



New conservative and regenerative treatments for cartilage and tendon lesions

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CHU de Liège - Université de Liège

Premier Séminaire Médical de la Pro League



Introduction

Introduction

Cartilage

Tendon

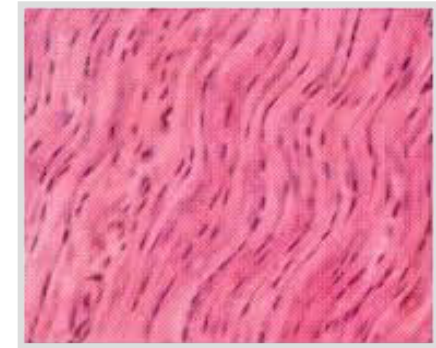


Introduction

Cartilage



Tendon

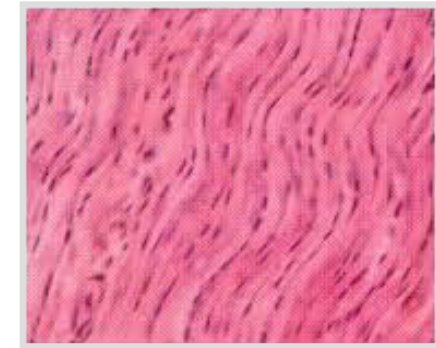


Introduction

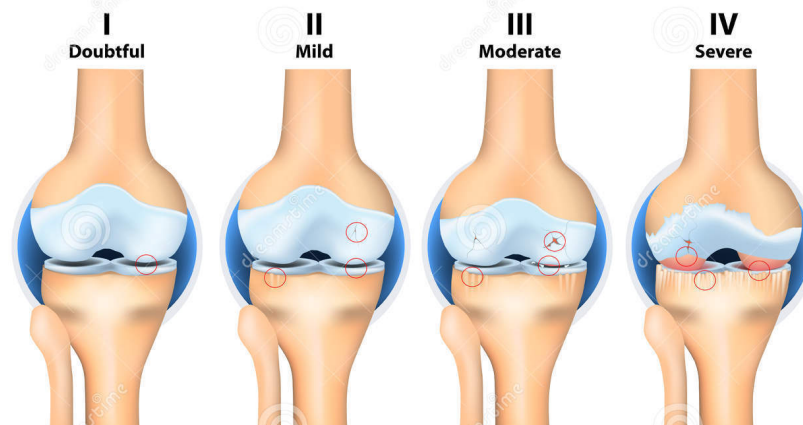
Cartilage



Tendon



STAGE OF KNEE OSTEOARTHRITIS



BASIC PRINCIPLE AND CORE SET

Combination of treatment modalities, including non-pharmacological and pharmacological therapies is strongly recommended

Core set - Information/Education

- Weight loss if overweight
- Exercise program (aerobic, strengthening)

STEP 1: Background treatment

if symptomatic

- (Paracetamol on a regular basis)
OR
- Chronic SYSADOA: prescription glucosamine sulfate and/or chondroitin sulfate ± as needed paracetamol

if still symptomatic ADD

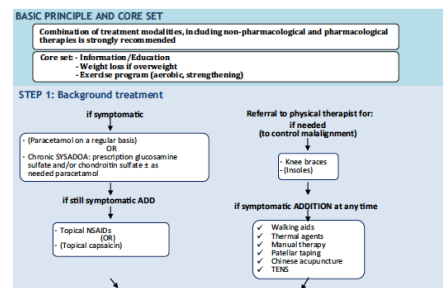
- Topical NSAIDs
(OR)
- (Topical capsaicin)

Referral to physical therapist for:
if needed
(to control malalignment)

- Knee braces
- (Insoles)

if symptomatic ADDITION at any time

- ✓ Walking aids
- ✓ Thermal agents
- ✓ Manual therapy
- ✓ Patellar taping
- ✓ Chinese acupuncture
- ✓ TENS



STEP 2: Advanced pharmacological management in the persistent symptomatic patient

if still or severely symptomatic

- Intermittent or continuous (longer cycles) oral NSAIDs

NORMAL GI RISK

- Non selective NSAID with PPI
- Cox-2 selective NSAID (consider PPI)

INCREASED GI RISK*

- Cox-2 selective NSAID with PPI
- Avoid non-selective NSAIDs

INCREASED CV RISK

- Prefer naproxen
- Avoid high-dose diclofenac and ibuprofen (if on low-dose aspirin)
- Caution with other non-selective NSAIDs
- Avoid Cox-2 selective NSAIDs

INCREASED RENAL RISK

- Avoid NSAIDs†

*Including use of low dose aspirin

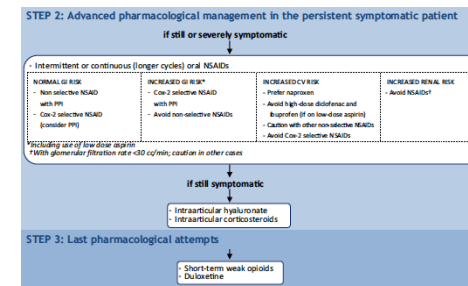
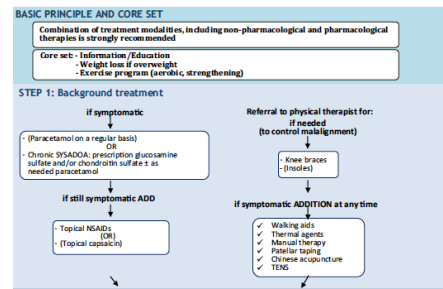
†With glomerular filtration rate <30 cc/min; caution in other cases

if still symptomatic

- Intraarticular hyaluronate
- Intraarticular corticosteroids

STEP 3: Last pharmacological attempts

- Short-term weak opioids
- Duloxetine



STEP 4: End-stage disease management and surgery

if severely symptomatic and poor quality of life

- Total joint replacement
- (Unicompartmental knee replacement)

if contraindicated

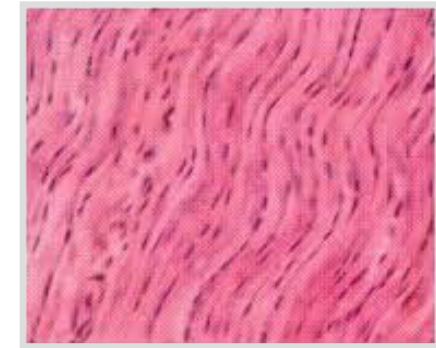
- Opioid analgesics

Introduction

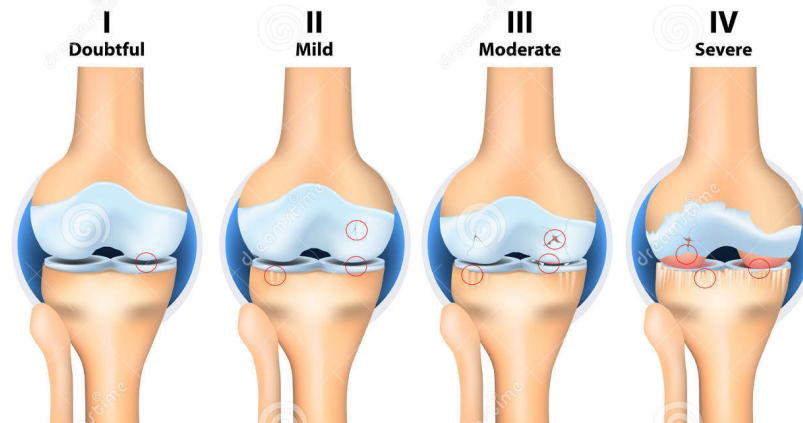
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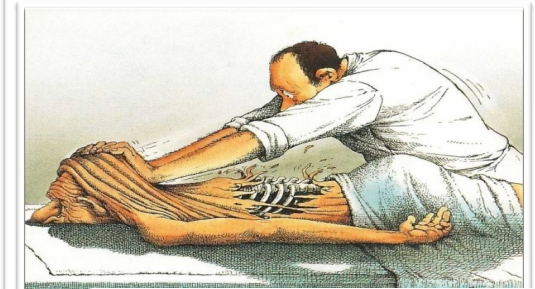


Tendon



STAGE OF KNEE OSTEOARTHRITIS





Conservative regenerative medicine



Conservative regenerative medicine

Regenerative biological treatment



Conservative regenerative medicine

Regenerative biological treatment



Augmenting body's physiology



Conservative regenerative medicine

Regenerative biological treatment



Augmenting body's physiology



Healing



Conservative regenerative medicine

Regenerative biological treatment



Augmenting body's physiology



Healing

- Prolotherapy



Conservative regenerative medicine

Regenerative biological treatment



Augmenting body's physiology



Healing

- Prolotherapy
- Platelet-Rich Plasma (PRP)



Conservative regenerative medicine

Regenerative biological treatment



Augmenting body's physiology



Healing

- Prolotherapy
- Platelet-Rich Plasma (PRP)
- Stem cells



Prolotherapy



Prolotherapy

Irritating agent (dextrose, zinc sulfate, phenol...)



Prolotherapy

Irritating agent (dextrose, zinc sulfate, phenol...)



Pathologic tissue



Prolotherapy

Irritating agent (dextrose, zinc sulfate, phenol...)



Pathologic tissue



Healing response

(collagen synthesis, chemoneuromodulation)



Prolotherapy

Irritating agent (dextrose, zinc sulfate, phenol...)



