



# Platelet Rich Plasma (PRP)

Russell M. Nord, MD

Washington Township Medical Foundation

Fremont, CA

California Orthopaedic Association

2011 Meeting

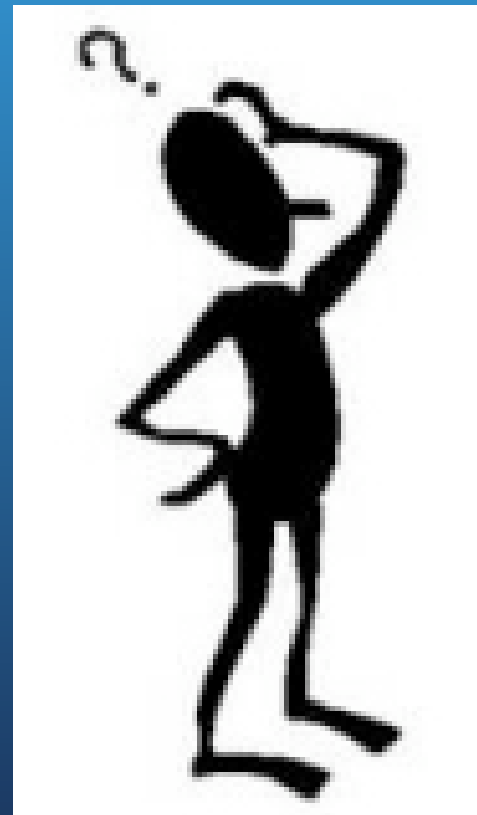


Washington Township  
Medical Foundation

Part of Washington Hospital Healthcare System

# Conflict of Interest

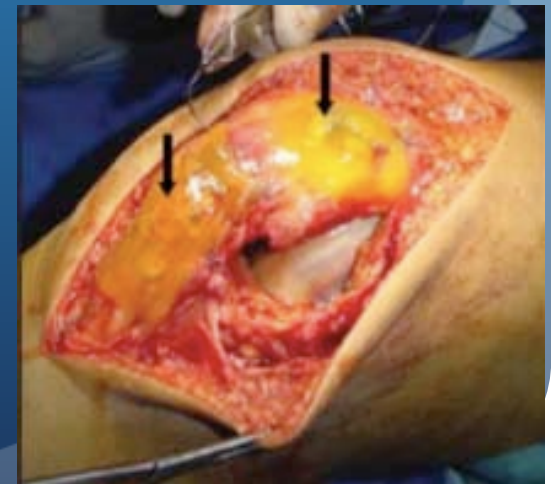
- I have no conflicts of interest relevant to this lecture...but there is a disclaimer.
  - Few solid conclusions
  - Introduction
  - Background
  - State of the art



# AAOS Now February 2011 PRP Forum

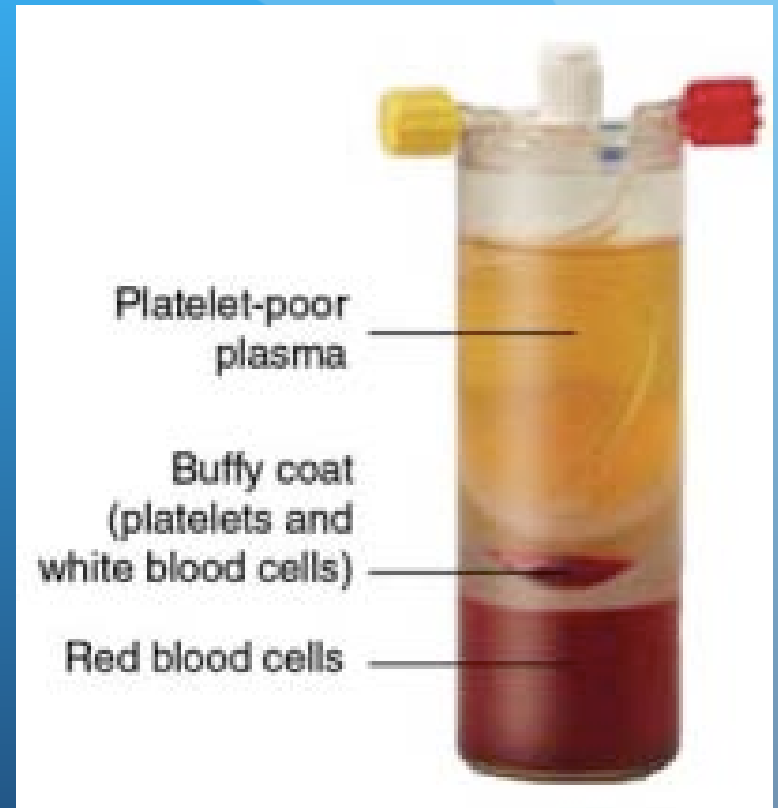
- “ This attention in print and electronic media has resulted in the dissemination of much misinformation and has elevated patient expectations to often unrealistic levels. As orthopaedic surgeons, we are ultimately responsible for interpreting the science, determining the appropriate indications, and counseling our patients about what PRP can and cannot accomplish.”

