

Orthobiologics

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Magic City Sports Medicine Conference



Disclosure

Conflict of Interest

BOC Approved Providers shall make public potential and actual conflicts of interest and financial gain associated with any programs, providers, program faculty or sponsors.

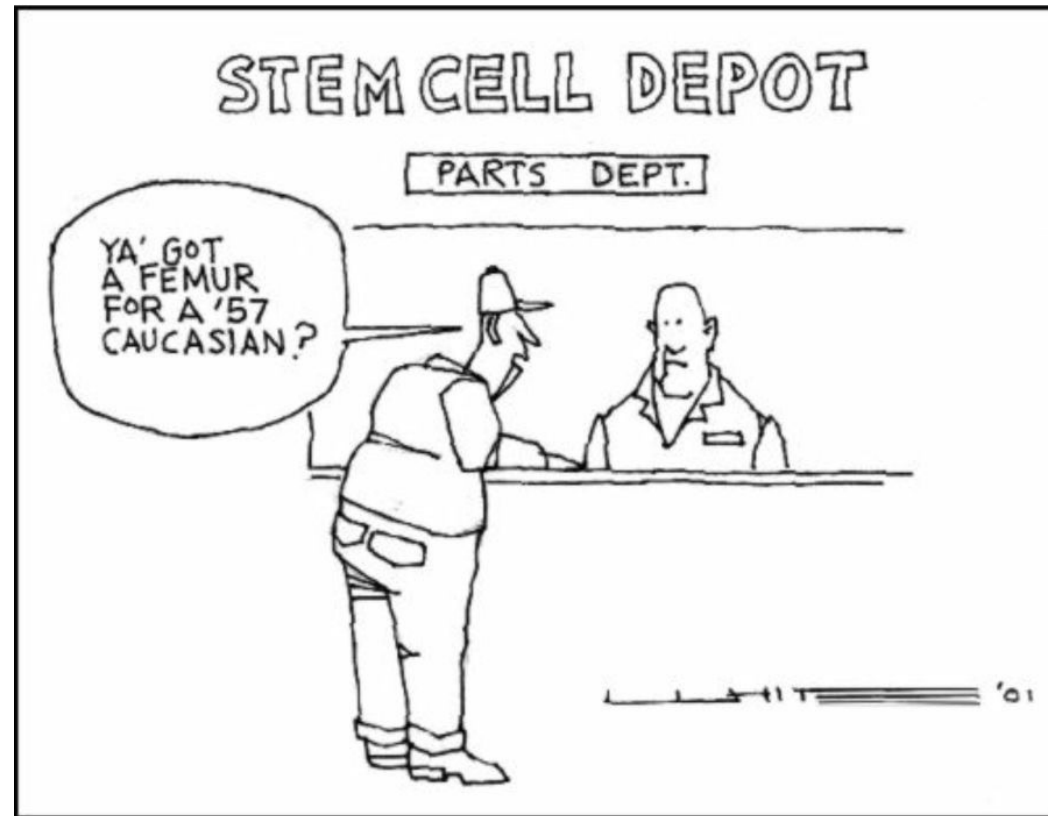
I am an employee of Ortho Montana and Athletic Medicine and Performance (AMP). AMP is the sponsor of this conference.

I have no other financial or personal conflicts of interest.

Objectives

- Discuss PRP use in orthopedics and the important variables
- Discuss what is a stem cell and how it is being used in orthopedics
- Review current research regarding these topics

Why?



Terminology

- Orthobiologics
- Regenerative medicine
- Prolotherapy
- Autologous blood injections
- Autologous conditioned serum
- PRP
 - Leukocyte rich
 - Leukocyte poor
- Stem Cell
 - Embryonic
 - Amniotic
 - Placental
 - Cord blood
 - Mesenchymal
 - Bone marrow
 - Adipose

Terminology

- “Orthobiologics” “Regenerative Medicine”
 - “refers to the use of biological substances to help musculoskeletal injuries heal quicker. They are used to improve the healing of fractured bones and injured muscles, tendons and ligaments and are derived from substances that are naturally found in body. When they are used in concentrations many times the normal, they can potentially help speed up the healing processes.”