Pathologic tissue

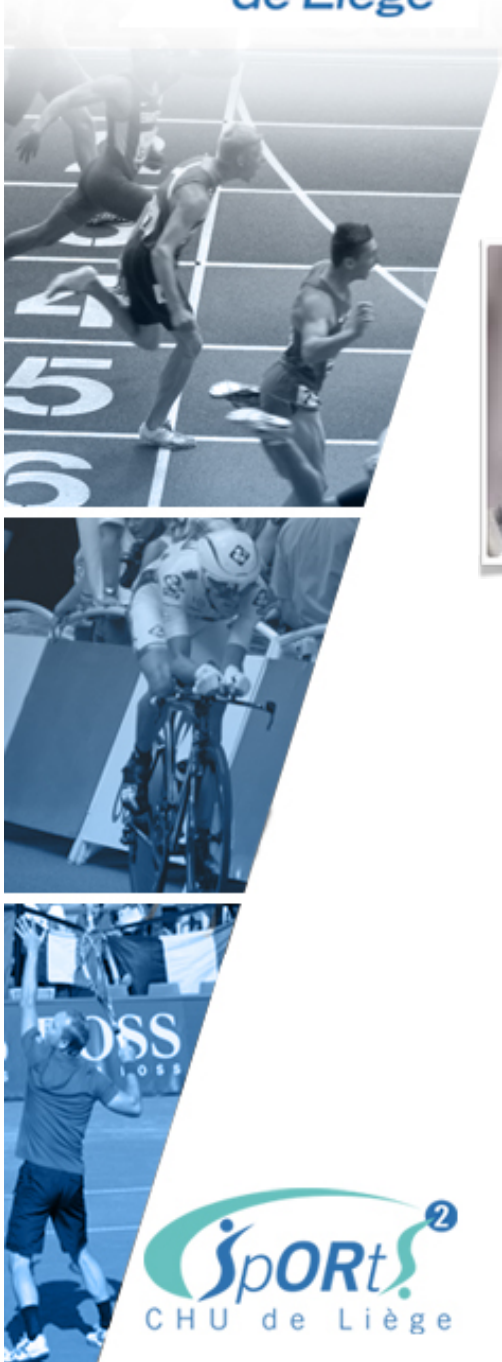


Healing response

(collagen synthesis, chemoneuromodulation)

Mechanism ????

Triggering inflammatory cascade



Prolotherapy

Irritating agent (dextrose, zinc sulfate, phenol...)



Pathologic tissue



Healing response

(collagen synthesis, chemoneuromodulation)

Mechanism ????

Triggering inflammatory cascade

Effective on pain (few quality trials !!!)



Platelet-Rich Plasma - PRP



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- Popular in sport



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- Removed from the doping list of the WADA



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- Popular in sport
- Removed from the doping list of the WADA
- Controversies in literature



Platelet-Rich Plasma - PRP

- Popular in sport
- Removed from the doping list of the WADA
- Controversies in literature
- No general agreement



What's PRP?



What's PRP?

- Centrifugation of **autologous** blood



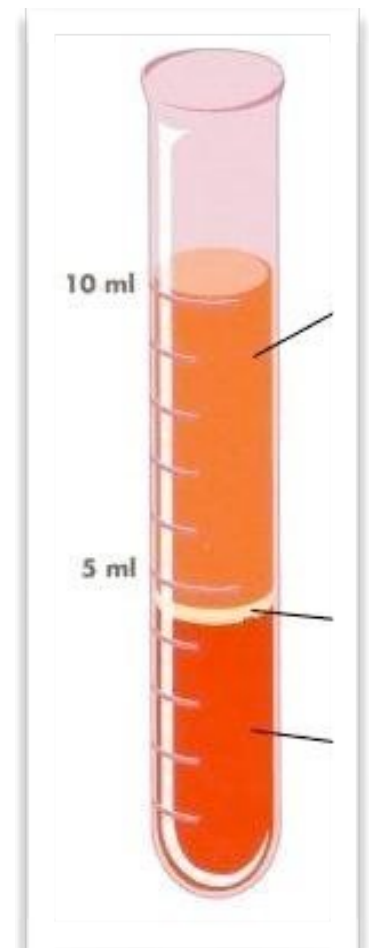
What's PRP?

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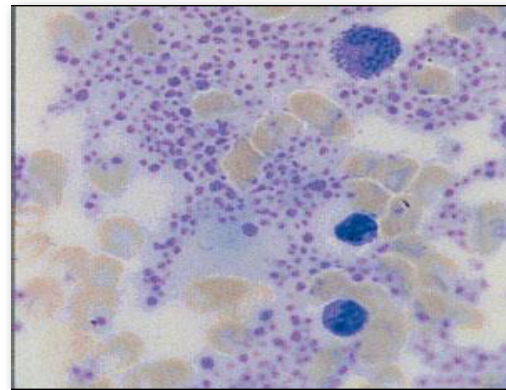
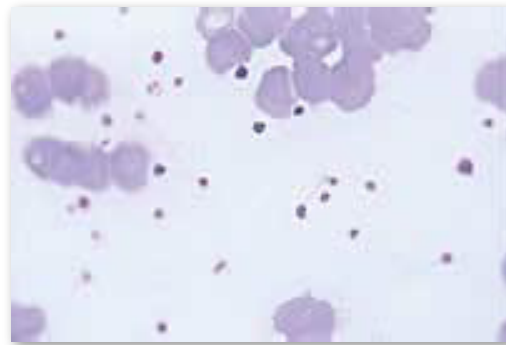


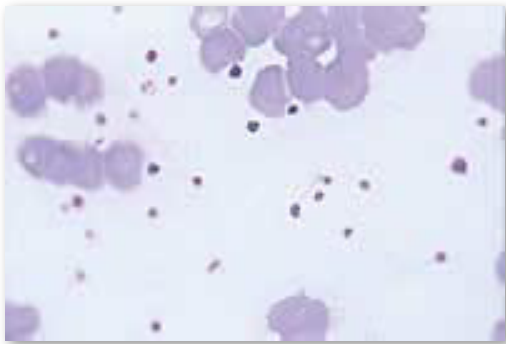
What's PRP?

- Centrifugation of autologous blood
- High concentration of platelets (3-10x)

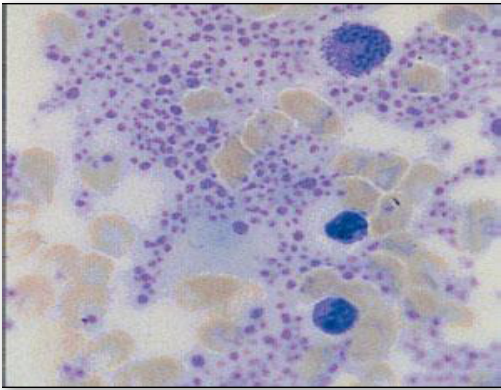




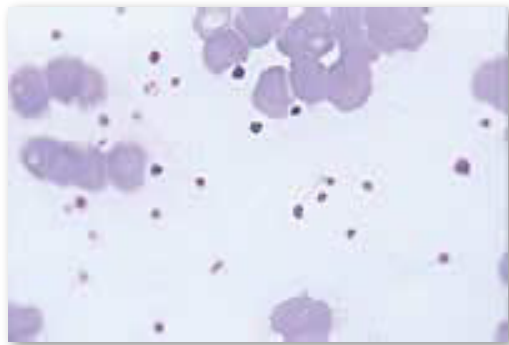




Blood



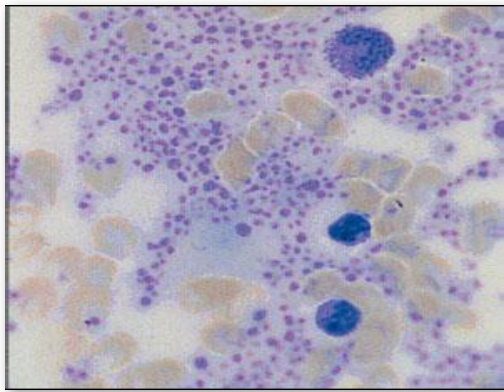
PRP



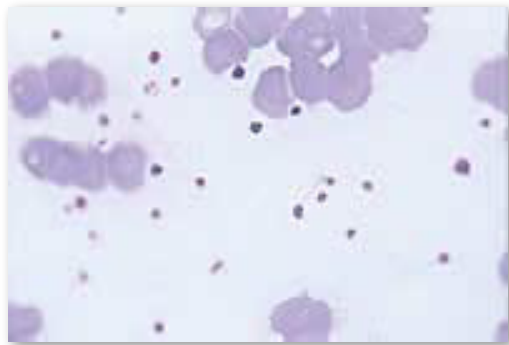
Blood

45% cellular
elements

55% plasma



PRP



Blood

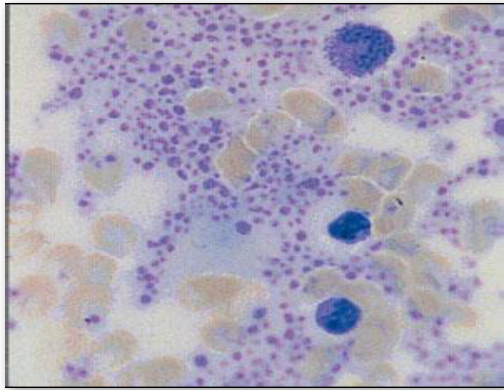
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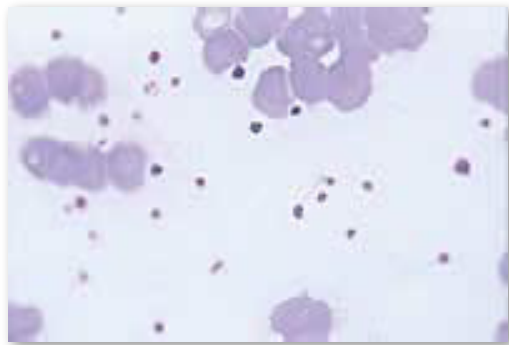
95% RC