- S. Terry Canale, MD and Frank B. Kelly, MD



# Outline

- Definition of PRP
  - Proposed mechanism of action
  - Preparation technique
  - Available preparations
- History of Use
  - Now used for almost anything
  - Safe, inexpensive, autologous
- Known Efficacy Data
- Coding
- Future Directions and Predictions



# What is PRP?

- Platelet-concentrated aliquot
  - 3-5x normal blood platelet concentration
  - Growth factor concentrate - *mixture of growth factors*
  - +/- WBCs
  - “Enhances healing”

AJSM. 2009;37:2259-72

TABLE 1

**Growth** Factors Identified Within Platelet-Rich Plasma and Their Physiologic Effect<sup>a</sup>

Factor	Target Cell/Tissue	Function
PD-EGF	Blood vessel cells, outer skin cells Fibroblasts, and many other cell types	Cell <b>growth</b> , recruitment Differentiation, skin closure Cytokine secretion
PDGF A + B	Fibroblasts, smooth muscle cells, chondrocytes, osteoblasts, mesenchymal stem cells	Potent cell <b>growth</b> , recruitment Blood vessel <b>growth</b> , granulation <b>Growth</b> factor secretion; matrix formation with BMPs (collagen and bone)
TGF- $\beta$ 1	Blood vessel tissue, outer skin cells Fibroblasts, monocytes TGF gene family includes the BMPs Osteoblasts—highest levels of TGF- $\beta$	Blood vessel ( $\pm$ ), collagen synthesis Growth inhibition, apoptosis (cell death) Differentiation, activation
IGF-I, II	Bone, blood vessel, skin, other tissues Fibroblasts	Cell <b>growth</b> , differentiation, recruitment Collagen synthesis with PDGF
VEGF, ECGF	Blood vessel cells	Cell <b>growth</b> , migration, new blood vessel growth Anti-apoptosis (anti-cell death)
bFGF	Blood vessels, smooth muscle, skin Fibroblasts, other cell types	Cell <b>growth</b> Cell migration, blood vessel <b>growth</b>

# How is PRP Administered?

- Autologous, sterile blood draw
  - Variable volume
  - ? Anesthesiologist
  - 18 gauge needle
    - Reduce platelet trauma and activation
- Anticoagulation
- Centrifugation
  - Variable durations
  - Variable number of cycles
- Sequestration of PRP
  - Syringe system
- +/- Activation with  $\text{CaCl}_2$  or thrombin
  - Rapid degranulation
- Application / injection of PRP at desired anatomic site
  - Many uses
  - ? Local anesthetic
    - pH changes
- Post injection
  - Observe for 20 mins for pain
  - ? Avoidance of NSAIDs for 3-4 weeks post-tx (prostaglandins)
  - Ice
  - Acetaminophen



# PRP Variability

- 15-20 companies making PRP products
- Patient variability
- Heterogeneous PRP formulations

**Table 2**

JAAOS. 2009;17:602-8

**Common Platelet-rich Therapy Preparation Systems\***

System	Volume of Blood (mL)	Centrifuge Time/Speed	Final PRP Volume (mL)	Final Platelet Concentration (compared with average)	Activator	Level of Growth Factors (compared with average)
Autologous Conditioned Plasma (Arthrex, Naples, FL) <sup>†</sup>	9	5 min/1,500 rpm	3-5	2-3x	None	PDGF (25x) EGF (5x) VEGF (11x) TGF-β1 (4x) IGF-1 (1x)
Cascade (Musculoskeletal Tissue Foundation, Edison, NJ) <sup>‡</sup>	9 or 18	First: 6 min/1,100g; Second: 15 min/1,450g	2 or 4	N/A	Calcium (forms a suturable clot for intraoperative use)	PDGF (N/A) EGF (5-10x) VEGF (5-10x) TGF-β1 (5-10x) IGF-1 (5-10x)
GPS III (Biomet, Warsaw, IN) <sup>§</sup>	27 or 54	15 min/1,900g	3 or 6	4-8x	Calcium chloride/thrombin	PDGF (N/A) EGF (3.9x) VEGF (6.2x) TGF-β1 (3.6x) IGF-1 (1x)
SmartPReP (Harvest Technologies, Plymouth, MA) <sup>  </sup>	20 or 60	14 min/1,000g	3 or 7	4.4-7.6x	Thrombin	PDGF (4.4x) EGF (4.4x) VEGF (4.4x) TGF-β1 (4.4x) IGF-1 (N/A)

Note: Data from manufacturers.