Terminology

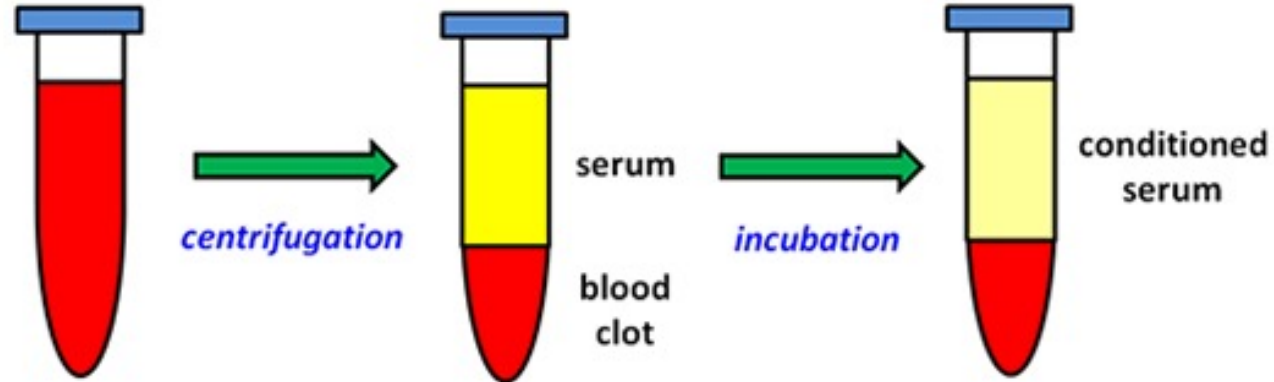
- Prolotherapy
 - Used as an injectant, hypertonic dextrose is hypothesized to stimulate native healing of damaged intra-articular and peri-articular soft tissue, including cartilage, ligaments, tendons, and fascial structures.
 - It has been termed a “regenerative” injection therapy due to these purported effects

Terminology

- Autologous blood injections
 - Whole blood injections
- Platelet-rich Plasma
 - PRP
 - Leukocyte rich
 - Leukocyte poor
- Autologous conditioned serum

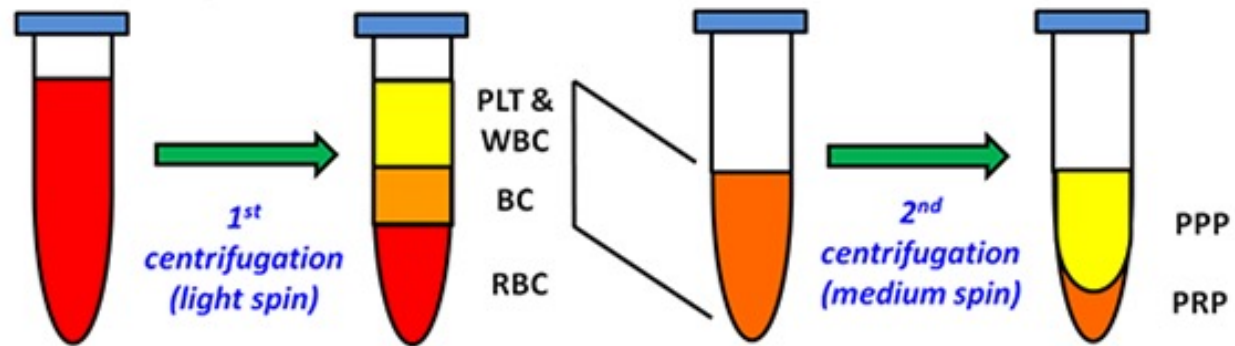
Preparation of conditioned serum

human blood sample
(no anticoagulant)



Preparation of platelet-rich plasma (PRP)

