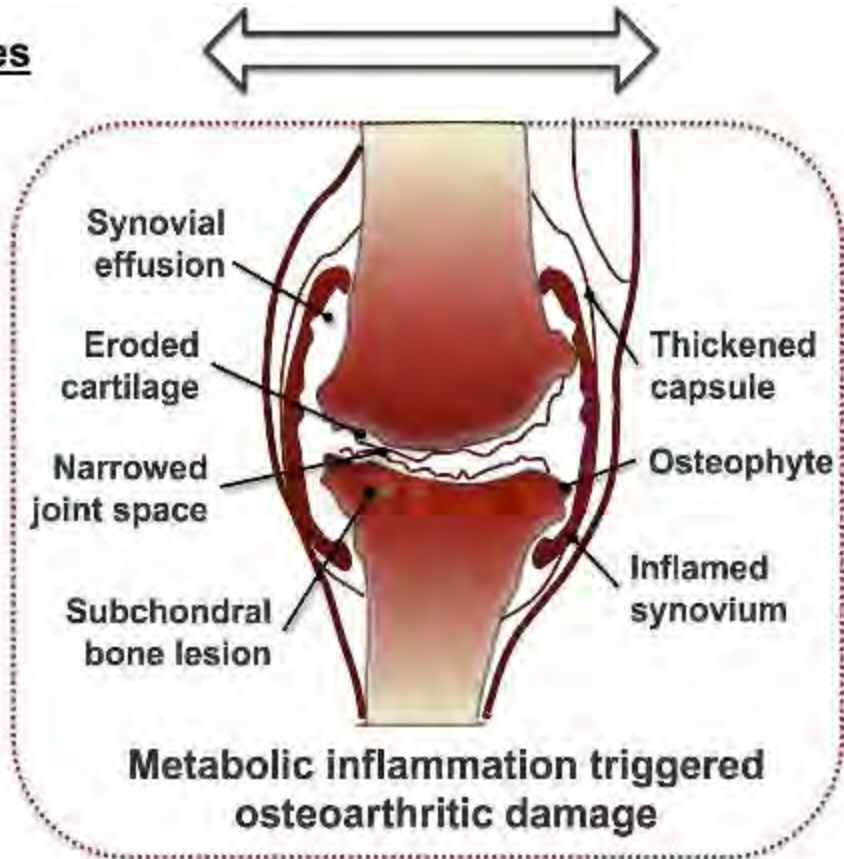
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Altered metabolites

Nutrients
Lipids ↑
Glucose ↑

Hormones
Estrogen ↓
Testosterone ↑
Vitamin D ↓

Others
Nitric oxide ↑
Reactive oxygen species ↑



Altered body composition

Body measures
BMI ↑
Waist/Hip Ratio ↑
Body fat ↑
Lean mass ↓
Muscle strength ↓



Synovium and chondrocyte-derived inflammatory mediators

Cytokines
IL-1, IL-8, IL-18, IL-6 ... ↑
TNF-α, LIF ↑
Chemokines ↑
IL-10, IL-4 ... ↓

MicroRNAs
miR-9, 16, 22, 103, 138, 222, 377 ... ↑
miR-26, 29a, 95, 140, 146a, 221, 337 ... ↓

Acute-phase components
CRP ↑
C3, C5 ↑
MAC ↑

Adipose tissue-derived inflammatory mediators

Adipokines
Leptin ↑
Resistin ↑
Visfatin ... ↑
Adiponectin ↓



Principles of Non-Operative Management of KJOA

Lifestyle Factors	Chemical Factors
Weight Management	Analgesia/ Inflammation – oral/ topical
Load Management	Non-prescription meds ; supplements
Exercise and Rehabilitation	Analgesia/ Inflammation - injections
Eating patterns and diet	Injections to improve loading
Psychological and behavioural factors	Injections claiming to offer regeneration



1 Diagnosis, grading and individualised management

- qOL = night pain, mobility, ADLs, squat ability
- Activity background, expectations, treatments
- Introduce concept of a 'journey' – management pathway, using understandable language
- Functional assessment
 - 6min walk test or 4 x 10m walks
 - 30 sec 'sit to stand' ; stair climb test
 - OARSI (2013) Dobson et al