Dragoo et al. AJSM. 2011. - 3<sup>rd</sup> party data, 3 preps.

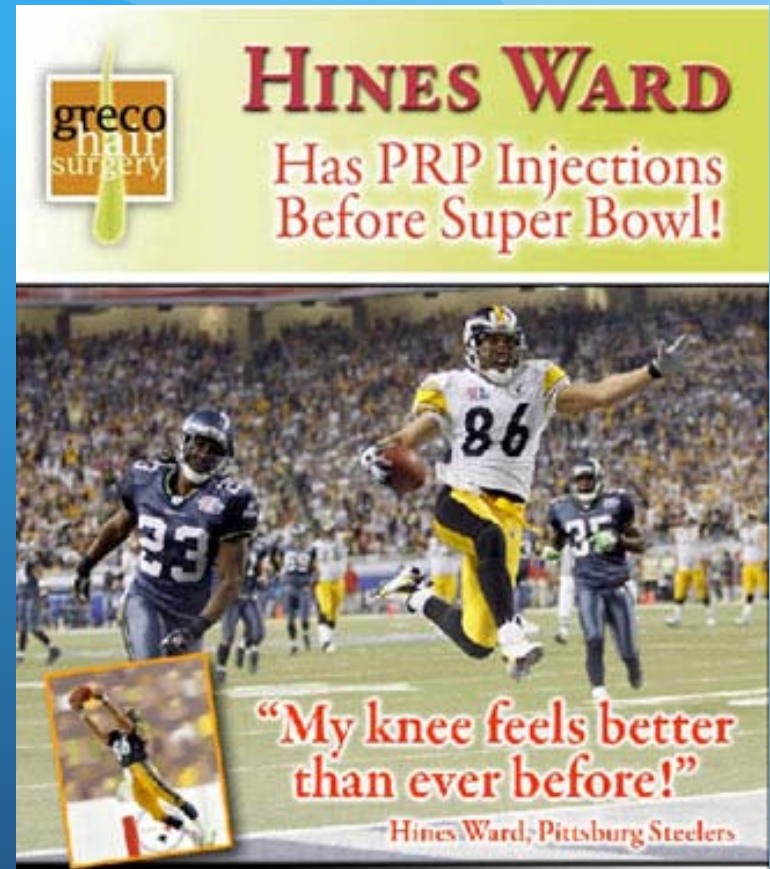
# History

- Began in late 1990's
  - Non-orthopedic literature
    - Dental / Maxillofacial
      - Bone Graft enhancement
        - Marx et al. 1998.
    - Plastic surgical literature
      - Improved cosmetic surgery recovery
  - Orthopaedic literature
    - Augmentation of spinal fusion and fracture healing

**The New York Times**

February 17, 2009

**A Promising Treatment for Athletes, in Blood**



greco hair surgery

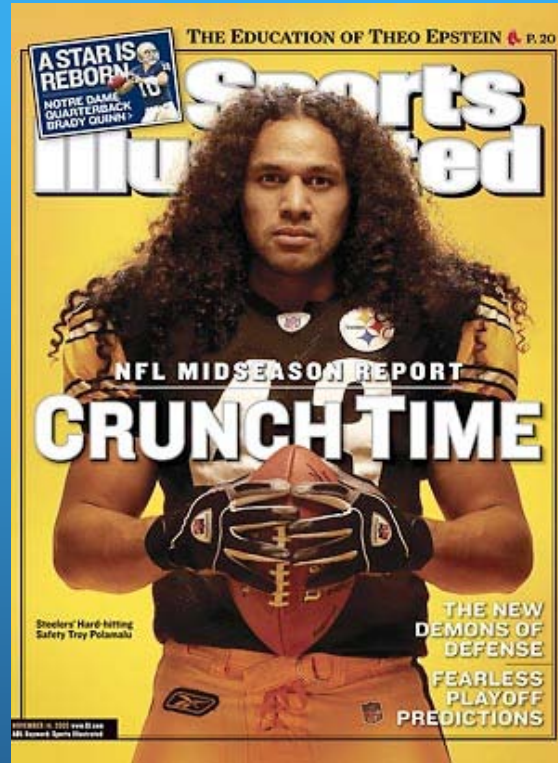
**HINES WARD**  
Has PRP Injections  
Before Super Bowl!