4% platelets

1% WC



PRP



Blood

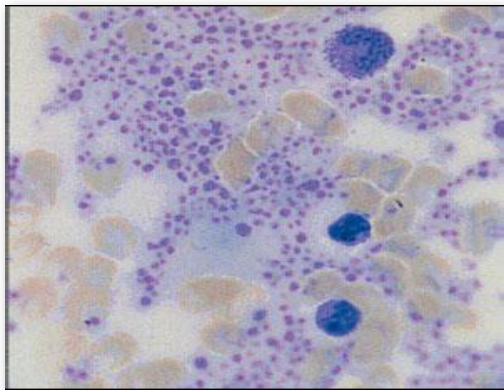
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PRP

45% cellular
elements

55% plasma

> 95% plaquettes

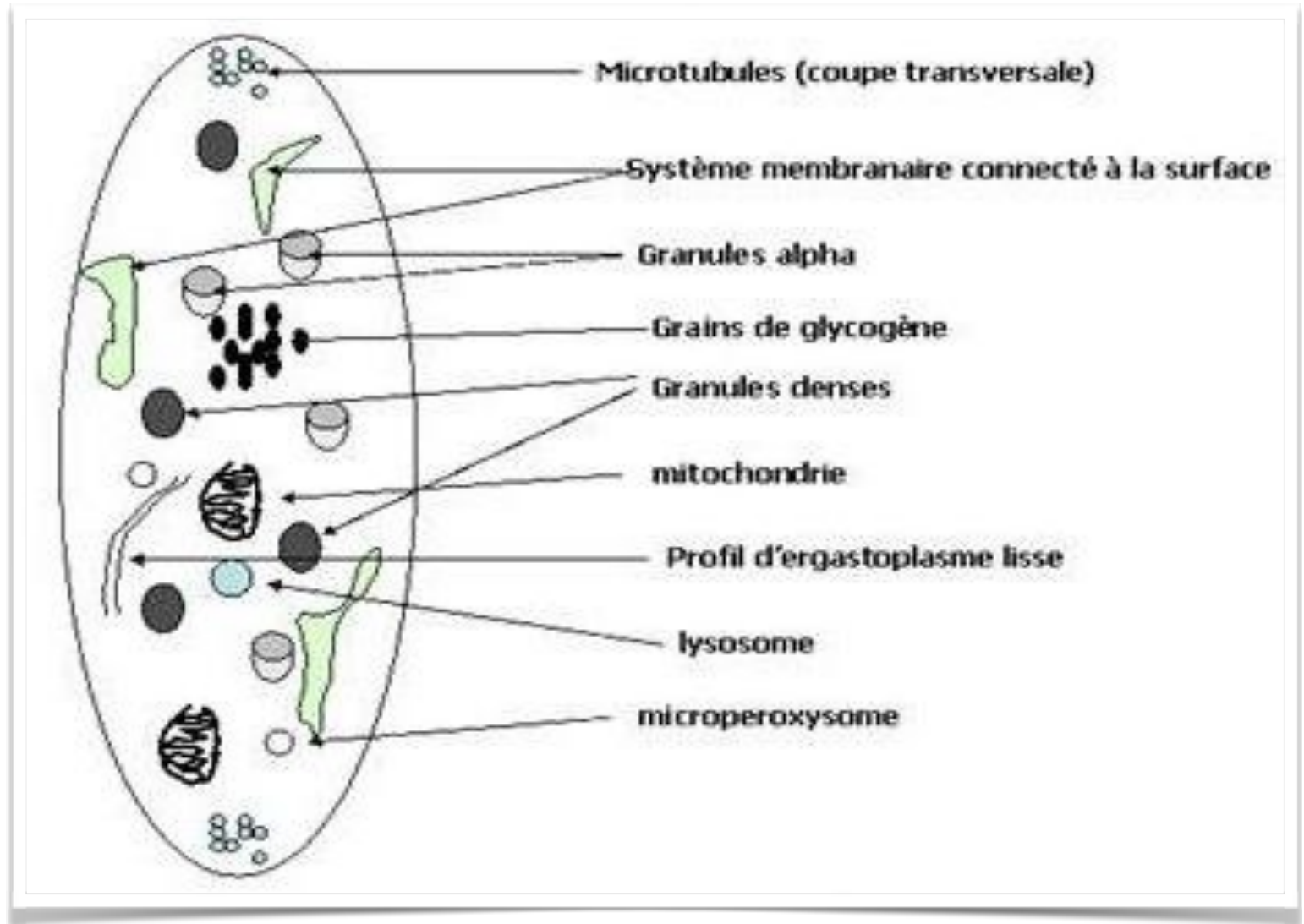
< 4% RC

< 1% WC

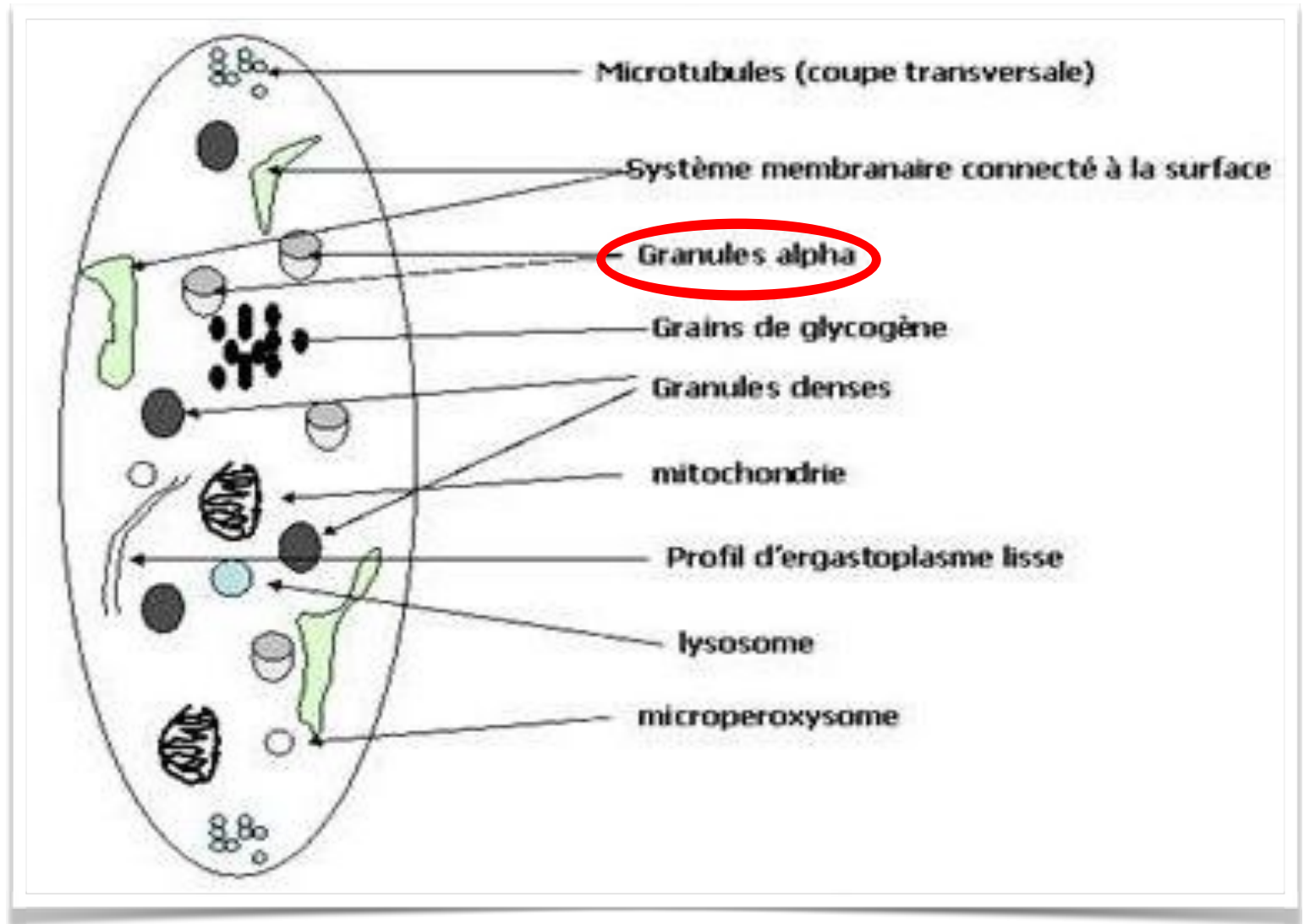
Platelets



Platelets



Platelets



Platelets



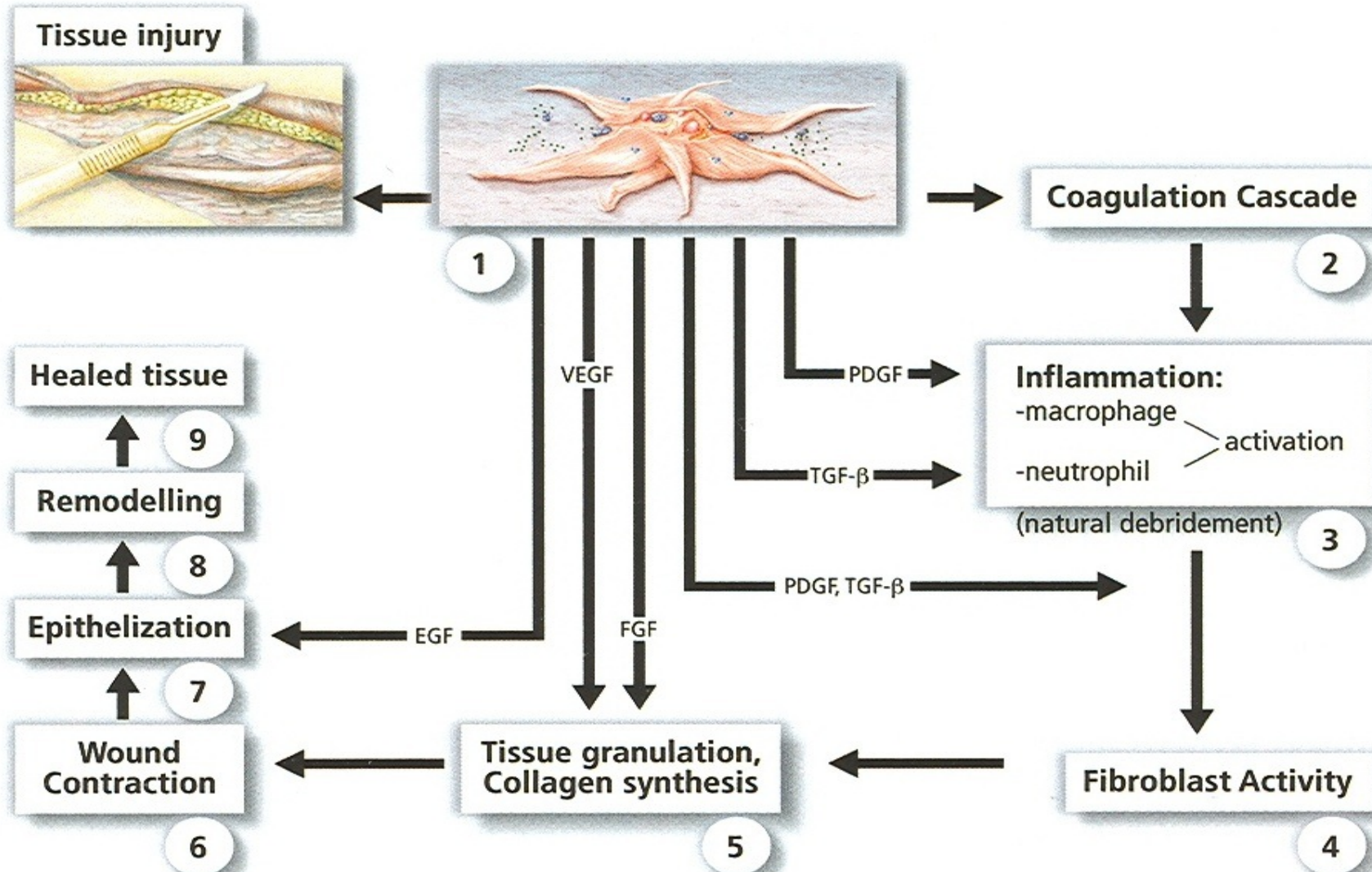
Platelets



- PDGF : stimulation production other GF
- TGF- β : cells proliferation and migration, collagen synthesis