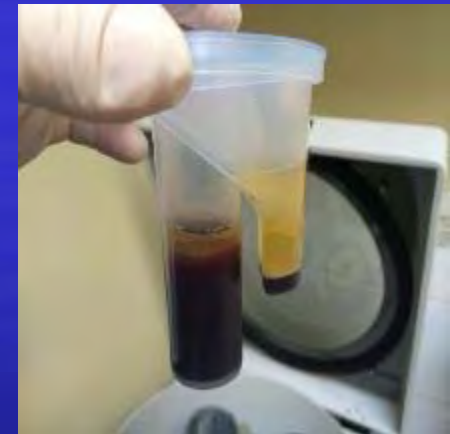


2 Manage Pain and Inflammation well

- Load management and analgesia
 - Ice ; paracetamol; topical therapies
- Anti-inflammatories
 - Oral NSAIDs – short-term, idiosyncratic, side-effects
 - Injectable cortisone for synovitis (short term)
 - 70% patients have relief for 3-12 weeks
- Supplements – non-TGA assessed
 - Omega 3 FA (eg Fish Oil) – varied quality and dose
- Platelet Rich Plasma (PRP) ??

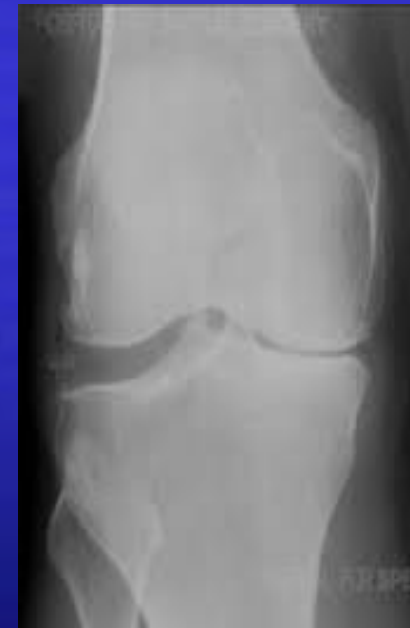
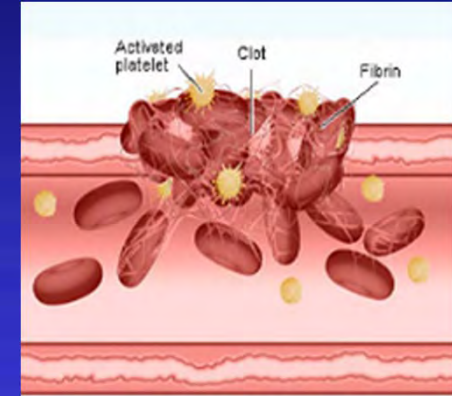
PRP and KJOA (Dr P Annett)

- Research unclear
- In those with a benefit most likely down regulation/modulation of inflammation
- Platelets are a rich source of bioactive molecules; 1100 different proteins
- **Does not produce chondrocyte proliferation**
- **No evidence for slowing disease progression**
- **No clear protocol**



Evidence for PRP Joint

- Knee joint Osteoarthritis
 - Patel 2013. AmJSM
- 156 knees
- 52 PRP, 50 X2 PRP, 46 Saline
- Significant improvement in first 2 groups from 2-3/52 to 6/12
- No difference between 1 & 2 PRP injections
- NS deteriorated



Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: a systematic review and meta-analysis

Augustinus B M Laudy,^{1,2} Eric W P Bakker,² Mark Rekers,³ Maarten H Moen^{4,5}



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3 Eating Patterns and Weight Management

- Weight and composition
 - Abdominal fat (peri-organ)
- BMI – using ht /wt

Class	BMI range
Underweight	<18.5
Normal /healthy	18.5-25
Overweight	25-30
Obesity Class I	30-35
Obesity Class V	50-60

- Eating Patterns
 - Self – control
 - Effects on hormones
- Diet and inflammation
 - Insulin resistance
 - High carbs and Omega 6
- Weight gain and load
- Part of an unhealthy lifestyle including 'comfort eating'

