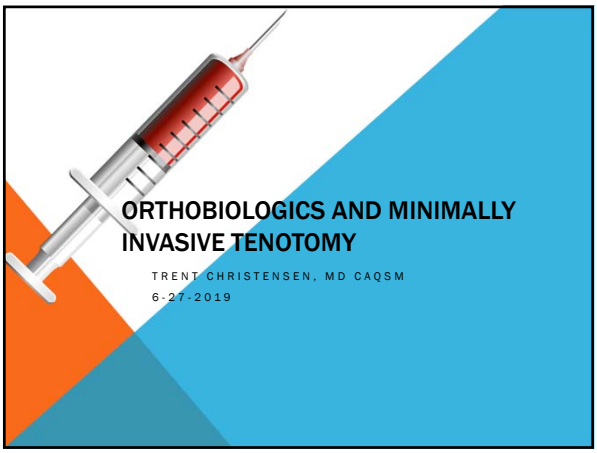


ORTHOBIOLOGICS AND MINIMALLY INVASIVE TENOTOMY

TRENT CHRISTENSEN, MD CAQSM

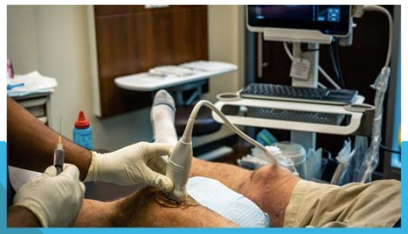
6-27-2019

DISCLOSURE

Neither I, Trent Christensen, nor any family member(s), have any relevant financial relationships to be discussed, directly or indirectly, referred to or illustrated with or without recognition within the presentation.

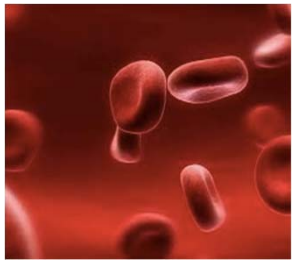
OBJECTIVES

- What types of biologics are out there?
- What is percutaneous tenotomy?
- Indications?
- Do they work?



ORTHOBIOLOGICS

- PLATELET-RICH PLASMA (PRP)
- AUTOLOGOUS BLOOD INJECTIONS (ABI)
- MESENCHYMAL STEM CELLS (MSCs)



PLATELET-RICH PLASMA (PRP)

What is it?:

- Platelet-rich plasma (PRP) is a blood concentrate rich in platelets and growth factors, which is derived from autologous centrifuged blood.
- Injected into sites of tendon injury or degenerative arthritis to promote healing or and pain reduction
- First used in early 1990s for maxillofacial surgery
- Early 2000s introduced into the ortho world

Mechanism of Action:

- Alpha granules >30 bioactive proteins (growth factors)
- Promote healing through GF triggering proliferation, differentiation, chemotaxis and tissue morphogenesis needed in tissue repair (PDGF, TGF-B, VEGF, EGF, HGF)
- Inhibit inflammation through anti-catabolic GF (PDGF, IGF-1, TGF-B)

PLATELET-RICH PLASMA (PRP)

- Currently >17 commercial PRP systems- Variability in plt conc, spin techniques, activating agents and leukocyte levels.

Leukocyte Rich

- High WBCs
- Ideal for areas that the body is not reacting with inflammation (tendinopathy)

Leukocyte Poor

- Low WBCs
- Ideal in areas where there's already an inflammatory response that we don't want to enhance (degenerative osteoarthritis)

PLATELET-RICH PLASMA (PRP)

Additional Information:

- 6 week recovery
- PRP therapy is rarely covered by standard insurance, but is typically covered by workers' compensation.
- $500-900 for PRP therapy.

PLATELET-RICH PLASMA (PRP)

Indication: Tendinosis, degenerative arthritis, muscle/tendon tears, chondromalcia, OCD, TKA, ACL reconstruction, non-union bone healing

PRP AND TENDINOPATHY

Am J Sports Med 2017

The effectiveness of platelet-rich plasma in the treatment of tendinopathy: A meta-analysis of randomized controlled clinical trials.

Fitzpatrick J, Bulsara M, Zheng MH.