- FGF : angiogenesis, cells proliferation and migration
- VEGF : angiogenesis
- HGF : cells proliferation and migration, angiogenesis
- IGF-1 : cells proliferation and migration, collagen and ECM synthesis





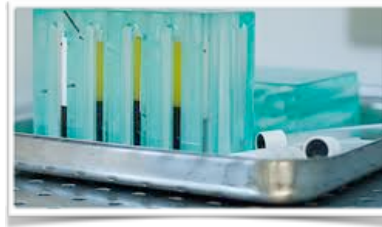
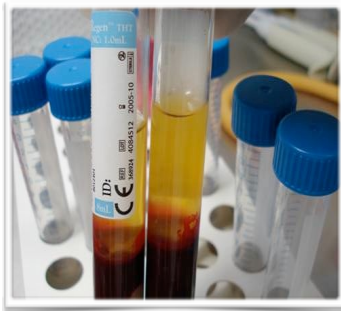
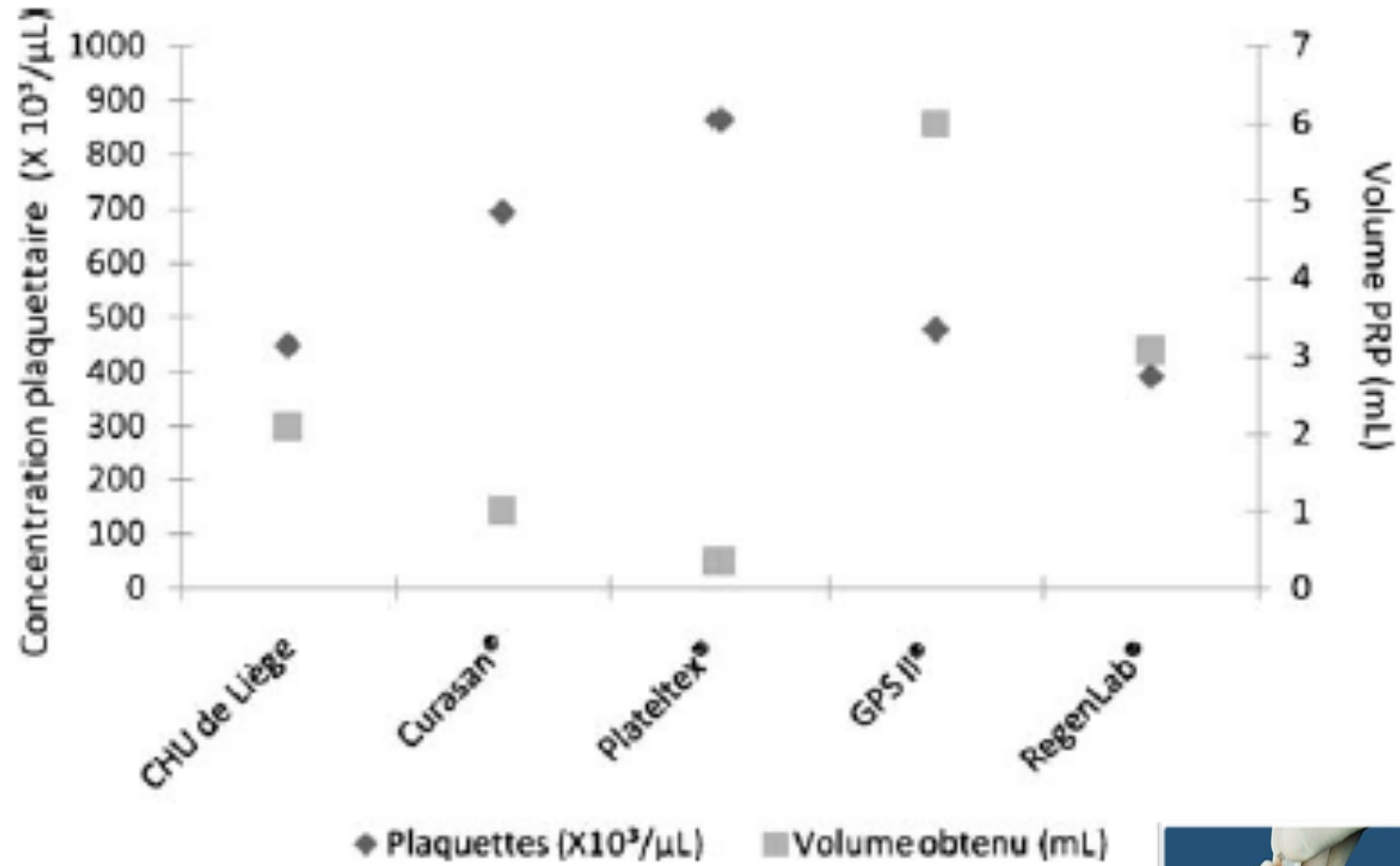




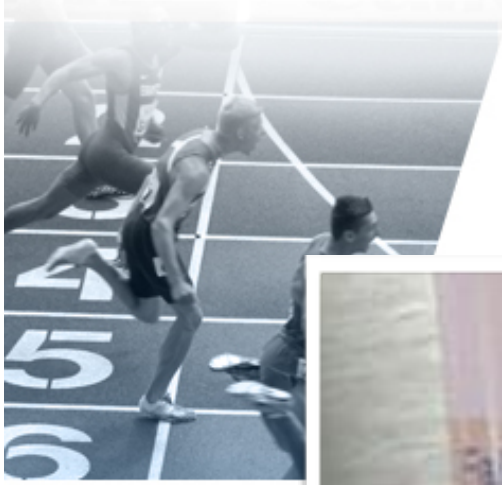


Pathologie Biologie 59 (2011) 157–160

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BIOLOGIE

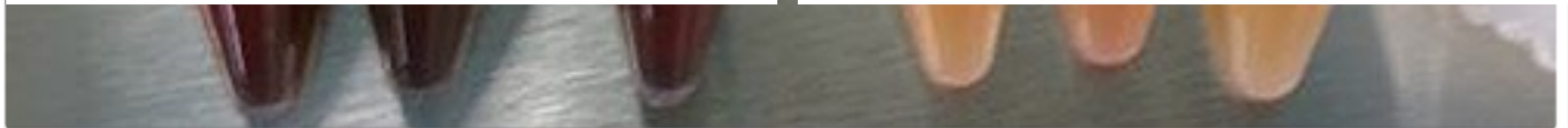


Red or yellow ?