Overweight and obese patients have accelerating

Weight Loss, Diet and Exercise

IDEA trial JAMA 2013, Messier et al

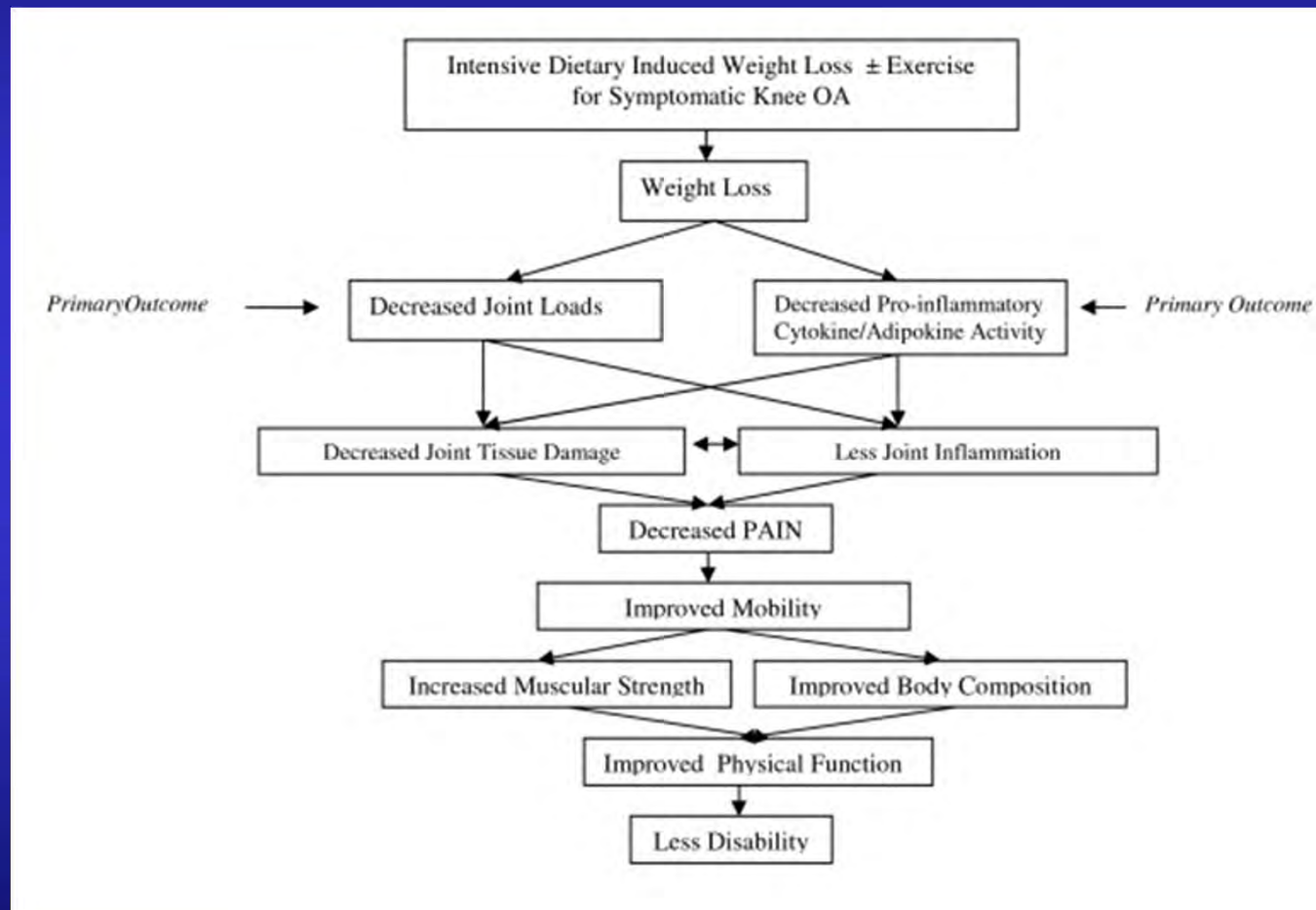
- Single blind, 18 month trial
 - 2006-2011
 - 454 overweight and obese
 - Age >55; BMI 27-41, KJOA
 - Interleukin -6 levels
 - WOMAC scores
 - Multiple other tests
- Findings – weight loss through diet and exercise gave superior results. **SPECTACULAR**