- 18 Studies with 1066 patients
- Tendon types: Achilles, RC, patellar, TE (common ext tendon)
- Primary outcome: decreased pain intensity and increased function
- Assessed 3,6, and 12 months
- Results: reported as standardized mean difference with CI 95%
  - LR-PRP strongly positive effect (SMD 36.38; 95% CI)
  - LP-PRP positive effect (SMD 26.77; 95% CI)
  - Corticosteroid effect (SMD 23.82; 95% CI)
  - Saline effect (SMD 14.62; 95% CI)

CONCLUSION: "There is good evidence to support single ultrasound guided injection LR-PRP in tendinopathy".

Level of Evidence: 1

PRP AND OA

Arthroscopy: The Journal of Arthroscopic & Related Surgery 2016

Efficacy of Intra-articular Platelet-Rich Plasma Injection in Knee Osteoarthritis: A Systematic Review

Meheux CJ, McCulloch PC, Lintner DM, Varner KE, Harris JD.

- 6 Studies with 739 patients (817 knees) symptomatic knee OA
- Primary outcome: Standardized Patient-reported outcome measures
- Assessed 6 and 12 months
- Results:
  - PRP significantly improved validated patient reported outcomes (pain, physical function, and stiffness) (WOMAC and IKDC)
  - Better than HA in improving patient outcomes. PRP (baseline) 52.36➔28.5 (6m)➔22.8 (12m) vs HA (baseline) 52.36 ➔ 43.4(6m) ➔38.1 (12m)

CONCLUSIONS: "In symptomatic knee OA, PRP injections results in significant improvement up to 12 months post-injection. Significantly better than HA".

Level of Evidence: 1

PRP SUMMARY

Strongly Recommend

- **PRP is an effective treatment of tendinopathy, including: Lateral epicondylosis, achilles tendinopathy, patellar tendinopathy, rotator cuff tendinopathy, and gluteal tendinopathy. (AJSM 2017, Arthroscopy 2017, J Orthop Traumatol 2016, AJSM 2019)**
- **PRP is an effective treatment for knee osteoarthritis. (Arthroscopy 2016, Arthroscopy 2015, BJSM 2015)**
- **PRP is superior to HA in the treatment of Knee OA. (Arthroscopy 2016, BJSM 2015)**

Weakly Recommend

- **PRP is likely an effective treatment for hip OA (Cartilage 2016)**
- **PRP is likely an effective treatment for plantar fasciitis (Int Orthopedics 2017)**
- **PRP is likely an effective treatment for cartilage injury (Int J Surg. 2017, World J Orthop 2016, Arthroscopy 2015)**

Other areas being studied

- **Primary rotator cuff repairs, acute hamstring injuries, Non-union bone healing, total knee arthroplasty, and ACL reconstruction. (Arthroscopy 2015, Int J Surgery 2016, Foot and Ankle Clinc 2016, Int J Surg. 2017, World J Orthop 2016, Arthroscopy 2016,**

AUTOLOGOUS BLOOD INJECTION (ABI)

What is it?:

- Whole blood with platelets (GF), WBCS and RBCs
- Injected into sites of tendon injury or degenerative arthritis to promote healing or and pain reduction

Mechanism of Action: Similar to PRP but no concentration of platelets, Leukocyte included, RBCs included.

AUTOLOGOUS BLOOD INJECTION (ABI)

Additional information:

- 6 week recovery
- ABI therapy is rarely covered by standard insurance, but is typically covered by workers' compensation.
- $300-500 for ABI therapy.

Indication: Tendinopathy

ABI AND TENDINOPATHY

Am J Sports Med 2017

The effectiveness of platelet-rich plasma in the treatment of tendinopathy: A meta-analysis of randomized controlled clinical trials.

Fitzpatrick J, Bulsara M, Zheng MH.