Red PRP ?

Yellow PRP ?





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}

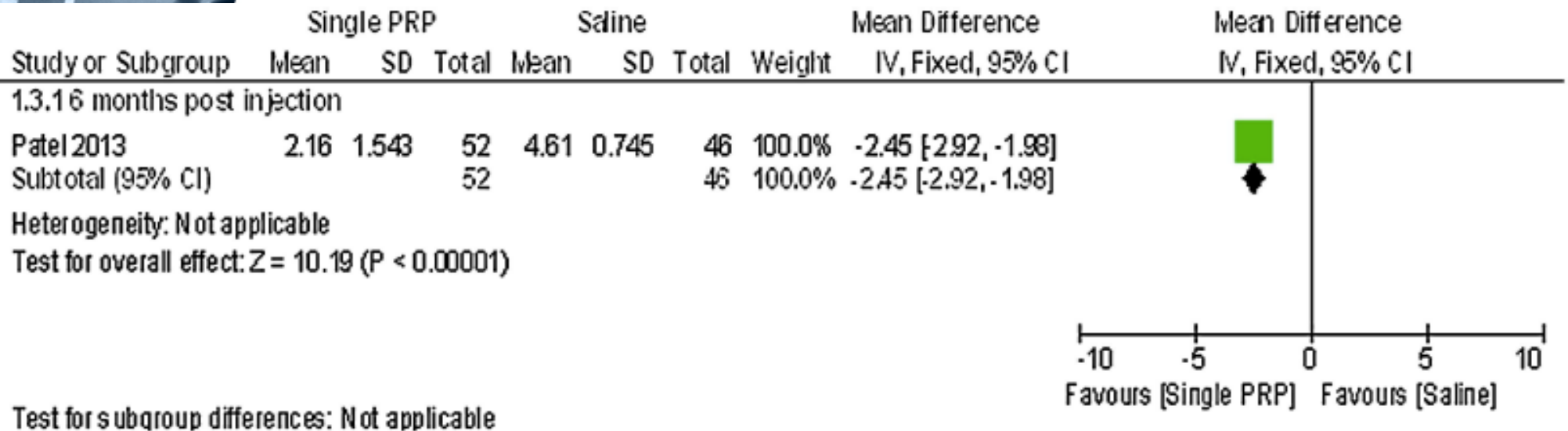


BJSM
The Journal of Sport
& Exercise Medicine

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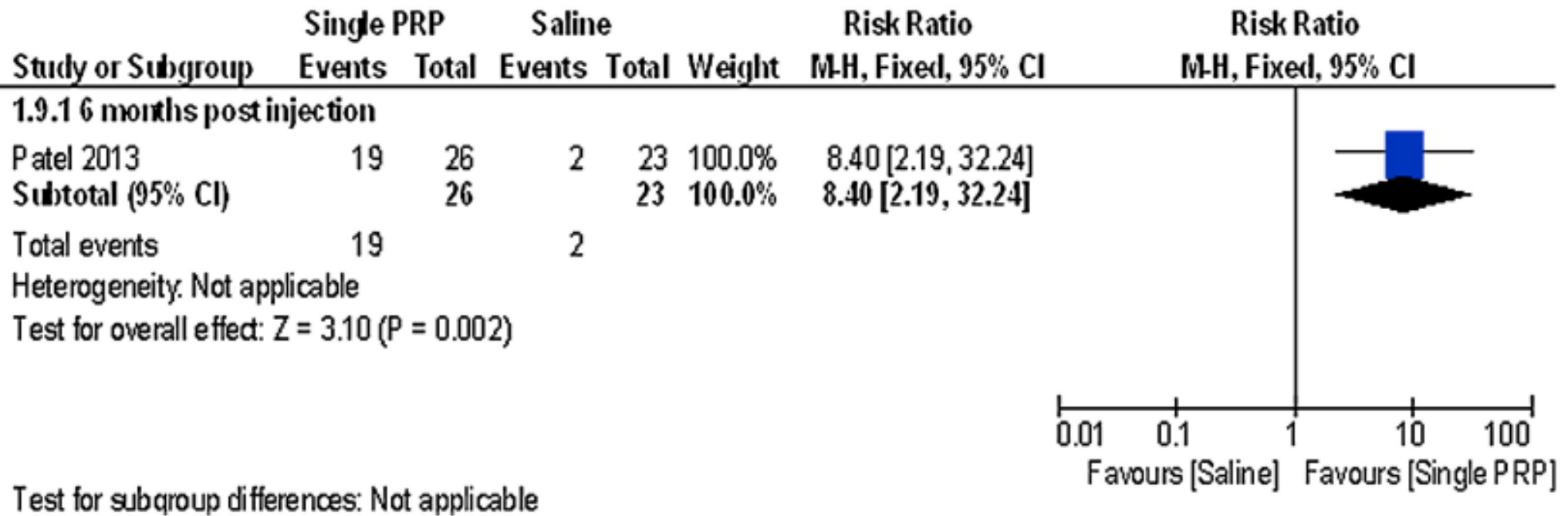
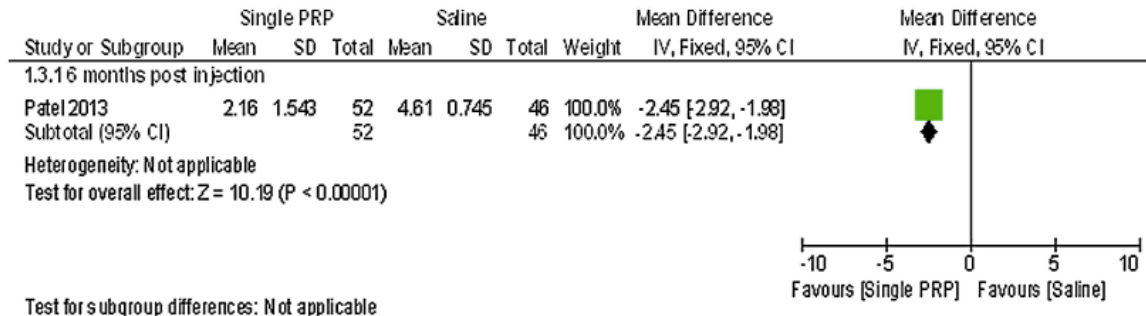
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Study or Subgroup	PRP		HA		Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Events	Total	Events	Total				

2.2.1 6 months post injection

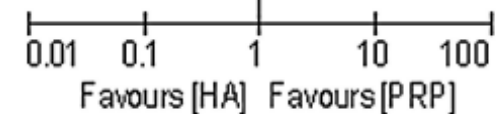
Sánchez 2012	34	89	21	87	80.9%	1.58 [1.00, 2.50]	
Vaquerizo 2013	26	48	5	48	19.1%	5.20 [2.18, 12.41]	
Subtotal (95% CI)		137		135	100.0%	2.27 [1.53, 3.38]	

Total events 60 26
Heterogeneity: $\chi^2 = 5.89$, $df = 1$ ($P = 0.02$); $I^2 = 83\%$
Test for overall effect: $Z = 4.05$ ($P < 0.0001$)