	Changes	in Weight	and BMI
Weight reduction	5-10%	10-20%	>20%
Pain reduction	15-25%	25-50%	>50%
Mobility	+	++	+++



WEIGHT LOSS, DIET AND EXERCISE

IDEA trial JAMA 2013, Messier et al



4 Manage Load and Exercise Safely

- pain reduction, better sleep and reduced inflammation

- Slower warm up
- Pursue the components of good health and manage load well (EULAR paper 2018, ACSEM recommendations)
- Cardiovascular exercise
 - > 150mins / week; HIIT training options
- Resistance training
 - Major groups, 2-3/week, 2-4 sets, 8-12 reps
 - Novice or >65yrs 35%1RM ; Experienced 75% 1RM
- Balance and Flexibility



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– 20-30 min, 2-3/week, Tai Chi, one legged standing

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4 Manage Load and Exercise Safely

- pain reduction, better sleep and reduced inflammation

- Load Management
 - Stick ; braces ; wedges
- Assessing reaction to activity
 - No sharp pain
 - Minimal after-pain / swelling
- Alternate activities – avoid lunges
 - Reduced impact
 - Walk, cycle, elliptical, aquatic, doubles and table tennis, boxing, dance, gardening...
 - Variety of positions
- Review as symptoms improve
 - Enjoy with others; active holidays



Use of Visco-supplementation

HA = Hyaluronic Acid

- High MWt solutions supplement the reduced hyaluronate concentrations
- KJOA synovial fluid exhibits very low HA levels
- Animal, synthetic or microbiological
- Bolus or regime of 3 injections
- Effects – to increase load-bearing ability:
 - Physical, Anti-Inflammatory, Anabolic, Analgesic, chondroprotective


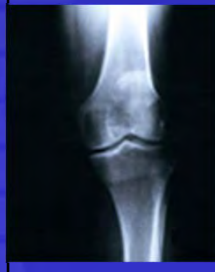
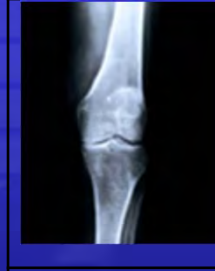




Results

No independent research
TGA approved

- Leighton et al
Rheumatology : Research
Reviews 2018
- Early to moderate OA do
better
- 75% who improve have a
better follow up injection
- Delayed time to primary
surgery

Relationship between x-ray grade and overall response

	Medical x-ray grade	Number of Knees	% Better or Much Better
	I	68	91%
	II	138	80%
	III	180	76%
	IV	57	58%

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5 Perform Key Exercises (20mins, 3/week)

- Strength

- Quads, gluteals
- Co-contractions



- Flexibility

- Quads, hamstring, hip flexor, ITB



- Control

- trunk

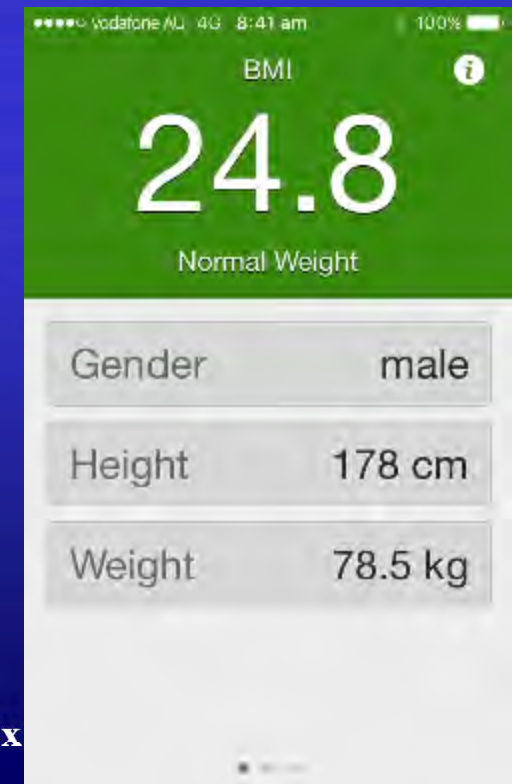
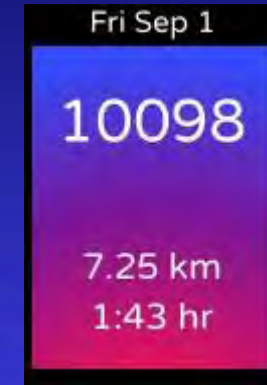