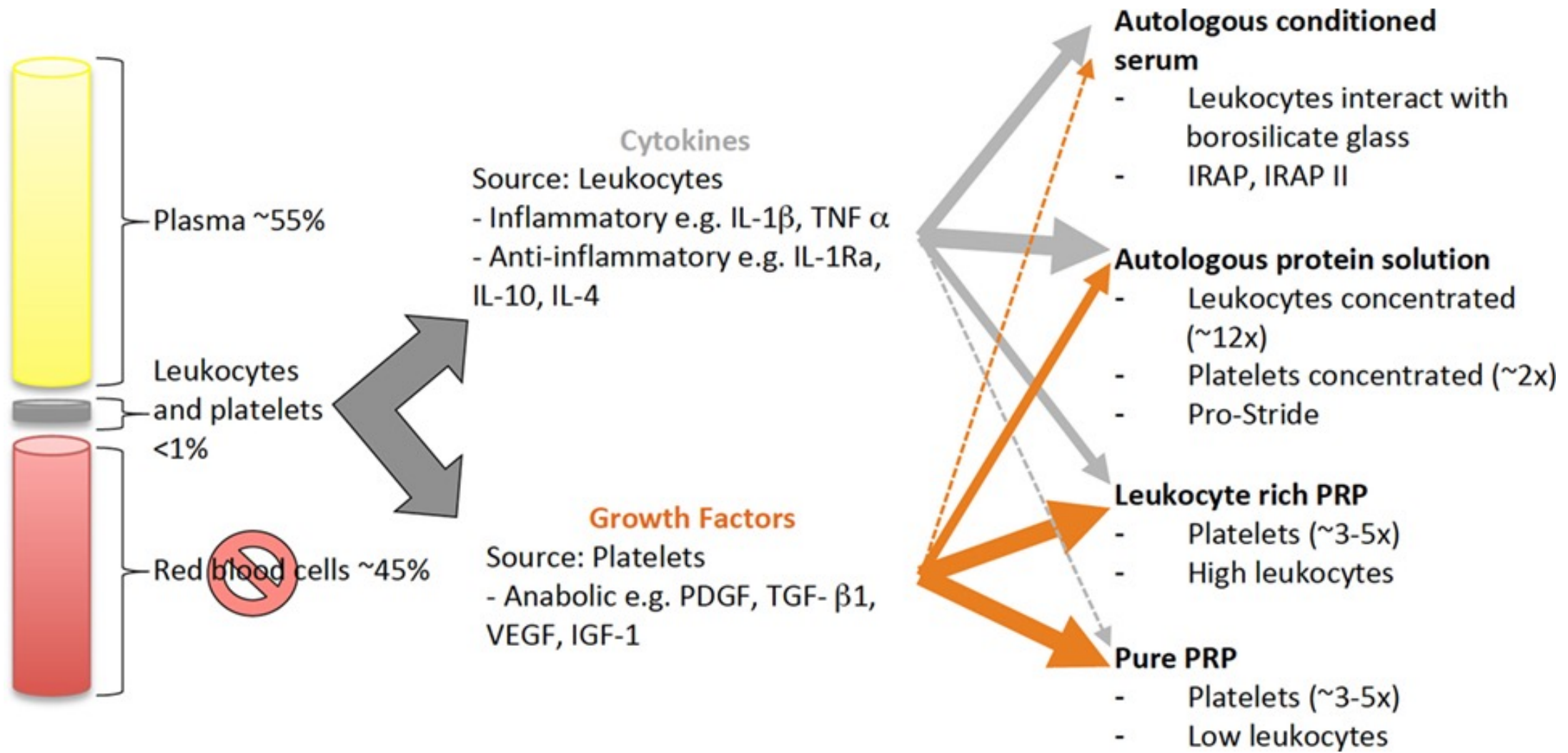
human blood sample
(with anticoagulant)