**“My knee feels better  
than ever before!”**  
Hines Ward, Pittsburgh Steelers



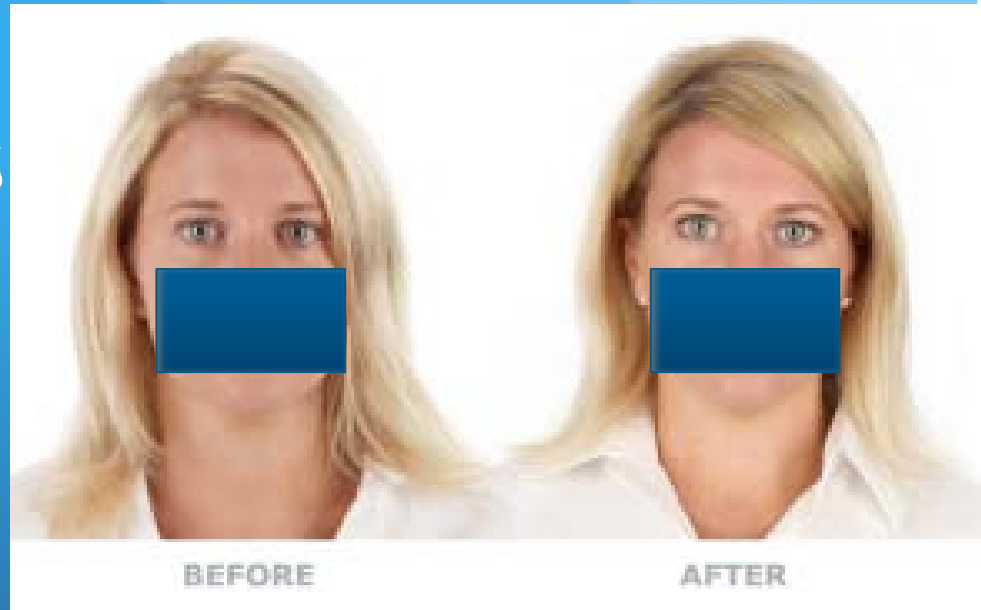
# High Profile Patients

- Allowed
  - NFL
  - MLB
  - NBA
  - WADA
  - IOC



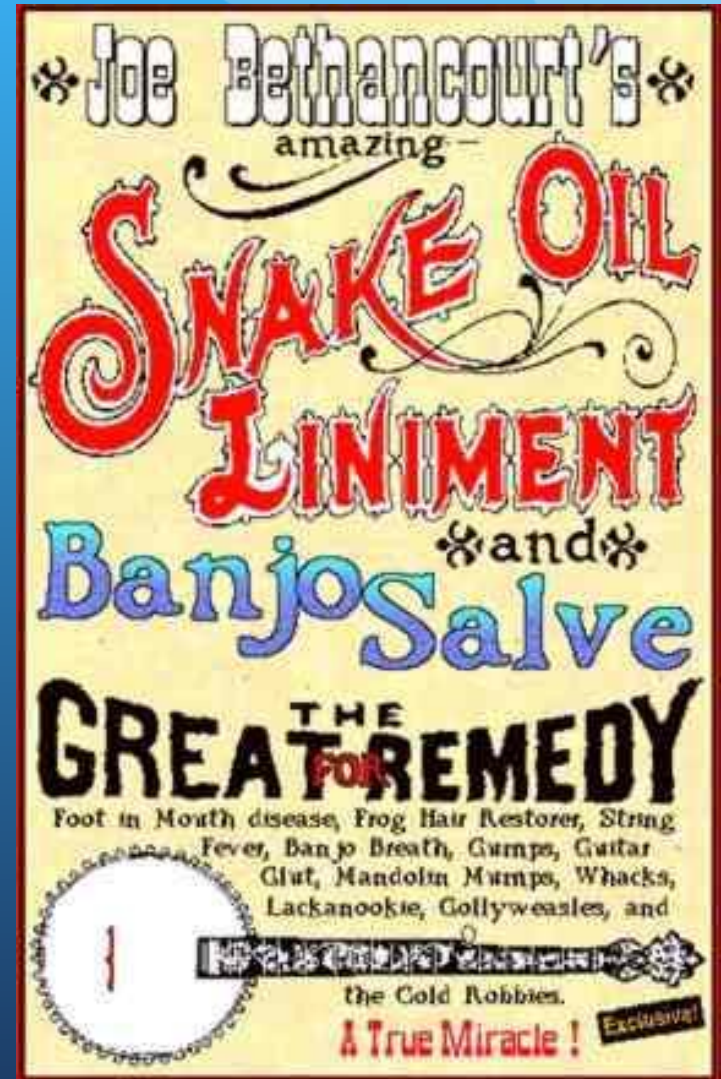
# Proposed Non-Orthopaedic Uses

- Cosmetic Blepharoplasty
- Treatment of male pattern baldness
- Plenty more...