- Balance



6 Review and Pursue Behaviour Change

- KJOA may control a patient's life
- Psychological and personality factors important
- 'Booster strategies' - follow-up calls, emails accountability and compliance
- Biometric monitoring effective in most patients
- Opportunities for change



7 Keep Up To Date with Research

- Understanding of obesity and diet modulated inflammation
- Finding ways to keep patients active
- Improving subchondral bone
- Looking at regenerative therapies
 - Stem Cells?



Invited Review

Why are MSCs therapeutic? New data: new insight

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*Conflict of interest statement: my
colleagues and I started Osiris
Therapeutics Inc. in late 1992. I
no longer own stock in Osiris,
neither do I have direct contact
with the company.*

Abstract

Adult marrow-derived mesenchymal stem cells (MSCs) are able to differentiate into bone, cartilage, muscle, marrow stroma, tendon–ligament, fat and other connective tissues. The questions can be asked, what do MSCs do naturally and where is the MSC niche? New insight and clinical experience suggest that MSCs are naturally found as perivascular cells, summarily referred to as pericytes, which are released at sites of injury, where they secrete large quantities of bioactive factors that are both immunomodulatory and trophic. The trophic activity inhibits ischaemia-caused apoptosis and scarring while stimulating angiogenesis and the mitosis of tissue intrinsic progenitor cells. The immunomodulation inhibits lymphocyte surveillance of the injured tissue, thus preventing autoimmunity, and allows allogeneic MSCs to be used in a variety of clinical situations. Thus, a new, enlightened era of experimentation and clinical trials has been initiated with xenogenic and allogeneic MSCs.