PLT = platelets
WBC = white blood cells
BC = buffy coat
RBC = red blood cells

transfer across
PLT, WBC & BC

PPP = platelet-poor plasma
PRP = platelet-rich plasma

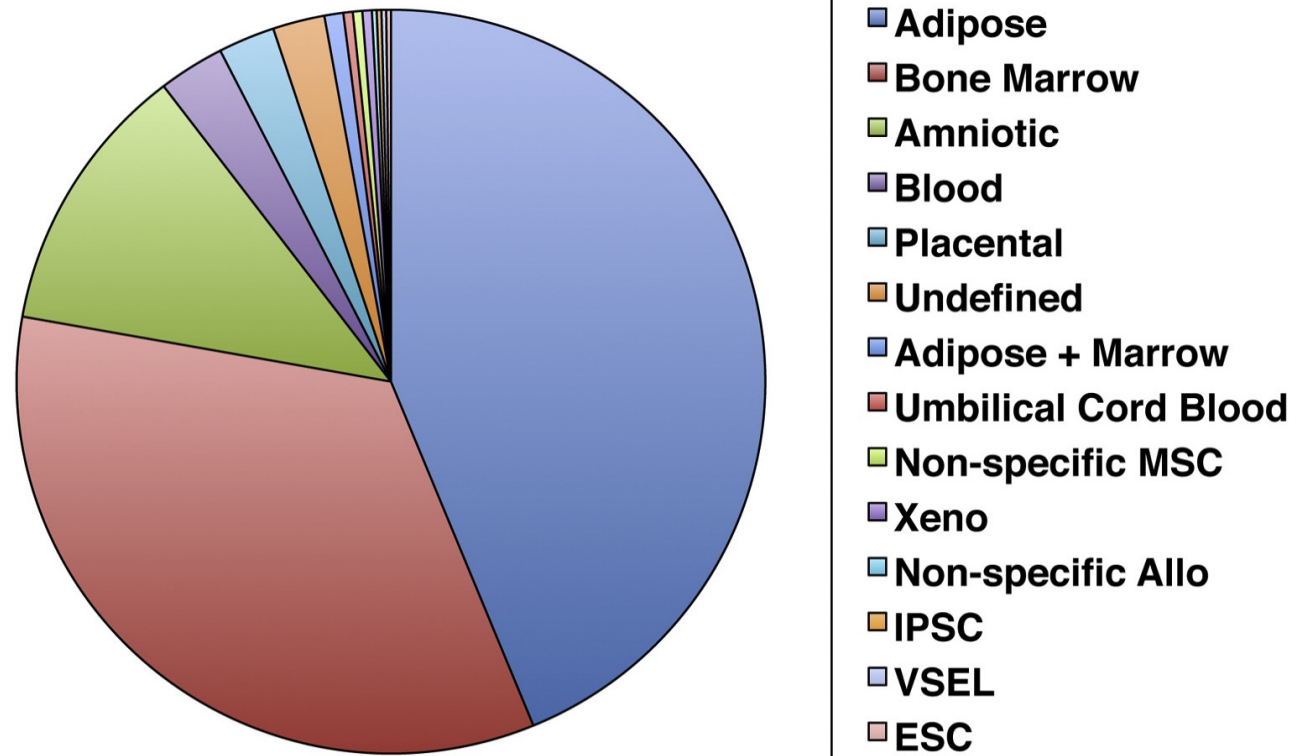


Terminology

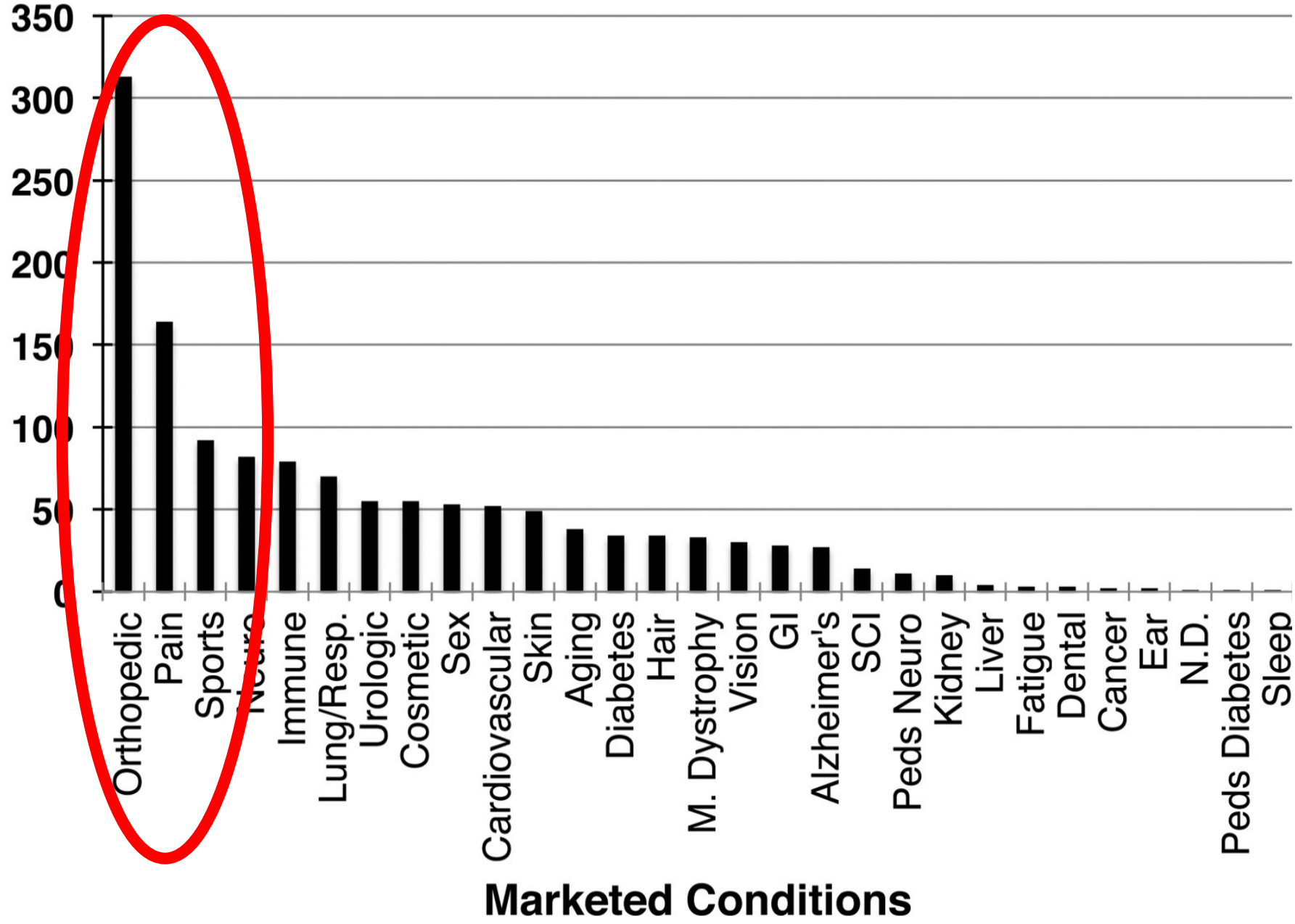
- Stem cell
 - A cell can be called a stem cell if it has the capacity to differentiate into multiple types of cells and the cell is able to self-renew
 - Mesenchymal (found in adults)
 - Embryonic (found early in development)

A

Marketed Stem Cell Types



B
Number of Businesses



“Regenerative” Medicine in Montana

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What is stem cell therapy?

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What are the potential benefits of stem cell therapy using MSC?

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REGENERATIVE THERAPY HELP
WITH NATURAL LUBRICATION

PRP

Platelet-Rich Plasma for Patellar

Current Reviews in Musculoskeletal Medicine (2018) 11:624–634

<https://doi.org/10.1007/s12178-018-9527-7>

PROTEIN-RICH PLASMA: FROM BENCH TO TREATMENT OF ARTHRITIS (S CHOATE AND J TOKISH, SECTION EDITORS)



Current Clinical Recommendations for Use of Platelet-Rich Plasma

Adrian D. K. Le^{1,2} · Lawrence Enweze¹ · Malcolm R. DeBaun¹ · Jason L. Dragoo¹

Published online: 23 October 2018

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Abstract

Purpose of Review This review evaluates current clinical literature on the use of platelet-rich plasma (PRP), including leukocyte-rich PRP (LR-PRP) and leukocyte-poor PRP (LP-PRP), in order to develop evidence-based recommendations for various musculoskeletal indications.

Recent Findings Abundant high-quality evidence supports the use of LR-PRP injection for lateral epicondylitis and LP-PRP for osteoarthritis of the knee. Moderate high-quality evidence supports the use of LR-PRP injection for patellar tendinopathy and of PRP injection for plantar fasciitis and donor site pain in patellar tendon graft BTB ACL reconstruction. There is insufficient evidence to routinely recommend PRP for rotator cuff tendinopathy, osteoarthritis of the hip, or high ankle sprains. Current evidence demonstrates a lack of efficacy of PRP for Achilles tendinopathy, muscle injuries, acute fracture or nonunion, surgical augmentation in rotator cuff repair, Achilles tendon repair, and ACL reconstruction.

Summary PRP is a promising treatment for some musculoskeletal diseases; however, evidence of its efficacy has been highly variable depending on the specific indication. Additional high-quality clinical trials with longer follow-up will be critical in shaping our perspective of this treatment option.