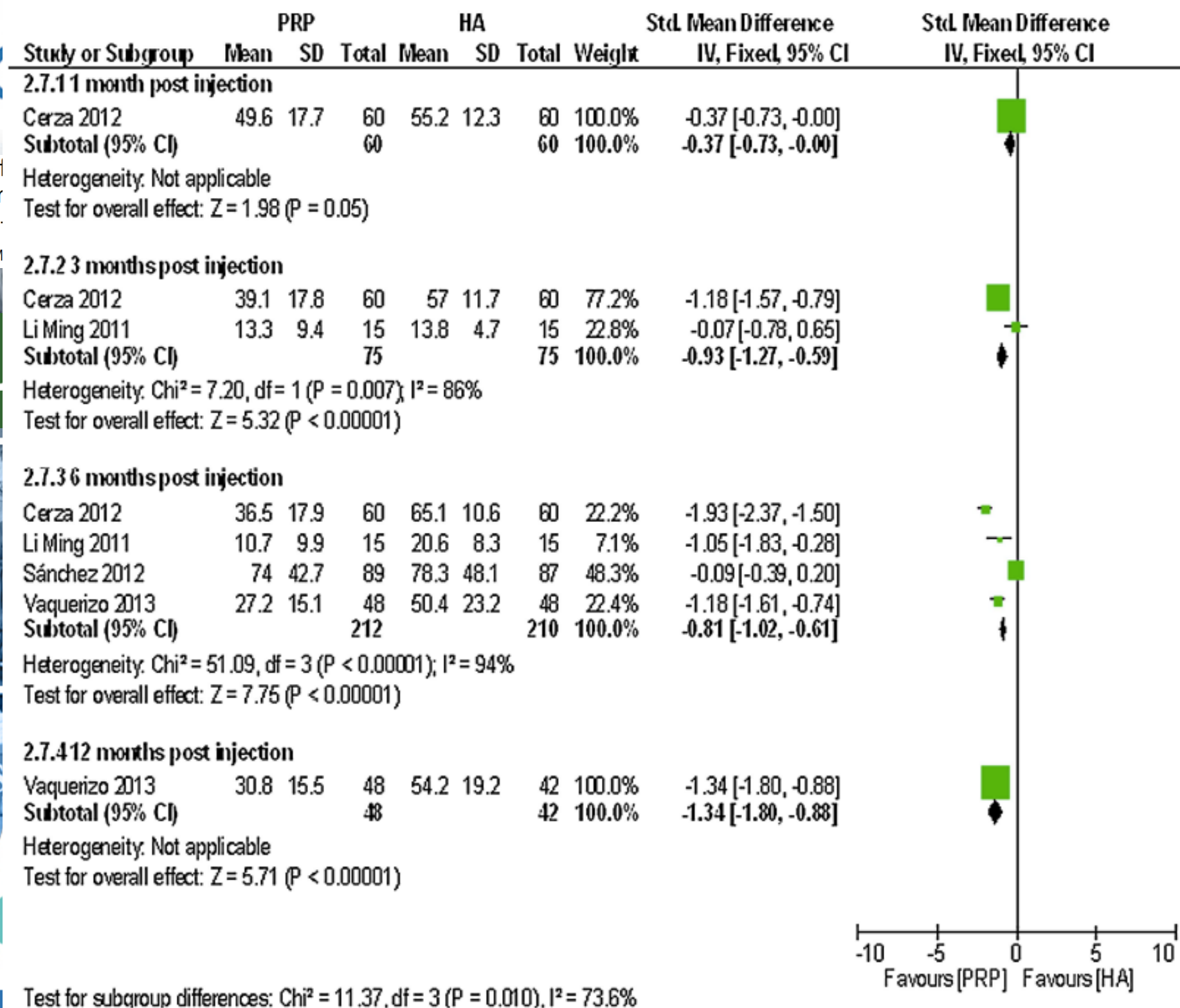
2.2.2 12 months post injection

Vaquerizo 2013	15	48	1	42	100.0%	13.13 [1.81, 95.20]	
Subtotal (95% CI)		48		42	100.0%	13.13 [1.81, 95.20]	

Total events 15 1
Heterogeneity: Not applicable
Test for overall effect: $Z = 2.55$ ($P = 0.01$)



Test for subgroup differences: $\chi^2 = 2.89$, $df = 1$ ($P = 0.09$), $I^2 = 65.4\%$



Tendinopathies



Tendinopathies

Platelet-rich plasma in the conservative treatment of painful tendinopathy: a systematic review and meta-analysis of controlled studies

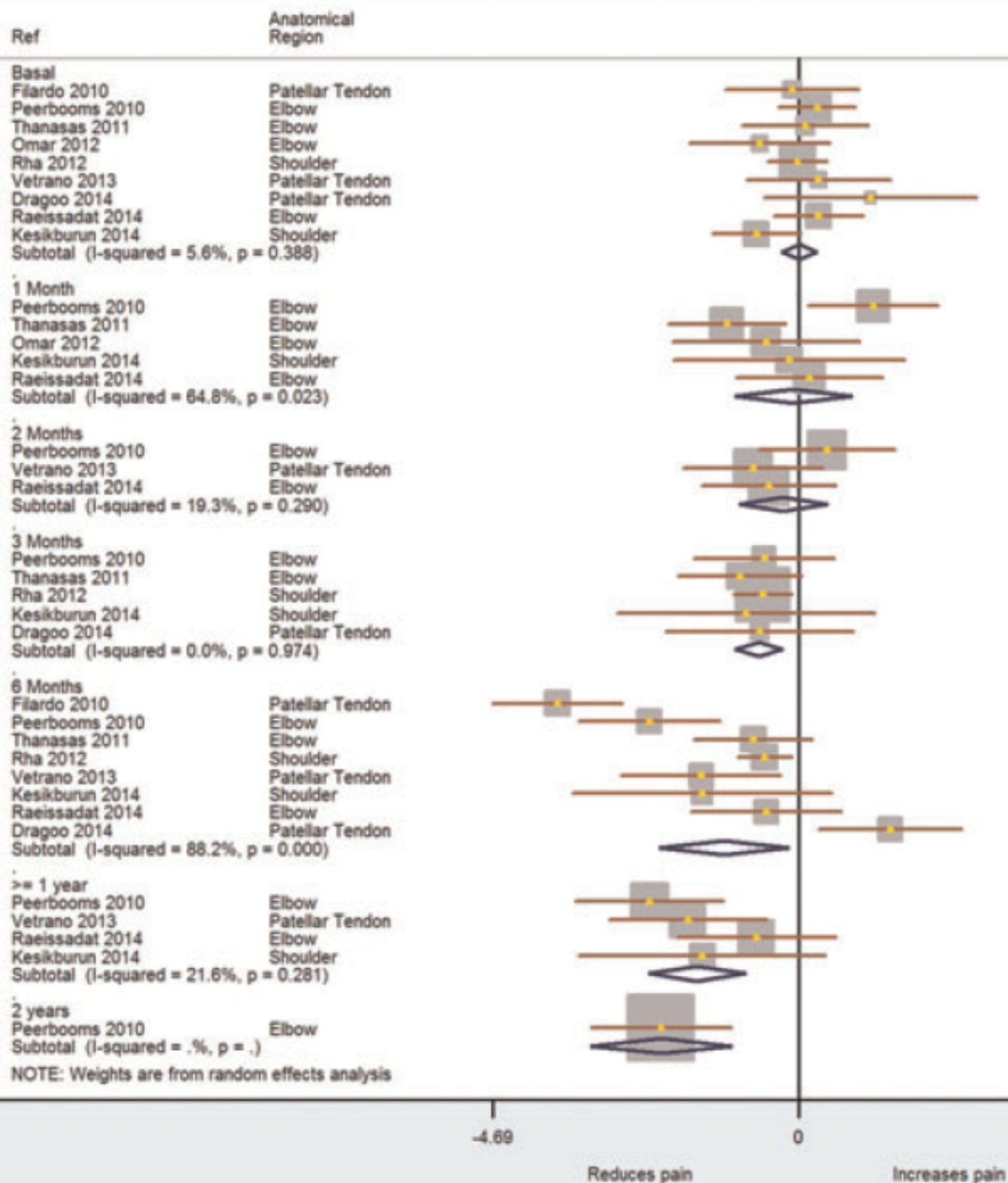
I. Andia[†], P. M. Latorre[‡], M. C. Gomez[‡], N. Burgos-Alonso[‡],
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BRITISH MEDICAL BULLETIN

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BRITISH MEDICAL JOURNAL



Tendinopathies



Tendinopathies

Strong evidence against platelet-rich plasma injections for chronic lateral epicondylar tendinopathy: a systematic review

Robert-Jan de Vos,^{1,2,3} Johann Windt,⁴ Adam Weir¹

British Journal of
Sports Medicine



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Background Chronic lateral epicondylar tendinopathy is frequent in athletes, and platelet-rich plasma (PRP) is being used increasingly in its treatment.

Objective To systematically review the literature on the efficacy of PRP injections for chronic lateral epicondylar tendinopathy.

Methods The databases of PubMed, EMBASE, CINAHL, Medline OvidSP, Scopus, Google Scholar, Web of Science and Cochrane Library were searched in October 2013. Inclusion criteria were a clinical diagnosis of chronic lateral epicondylar tendinopathy, a randomised controlled trial, an intervention with a PRP injection and the outcome measures described in terms of pain and/or function. One author screened the search results and two authors independently assessed the study quality using the Physiotherapy Evidence Database (PEDro) score. A study was considered to be of high quality if its PEDro score was ≥ 6 . A best evidence synthesis was used to identify the level of evidence.

Results 6 studies were included, of which four were considered to be of high quality. Three high-quality studies (75%) and two low-quality studies showed no significant benefit at the final follow-up measurement or predefined primary outcome score when compared with a control group. One high-quality study (25%) showed a beneficial effect of a PRP injection when compared with a corticosteroid injection (corticosteroid injections are harmful in tendinopathy). Based on the best evidence synthesis, there is strong evidence that PRP injections are not efficacious in chronic lateral epicondylar tendinopathy.

Conclusions There is strong evidence that PRP injections are not efficacious in the management of chronic lateral elbow tendinopathy.





- Autologous





- Autologous
- Antibacterial effect





- **Autologous**
- Antibacterial effect
- **No anesthetics**





- Autologous
- Antibacterial effect
- No anesthetics
- No NSAIDs





- **Autologous**
- Antibacterial effect
- **No anesthetics**
- **No NSAIDs**
- US guidance



Rehabilitation



Rehabilitation

- After painful period —> **sub-maximum eccentric rehabilitation** + stretching



Rehabilitation

- After painful period —> **sub-maximum eccentric rehabilitation** + stretching
- **Best results** if rehabilitation protocol



Rehabilitation

- After painful period —> **sub-maximum eccentric rehabilitation** + stretching
- **Best results** if rehabilitation protocol
- **Eccentric** > concentric (Kaux 2013)



Rehabilitation

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- **Eccentric** > concentric (Kaux 2013)
- Reathletisation



Rehabilitation

- After painful period —> **sub-maximum eccentric rehabilitation** + stretching
- **Best results** if rehabilitation protocol
- **Eccentric** > concentric (Kaux 2013)
- Reathletisation
- Orthoses or strapping (?)