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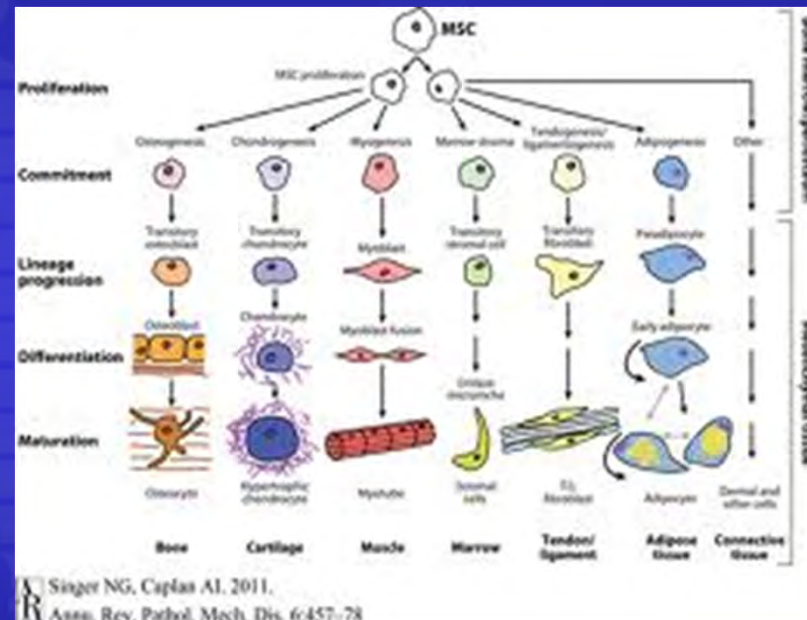
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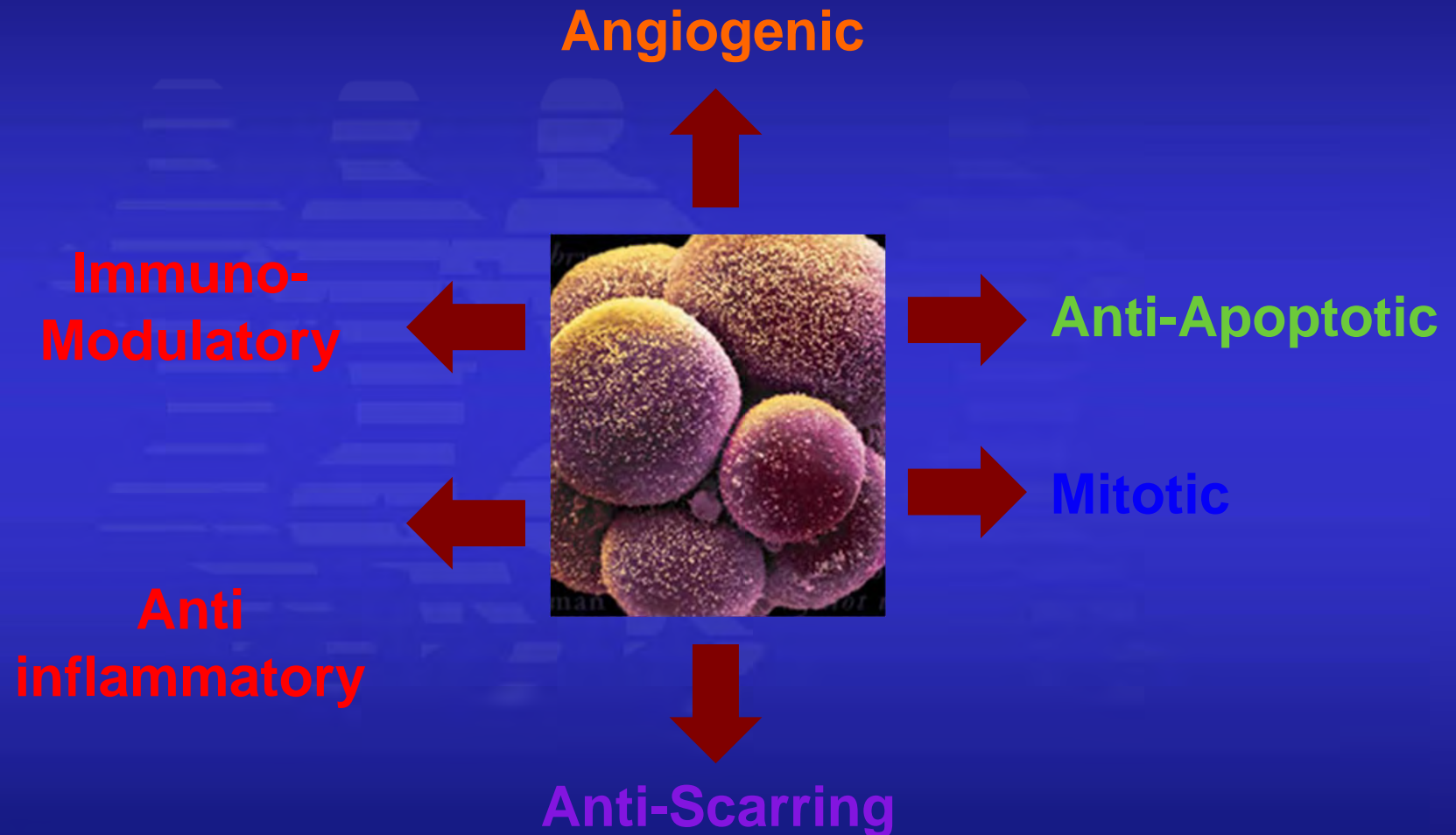
What are Mesenchymal Stem Cells?

(Courtesy Dr D Kuah)

- Secretions – major driver of the therapeutic effect
- Mixed cell populations - produce a potent mixture of secretions
- Strong evidence- from cell therapy in cartilage injury models in animals



MSCs – ‘secretion factories’ Fat or bone marrow derived



Cartilage regeneration and/or modification of OA disease demonstrated in many animal models

ARTHRITIS & RHEUMATISM
Vol. 48, No. 12, December 2003, pp 3464–3474
DOI 10.1002/art.11365
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Stem Cell Therapy in a Caprine Model of Osteoarthritis

J. Mary Murphy,¹ David J. Fink,¹ Ernst B. Hunziker,² and Frank P. Barry¹

Enhanced early chondrogenesis in articular defects following arthroscopic mesenchymal stem cell implantation in an equine model