Keywords Platelet-rich plasma · PRP · Orthobiologics · Regenerative medicine · Tendinopathy · Osteoarthritis

Keywords: knee; patellar tendon; platelet-rich plasma; musculoskeletal; rehabilitation; injection; pain

Stem Cells

Review

REVIEW ARTICLES

The Surgical Applications of Biologics in Sports Medicine

Barber, F. Alan MD, FACS [Author Information](#) 

Sports Medicine and Arthroscopy Review: December 2018 - Volume 26 - Issue 4 - p 196-199

doi: 10.1097/JSA.0000000000000219

 Metrics

Abstract

Over the past 25 years an increased appreciation of the positive impact of biologic interventions has driven significant advances in the surgical treatment of shoulder and knee conditions. These biologic adjuncts to treatment promote improved outcomes and have set the stage and increased research and development in this arena.

therapy for tendon disorders in clinical practice is currently not advised.

Cost of Orthobiologics

Region	Mean Platelet-Rich Plasma Cost, n = 818	Mean Stem Cell Cost, n = 288
Midwest, \$	703 ± 346	3008 ± 1276
Northeast, \$	733 ± 466	2736 ± 1429
South, \$	654 ± 361	2462 ± 1470
West, \$	778 ± 383	3102 ± 2062
<i>P</i>	0.01	0.07

Ethical considerations

- Profit vs best interest of the patient
- Origin of the stem cells
 - Embryonic have the best differentiation potential but also the highest risk for tumor development
 - Also require destruction of embryo for harvesting
- FDA “Minimal manipulation”

FDA

Table 1. Food and Drug Administration 361 Versus 351 Product Chart

Category	HCT/P That:	Regulation	Examples
361 products	<ul style="list-style-type: none"> • The HCT/P is minimally manipulated; • The HCT/P is intended for homologous use only; • The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage; and either: • (i) the HCT/P does not have a systemic effect and is not dependent on the metabolic activity of living cells for its primary function; or (ii) the HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and (a) is for autologous use; (b) is for allogeneic use in a first-degree or second-degree blood relative; or (c) is for reproductive use. 	<ul style="list-style-type: none"> • HCT/P is regulated solely under section 361 of the PHSA, and regulations in 21 CFR Part 1271 • No premarket approval required • Follow Current Good Tissue Practices (CGTPs) • Donor eligibility determination 	<ul style="list-style-type: none"> • Bone (include demineralized bone) • Tendons • Cartilage • Skin • Pericardium • Dura matter • Embryos • Ligaments • Fascia • Ocular tissue • Vascular grafts (except preserved umbilical cord veins) • Hematopoietic stem cells derived from peripheral or umbilical cord blood
351 products	<ul style="list-style-type: none"> • Fail to meet criteria for 361 products • Regulated as a drug, device, and/or biological product depending on the primary mode of action 	<ul style="list-style-type: none"> • HCT/P is regulated under section 351 of the PHS ACT • Regulated under the Federal Food, Drug, and Cosmetic Act (FD&C) and applicable regulations • CGTPs and Current Good Manufacturing Practices (cGMP) • Premarket approval, safety, and effectiveness • Investigational New Drug (IND) 	<ul style="list-style-type: none"> • Cultured cartilage cells • Cultured nerve cells • Lymphocyte immune therapy • Gene therapy products • Human cloning • Human cells used in therapy involving the transfer of genetic material • Unrelated allogeneic hematopoietic stem cells • Unrelated donor lymphocytes for infusion

CFR, Code of Federal Regulations; HCT/P, human cells, tissues, and cellular and tissue-based product; PHSA, Public Health Service Act.

Future of Sports Medicine

Clinical Sports Medicine Update

A Practical Guide for the Current Use of Biologic Therapies in Sports Medicine



Joseph D. Lamplot,^{*} MD, Scott A. Rodeo,[†] MD, and Robert H. Brophy,^{**‡} MD, MS
*Investigation performed at Washington University School of Medicine,
Chesterfield, Missouri, USA*