Second infiltration ?



Second infiltration ?

Using platelet-rich plasma to treat jumper's knees: Exploring the effect of a second closely-timed infiltration

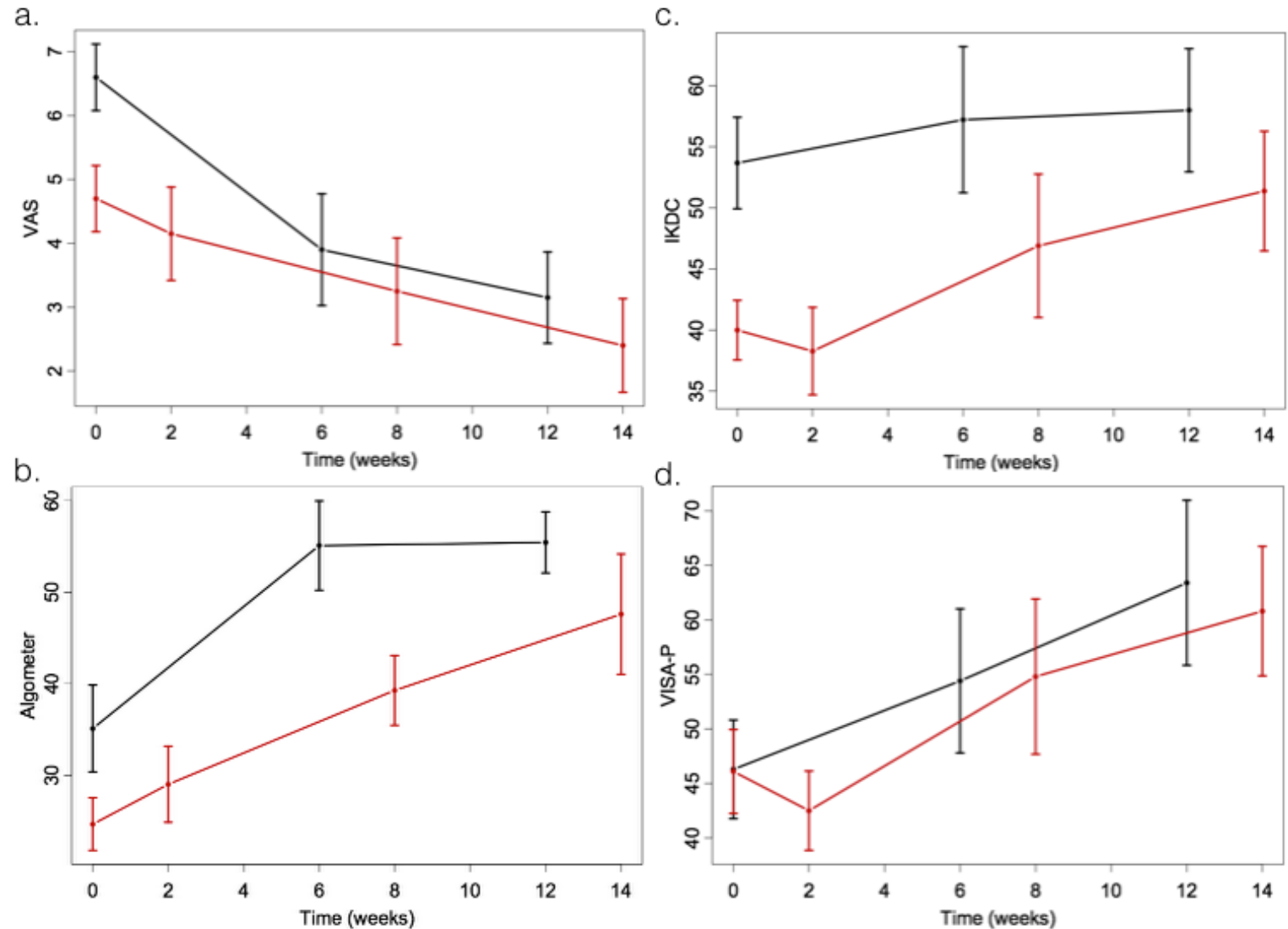
J.F. Kaux^{a,*}, J.L. Croisier^b, B. Forthomme^b, C. Le Goff^c, F. Buhler^b, B. Savanier^b, S. Delcour^c, A. Gothot^c, J.M. Crielaard^a