- 7 of 18 studies were ABI
- Tendon types: Achilles and TE (common ext tendon)
- Primary outcome decreased pain intensity and increased function
- Assessed 3,6, and 12 months
- Results: reported as standardized mean difference with CI 95%
  - LR-PRP strongly positive effect (SMD 36.38; 95% CI)
  - **ABI strongly positive effect (SMD 36.14; 95% CI)**
  - LP-PRP positive effect (SMD 26.77; 95% CI)
  - Corticosteroid effect (SMD 23.82; 95% CI)
  - Saline effect (SMD 14.62; 95% CI)

CONCLUSIONS: There is good evidence to support single ultrasound guided injection ABI in tendinopathy.

Level of Evidence: 1

* Adverse Events

ABI AND TENDINOPATHY

J Am Podiatr Med Assoc 2006

Comparison of Injection Modalities in the treatment of plantar heel pain: a Randomized Controlled Trial.

Kilar E, Celikbas E, Akkaya S, Demirkan F, Kilic BA.

- RCT, 44 patients, 6-mo f/u, VAS pain score
  - Statistical significant improvements in pain
  - Superior to CSI

Br J Sports Med 2007

Ultrasound Guided Dry Needling and Autologous Blood Injection for Patellar Tendinosis

James S, Ali K, et al. M,.

- Prospective Cohort, 47 knees, 44 patients, 15-mo f/u, VISA pain score
  - Statistical significant improvements in pain
  - Sonographic improvements of interstitial tears

AUTOLOGOUS BLOOD SUMMARY

Strongly Recommend

- **ABI is an effective treatment of tendinopathy, including: Lateral epicondylosis and achilles tendinopathy. (AJSM 2017)**

Appears promising, but insufficient Evidence to Recommend

- **ABI is possibly an effective treatment for plantar fasciitis and patellar tendinopathy (JAPMA 2006 , BJSM 2007)**

Insufficient Evidence to Recommend

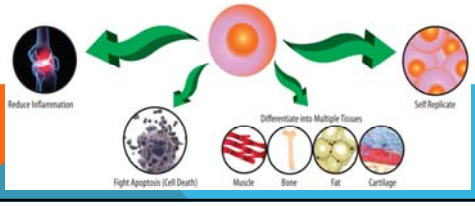
- **Insufficient evidence for ABI in treatment degenerative OA**
- **ABI has not been studied enough to recommend for other indications**

MESENCHYMAL STEM CELLS (MSCS)

What are they?:

- **Mesenchymal- (hematopoetic already differentiated) able to differentiate into into multiple cell lineages.**
- **Reservoirs adipose tissue, bone marrow, blood, periosteum, muscle and cartilage.**

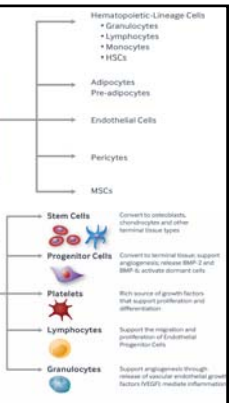
Mechanism of Action: Regenerative potential as undifferentiated stem cells have potential to become multipotent and can differentiate into bone, cartilage, tendon, ligament, and fat cells (Pittenger- Science 1999). Growth Factors present to activate the MSCs.



MESENCHYMAL STEM CELLS (MSCS)

Two main types:

- **Adipose: Fat extraction (gluteal vs stomach area)**
- **BMAC: Bone marrow aspirate concentrate (Iliac Crest)**



ADSC VS BDSC

Am J Sports Med 2019

Single-Cell Profiles and Clinically Useful Properties of Human Mesenchymal Stem Cells of Adipose and Bone Marrow Origin

Zhou W, Lin J, et al.

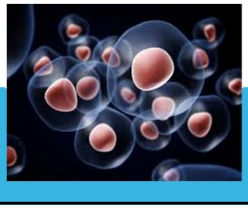
- ADSM higher homogeneity
- ADSM higher survival in hypoxic and nutrient deficient environments
- ADSM lower immunogenicity

CONCLUSION: "ADSM provide better stability in treatment of OA"

MESENCHYMAL STEM CELLS (MSCS)

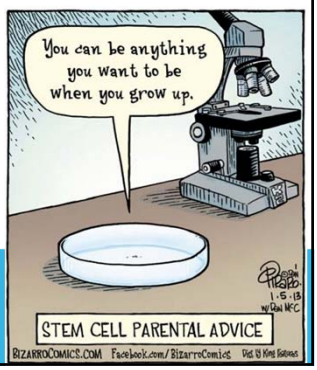
Additional Information:

- **6 week recovery**
- **MSCs therapy is rarely covered by standard insurance, but often by workers' compensation.**
- **$2,500- $10,000 for MSC therapy.**
- **Contraindication: Cancer w/i 5 years**



MESENCHYMAL STEM CELLS (MSCS)

Indication: Tendinosis, degenerative arthritis, muscle/tendon tears, chondromalcia, chondral defects, surgical enhancement



MSCS AND OA/CARTILAGE DEFECT

J Bone Joint Surg Am. 2016

Intra-articular Cellular Therapy for Osteoarthritis and Focal Cartilage Defects of Knee: A Systematic Review of the Literature

Jorge Chahla, MD, Nicolas S. Piuzzi, MD, et al.

- 6 Studies (**4 level II, 2 level III**) with 300 knees
- 3 studies knee OA, 3 focal cartilage loss
- Primary outcome: Standardized Patient-reported outcome measures
- F/U 12-36 months (mean 21m)
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - All 6 studies showed moderate benefit

CONCLUSION: Studies showed moderate benefit, but lack of **unblinded** methodologies do not control for patient or clinician bias and thus NO definite conclusion can be drawn.

Level of Evidence: III

MSCS AND KNEE OA

Br J Sports Med. 2017

Stem Cells Injections in Knee Osteoarthritis: A Systematic Review of the Literature

Pas HI, Winters M, Haisma HJ, Koenis MJ, Tol JL, Moen MH.

- 6 Studies (5 RCTs, 1 Non-RCT) with 310 patients
- Primary outcome: Standardized Patient-reported outcome measures
- Secondary outcome: radiographic and histological (based on arthroscopy)
- F/U 24-48 months
- Results: Due to heterogeneity of studies meta-analysis not performed
  - Six trials with high risk of bias showed level-3 or level-4 evidence in favor of MSCs
  - Superior radiographic outcomes favored stem cells
  - Superior histological outcomes reported in two trials

CONCLUSION: "In the absence of high-level evidence, we do not recommend stem cell therapy for KOA"

Level of Evidence: III

MSCS AND OA/CARTILAGE DEFECT

Am J Sports Med 2017

Intra-articular Mesenchymal Stem Cell Therapy for the Human Joint: A Systematic Review

McIntyre J, Jones I, et al.

- 28 Studies with 584 patients (523 knees, 61 foot/ankles, 5 hips)
- 14 studies OA, 14 focal cartilage loss
- 13 BDSC, 12 ADSC, 3 synovial/peripheral blood
- Primary outcome: Standardized Patient-reported outcome measures
- F/U mean 24.4m
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - All 28 studies showed moderate benefit in at least one clinical outcome measure
  - NO adverse events

CONCLUSION: "Strong evidence MSC's safe, with generally positive clinical outcomes"

Level of Evidence: III

MSCS AND OA/CARTILAGE DEFECT

Arthroscopy 2019

Intra-articular Mesenchymal Stem Cells in Osteoarthritis of the Knee: A Systematic Review of Clinical Outcomes and Evidence of Cartilage Repair

Chul-Won Ha, Yong-Beom Park, et al.

- 17 Studies (6 RCTs, 8 prospective, retrospective analysis)
- 8 BDSC, 8 ADSC, 1 umbilical
- Primary outcome: Standardized Patient-reported outcome measures and/or Cartilage repair (MRI, arthroscopy)
- F/U up to 28m
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - 15/17 studies improved clinical outcomes
  - 9/11 studies improved MRI
  - 6/7 studies improved 2nd look arthroscopy
  - NO adverse events

CONCLUSION: "Intra-articular MSCs provide improvements in pain and function in knee OA at short-term (28m) f/u. Evidence efficacy in cartilage repair."

Level of Evidence: III

MCS AND TENDON DISORDERS

Br J Sports Med. 2017

No Evidence for the Use of Stem Cell Therapy for Tendon Disorders: A Systematic Review

Pas HI, Moen MH, Haisma HJ, Winters M.