Markus M. Wilke¹, Daryl V. Nydam², Alan J. Nixon^{1,*} Issue

Article first published online: 2 APR 2007

DOI: 10.1002/jor.20382



Journal of Orthopaedic Research
Volume 25, Issue 7, pages 913–925, July 2007

STEM CELLS

TRANSLATIONAL AND CLINICAL RESEARCH

Injectable Mesenchymal Stem Cell Therapy for Large Cartilage Defects—A Porcine Model

KEVIN B.L. LEE, JAMES H.P. HUI, IM CHIM SONG, LENNY ARDANY, ENG HIN LEE

The Department of Orthopaedic Surgery, National University of Singapore, and the Department of Experimental Surgery, Singapore General Hospital, Singapore, Republic of Singapore

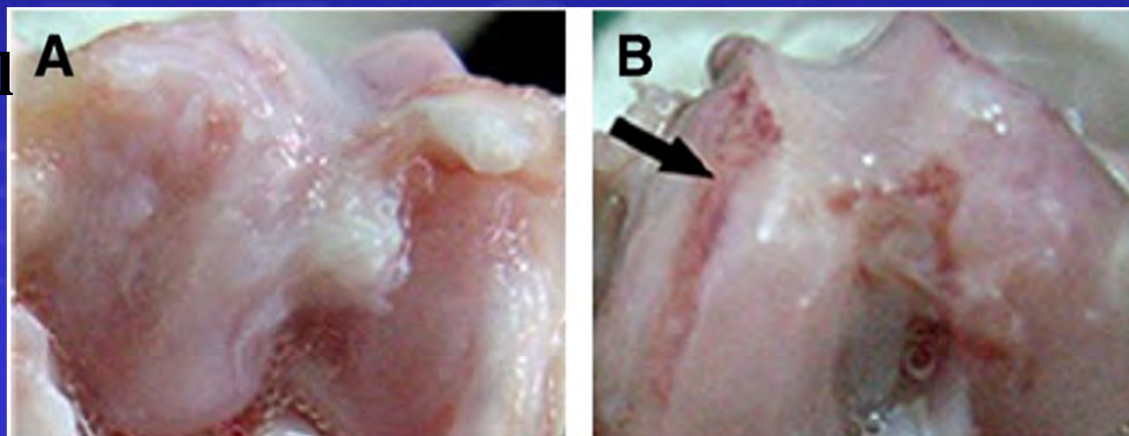
15 November 2018

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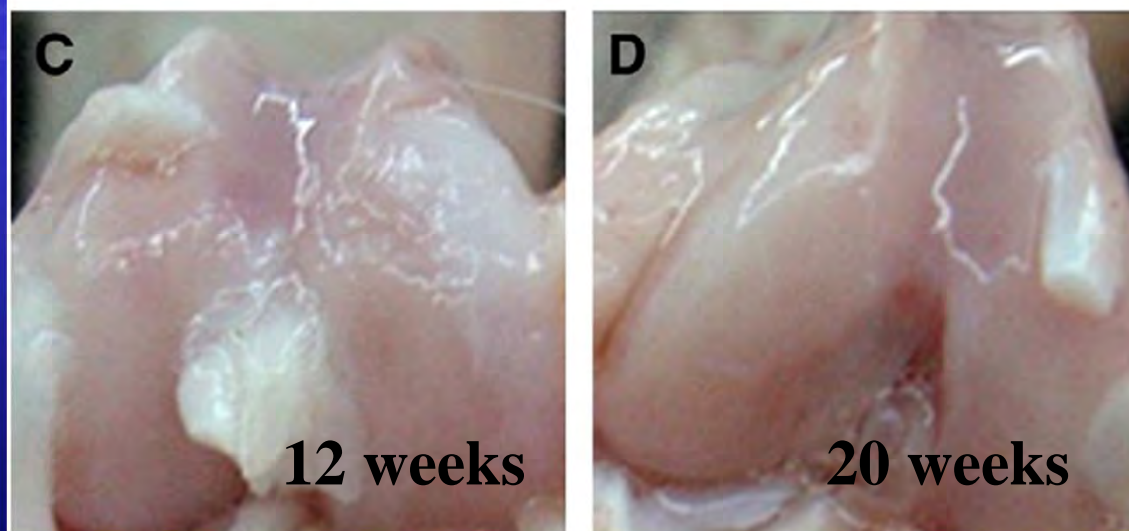
Treatment of osteoarthritis with infrapatellar fat pad derived mesenchymal stem cells in Rabbit