Over the past decade, there has been an increased interest in the use of biologic therapies in sports medicine. Although these technologies are in relatively early stages of development, there have been substantial increases in marketing, patient demand, and clinical utilization of biologics, including platelet-rich plasma, bone marrow aspirate concentrate, and other cell-derived therapies. Direct-to-consumer marketing of biologics has also proliferated but is largely unregulated, and clinicians must accurately convey the safety and efficacy profiles of these therapies to patients. Because most insurance companies consider biologic treatments to be experimental or investigational for orthopaedic applications given the lack of high-quality evidence to support their efficacy, patients receiving these treatments often make substantial out-of-pocket payments. With a range of treatment costs among centers offering biologics, there is a need for appropriate and sustainable pricing and reimbursement models. Clinicians utilizing biologics must also have a thorough understanding of the recently clarified Food and Drug Administration guidelines that regulate the clinical use of cell and tissue products. There is a lack of consensus on the optimal preparation, source, delivery method, and dosing of biologic therapies, which has been exacerbated by a lack of sufficient experimental detail in most published studies. Future research must better identify the biologic target of treatment, adhere to better standards of reporting, and better integrate researchers, industry, and regulatory bodies to optimize applications.

Keywords: biologics; platelet-rich plasma; PRP; bone marrow aspirate; BMAC; stem cells

Take Home Points

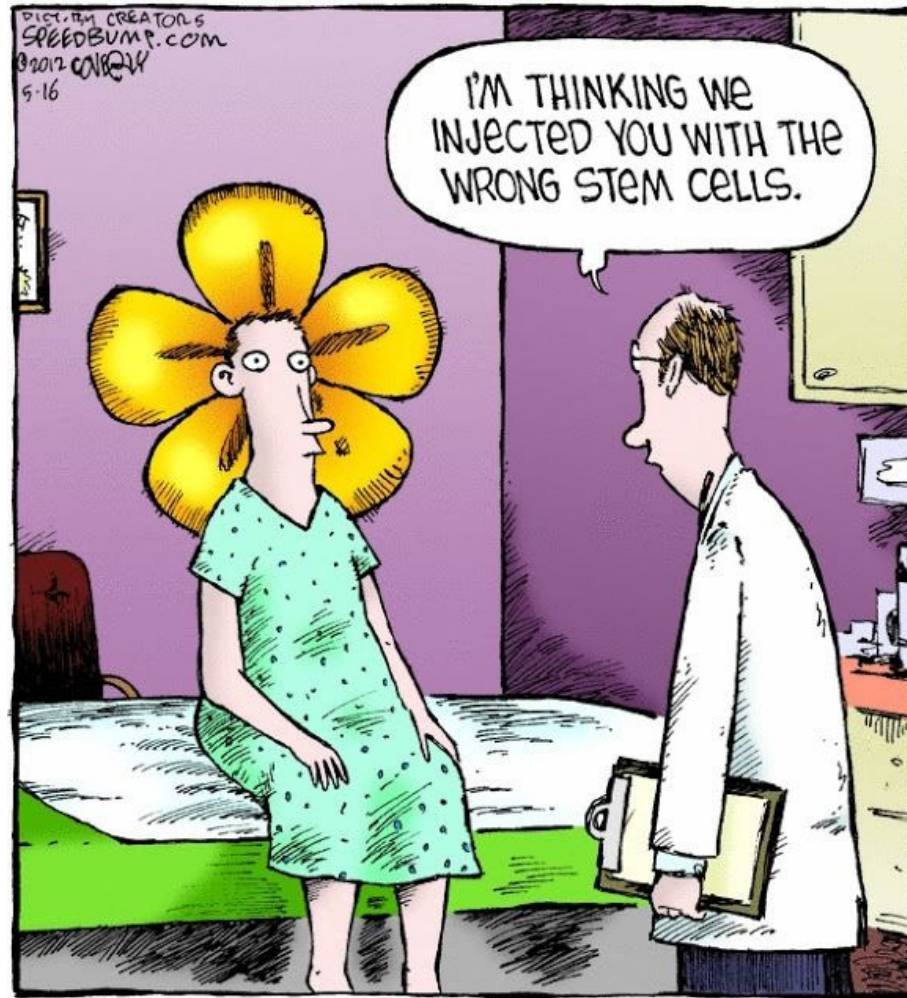
- Studies provided strong evidence for symptomatic treatment of knee OA and chronic tendonitis with PRP
- Stem cells are not the fountain of youth... yet
- More research is needed not only for the best method of obtaining cells, but also processing them, injecting them, quality testing them as well as the rehab after injection

me: stem cells can turn into any cell they want right?

adult stem cell:



Questions?



Resources

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Thank you!