- 4 Studies (1 non-RCT, 3 case-series) with 79 patients
- Patellar tendinopathy, lateral epicondylar tendinopathy and RC tears.
- Primary outcome: Standardized Patient-reported outcome measures or MRI analysis cuff healing/re-tear rates.
- F/U 12 months-10 years
- Results:
  - Patellar and TE statistical sig improvement compared to baseline
  - Decreased cuff re-tear rates compared to matched controls

CONCLUSION: Insufficient evidence for MSCs in treatment tendon disorders

Level of Evidence: IV

MSCS SUMMARY

Growing evidence to Recommend

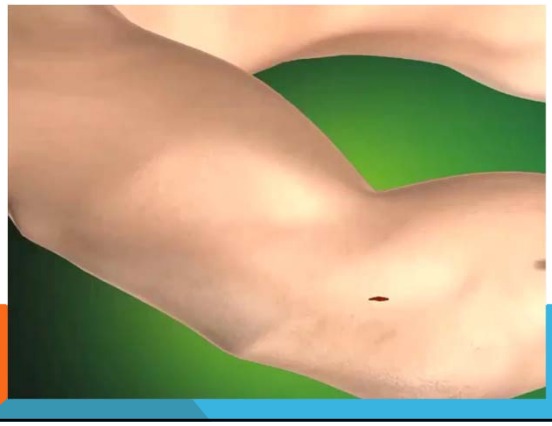
- MSCs are likely an effective treatment for knee OA, cartilage defects, probably multiple joint DJD (JBJS 2016, BJSM 2017, arthroscopy 2019, AJSM 2019)

Insufficient Evidence to Recommend

- Insufficient evidence for MSCs in treatment tendon disorders (BJSM 2017)
- MSCs have not been studied enough to recommend for other indications

TENEX TENOTOMY

- Ultrasound-guided percutaneous tenotomy
- Use ultrasonic energy to cut out portions of pathologic tendon, scar tissue and/or calcium
- Based on phacoemulsification used for treatment cataracts



PERCUATEOUS TENOTOMY TENNIS ELBOW

Am J Sports Med 2015

Ultrasonic Percutaneous Tenotomy for Recalcitrant Lateral Elbow Tendinopathy: Sustainability and Sonographic Progression at 3 years

Sang CP, Mohan C, et al.

- 20 patients
- Primary outcome: Standardized Patient-reported outcome measures
- F/U 1, 3, 6, 12 and 36m
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - VAS and DASH score
  - MSK US 3, 6, 36m
  - NO adverse events

CONCLUSION: "Percutaneous tenotomy provided sustained pain relief and functional improvement for tennis elbow at 3-year f/u. Sonographic evidence of healing".

Level of Evidence: IV

PERCUATEOUS TENOTOMY ELBOW

J Shoulder Elbow Surg 2015

Percutaneous Ultrasonic Tenotomy for Chronis Ebow Tendinosis: a Prospective Study

Barnes DE, Beckley JM, et al.

- 19 patients
- Primary outcome: Standardized Patient-reported outcome measures
- F/U 1.5, 3, 6, and 12m
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - VAS, MEPS and DASH score
  - NO adverse events

CONCLUSION: "Percutaneous tenotomy safe and effective treatment for chronic lateral or medial tendinopathy up to 1-year after procedure."

Level of Evidence: IV

PERCUATEOUS TENOTOMY VS PRP

J Shoulder Elbow Surg 2019

Platelet-rich Plasma vs Tenex in the treatment of medial and lateral epicondylitis

Boden A, Scott M, et al.

- 62 patients (32 PRP, 30 Tenex)
- Primary outcome: Standardized Patient-reported outcome measures
- F/U 1.5, 3, 6, and 12m
- Results: Due to **heterogeneity of studies** meta-analysis not performed
  - VAS and QDASH score
  - NO adverse events
  - NO difference between the two

CONCLUSION: "PRP and Tenex procedures were both successful in proving clinically and statistically significant improvement in pain and function."

Level of Evidence: IV

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THANK YOU!

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