F.S. Toghraie ^a, N. Chenari ^b, M.A. Gholipour ^a, Z. Faghih ^b, S. Torabinejad ^c, S. Dehghani ^a, A. Ghaderi ^{b,d,*}

Control



MSC



Regulations and Use

- Differ greatly country to country (and even by state). No TGA approval.
- Differ according to type of stem cells, and degree of manipulation
- Haemopoietic/ bone marrow/fat/blood/ etc
- Research use only ACSEP
- It is an invasive procedure
- Vulnerable patients



Summary

- KJOA can create severe disability with altered qOL
- Better understanding of the pathogenesis has provided options with dietary changes, weight reduction and exercise therapies
- Therapies for articular cartilage 're-growth' remains unclear
- Careful, individual follow-up is best practice

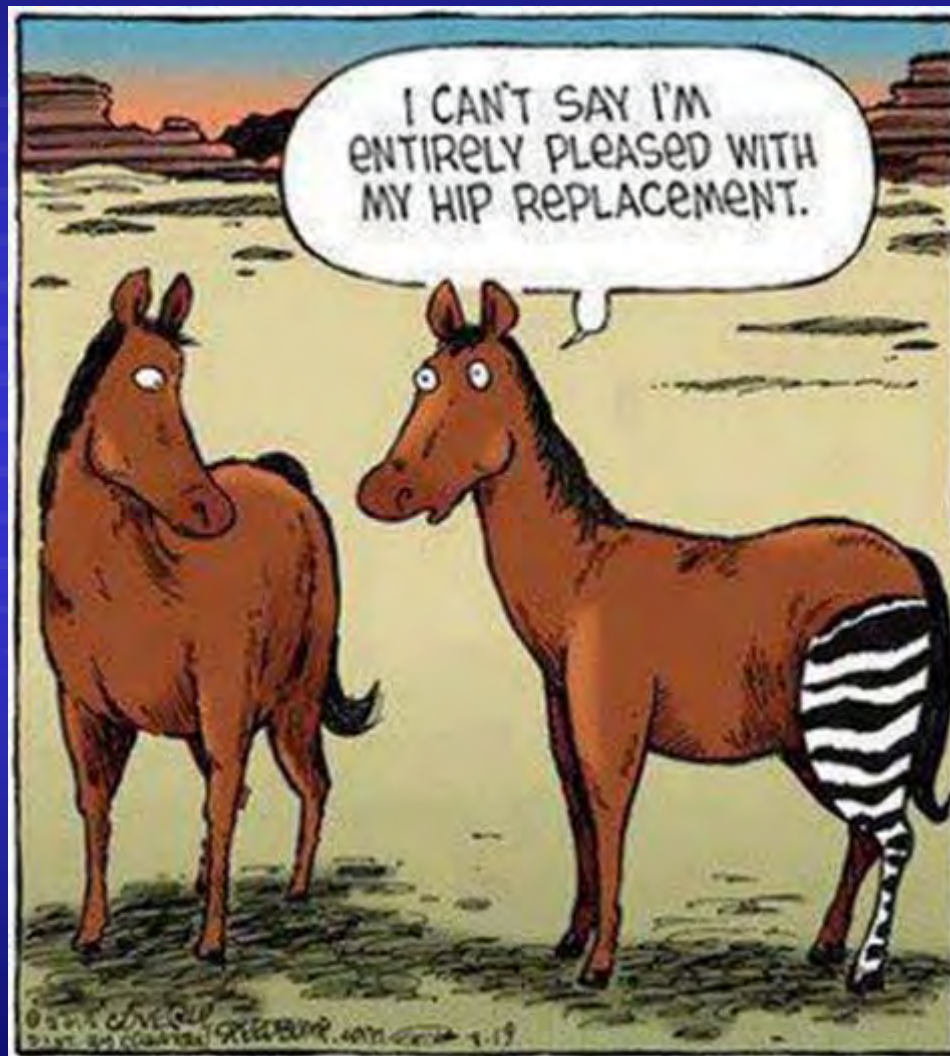


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Thank you



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