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Stem cells



Stem cells

- The most recent biological treatment



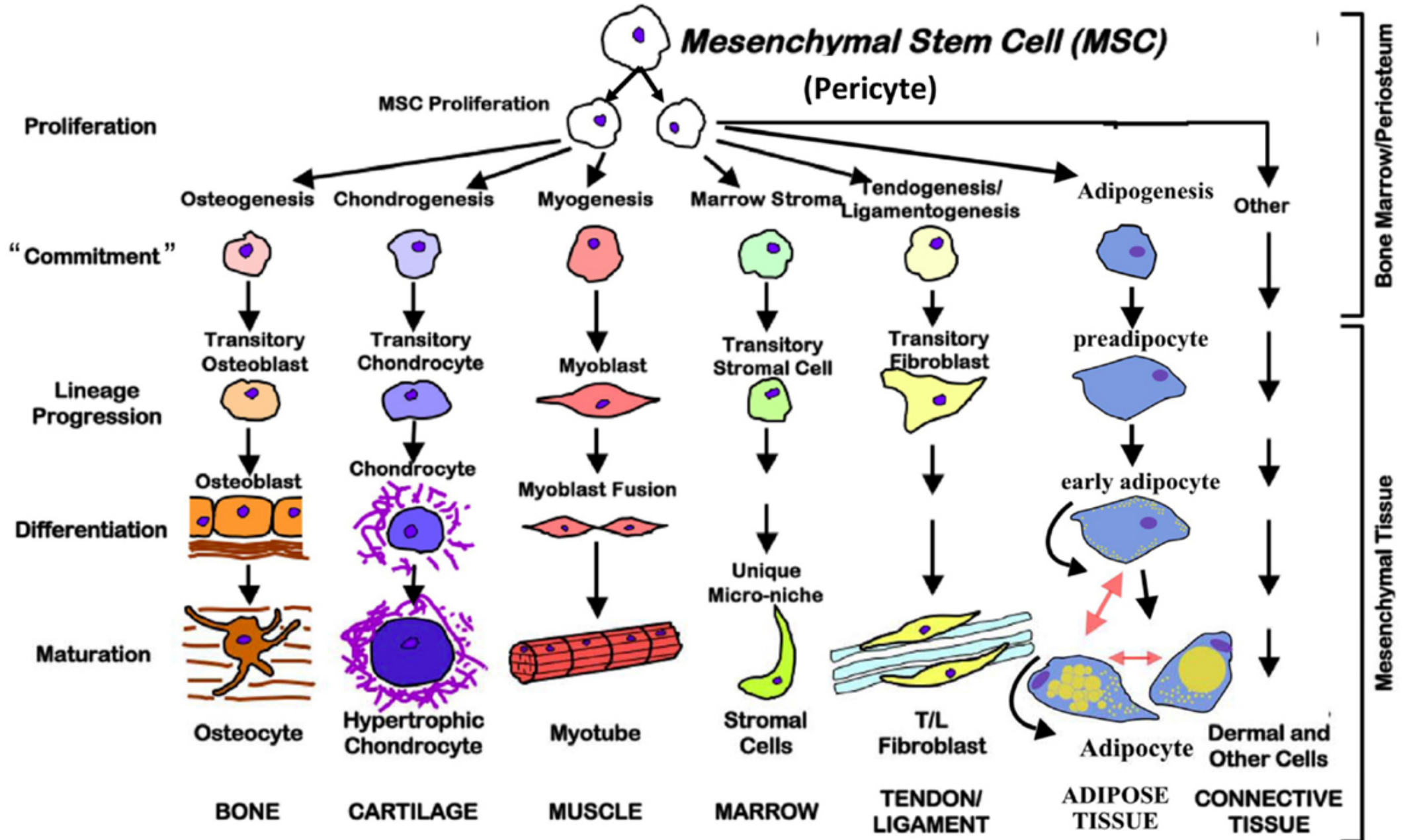
Stem cells

- The most recent biological treatment
- Multipotent stromal cells



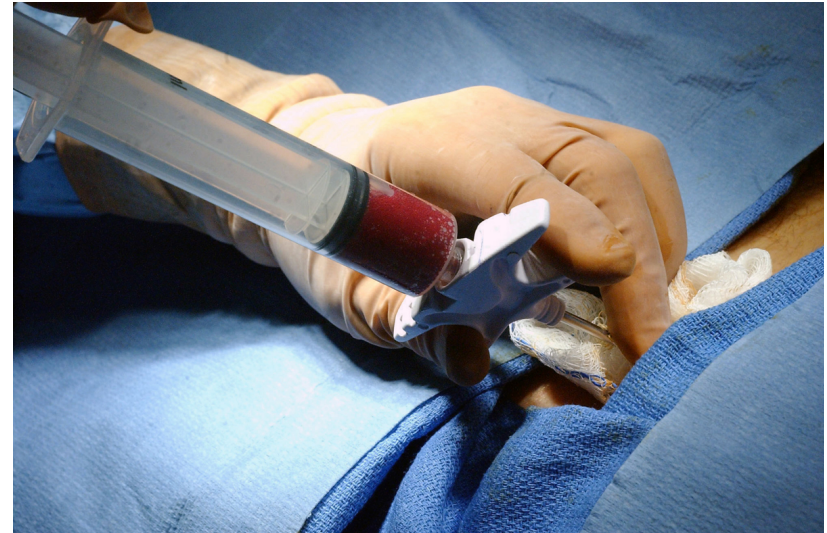
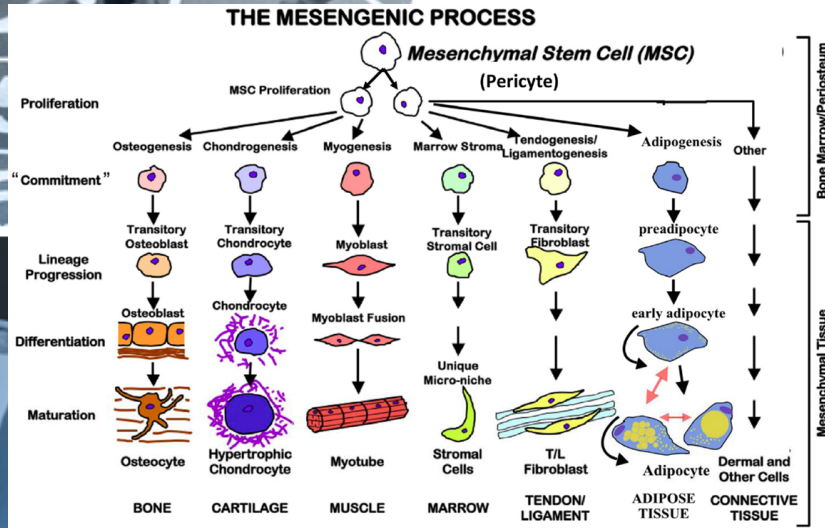
Stem cells

THE MESENGENIC PROCESS



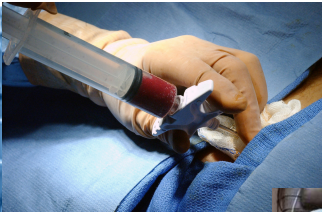
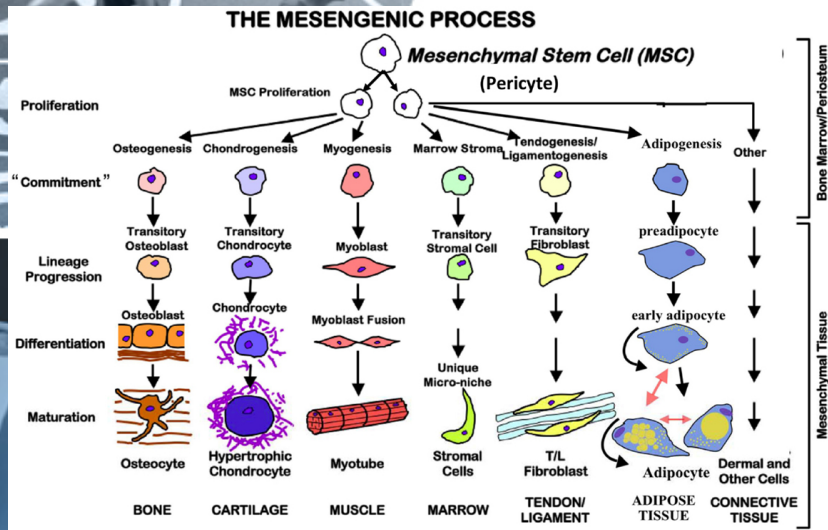
Stem cells

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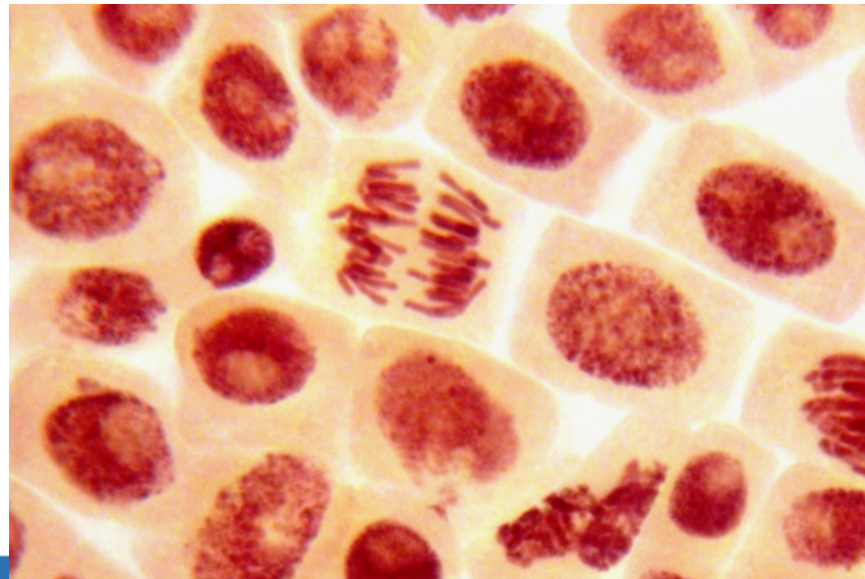
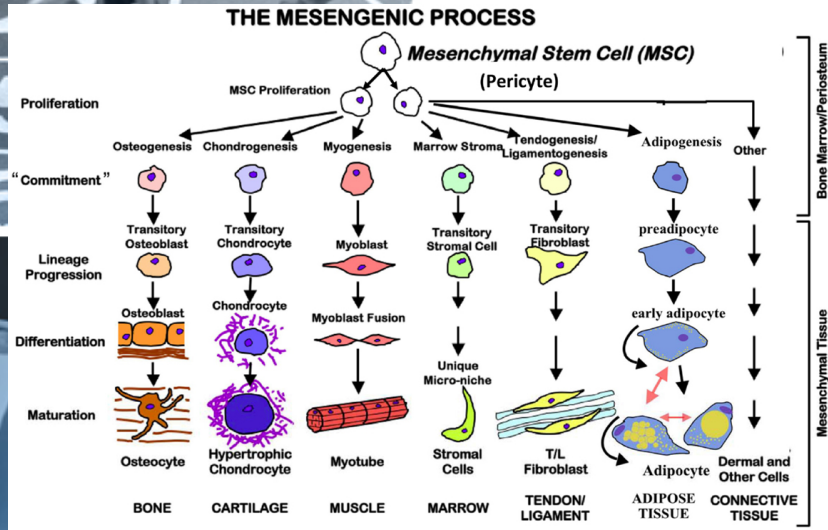
Stem cells

- The most recent biological treatment
- Multipotent stromal cells



Stem cells

- The most recent biological treatment
- Multipotent stromal cells







- Literature **stem cells** therapies for **orthopaedic** conditions:
 - basic science
 - animal studies
 - case reports
 - case series
 - cohort studies



Cartilage



Cartilage

Mesenchymal
stem cells



Cartilage

**Mesenchymal
stem cells**



**Repair 20 X 30 mm
lesion of medial
femoral condyle**



Cartilage

Mesenchymal
stem cells



Repair 20 X 30 mm
lesion of medial
femoral condyle



Smooth tissue



Cartilage

**Mesenchymal
stem cells**



**Repair 20 X 30 mm
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Smooth tissue



**Decrease pain,
increase range of
motion**



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Smooth tissue



Decrease pain,
increase range of
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Filling the defect on
imaging (minor flaw
still detectable)



Cartilage

Mesenchymal
stem cells



Repair 20 X 30 mm
lesion of medial
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Smooth tissue



Decrease pain,
increase range of
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Filling the defect on
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Layers of fibrous
tissue, hyaline-like
cartilage, chondral
bone



Tendinopathies





Tendinopathies

- Epicondylitis - Achilles tendinopathies





Tendinopathies

- Epicondylitis - Achilles tendinopathies
- US-guided





Tendinopathies

- **Epicondylitis - Achilles tendinopathies**
- US-guided
- **Safety** of using allogenic stem cells





Tendinopathies

- **Epicondylitis - Achilles tendinopathies**
 - US-guided
 - **Safety** of using allogenic stem cells
 - **Ectopic bone** into some tendon samples
- ➡ Driving stem cells toward tenogenic lineage prior to injection





Tendinopathies

- **Epicondylitis - Achilles tendinopathies**
 - US-guided
 - **Safety** of using allogenic stem cells
 - **Ectopic bone** into some tendon samples
- ⇒ Driving stem cells toward tenogenic lineage prior to injection
- **Tendon loading** ⇒ Tenogenic differentiation and biomechanical properties of the tissue engineered constructs containing stem cells



Conclusion



Conclusion

- Regenerative biological treatment



Conclusion

- Regenerative biological treatment
- Augmenting body's physiology



Conclusion

- Regenerative biological treatment
- Augmenting body's physiology
- (Prolotherapy) - PRP - Stem cells



Conclusion

- Regenerative biological treatment
- Augmenting body's physiology
- (Prolotherapy) - PRP - Stem cells
- Encouraging results



Conclusion

- Regenerative biological treatment
- Augmenting body's physiology
- (Prolotherapy) - PRP - Stem cells
- Encouraging results
- RCT needed





Université
de Liège



Thank you...

Questions ?

Lien ORBI : <http://hdl.handle.net/2268/195257>

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