# Science or Enthusiasm?

- Treats previously untreatable condition
  - Tendinopathy
- Potential utility in a broad spectrum of pathologies
- Limited efficacy data
- Inexpensive
- Safe
  - Autologous
  - ?WBCs in joint
  - Standard contraindications
- We must acknowledge our knowledge gaps...or else.



# Outcomes Data - Non-Operative

- Achilles tendinopathy -

- De Vos, et al. 2010.
  - Double blind, placebo controlled, randomized, 54 patients, No benefit at 6 mos.

- Acute Achilles tendon injury

- Virchenko and Aspenberg. 2006.
  - Greater initial tendon strength in rat model at 14 days when exposed to mechanical loading.

- Lateral epicondylitis

- Peerbooms, et al. 2010.
- RCT, 100 patients
  - Goal: 25% VAS or DASH reduction at 1 year
  - 73% with PRP
  - 50% with corticosteroid

- Patellar tendinitis

- Kon, et al. 2009
  - Uncontrolled. 3 weekly injections. 20 patients. 80% satisfied at 6 mos.

- Muscle injuries

- Sanchez et al. 2005. Poster
  - 20 patients. Recovered in half the "expected" time.
- Hammond et al. 2009.
  - Improved mechanical testing in rat model

- Plantar fasciitis

- Barrett and Erredge. 2004.
  - 6/9 patients w/ complete relief at 2 mos

- Knee osteoarthritis / cartilage degen

- Kon, et al. 2010.
  - 3 weekly injections. 100 pts, 1 year f/u
  - Scores improved throughout (IKDC, VAS)
    - Best in young w/ low deg of degen
    - Drop somewhat after 6 mos
  - RCT underway with HA
    - Prelim: similar, painful PRP injection

- Grade 2 MCL Injuries

- Mandelbaum and Gerhardt. Unpublished.
  - 27% reduction in return to play time.

# Outcomes Data - Operative

- Rotator cuff repair

- Castricini, et al. 2010.
  - Randomized, controlled - 87 patients total
    - No difference at 16 months
- Randelli et al., 2011
  - Randomized, controlled - 53 patients total
    - No difference at 6, 12 or 24 months

- Achilles tendon repair

- Schepull et al. 2011.
  - Randomized, controlled, prospective, single-blinded trial
    - 16 with PRP, 14 controls, 1 year f/u
    - No differences, possibly lower Achilles Tendon Total Rupture Score with PRP
- Sanchez, et al. 2007.

- 6 cases, 6 controls. PRP patients with earlier functional ROM, jogging, training, smaller cross-section and no wound complications.

- ACL

- No studies to strongly support use
- Radice, et al. 2010.
  - Graft homogeneity on MRI at 6 months instead of 1 year

- Cartilage restoration

- Gobbi, 2009 presentation
  - 20 patients, PRP with collagen membrane. At 20 months, improved IKDC and Lysholm scores and near-pre-injury Tegner scores and hyaline like tissue on pathology.
- Sun, et al. 2009.
  - Rabbit model - PRP in PLGA scaffold helps heal osteochondral defects

- Total Knee Arthroplasty

- Berghoff, et al. 2006.
  - 71 experimental, 66 controls. PRP in tissue prior to closure. Less blood loss, shorter hospital stay, 5 deg more ROM at 6 wks with PRP.

- Spinal Fusion

- Hartmann, et al. 2010.
  - Clinical study: No improvement in fusion rate
- Rao, et al. 2009.
  - No improvements in rat model

- Femur Fractures

- Simman, et al. 2009.
  - Accelerated bone healing in rat femurs

# Future Directions

- Improved high-level prospective studies
- Define and classify types of PRP
- Elucidate which works best in what setting
- **Prediction:** Isolated high-quality studies on specific proprietary formulations used for a discrete pathology will yield outcome data that cannot be extrapolated to other formulations or pathologies.
  - “Islands of data”



# Conclusions

- Identify low-morbidity applications
  - Appropriate for use with limited data
- Appropriate disclosure to patients
- 0232T code
  - Often not covered
  - Out-of-pocket expenses
- Follow the developments in the literature
- Best Review Paper
  - Foster, et al. AJSM. 2009. 37(11):225-72.
  - AAOS Now PDF

