PROLOATHERAPY

What is it and why is Prolotherapy the foundation of Regenerative Medicine?

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My Experience

• 25 years Prolotherapy
• 15 years PRP
• 10 years Stem cells
• Interventional Pain/PMR
PROLOTHERAPY

YOU NEED TO LEARN THIS TECHNIQUE!!
OBJECTIVES

- Why you need to know this to do RIT
- Definition
  - Understanding how prolotherapy works
- Studies in the literature
- Indications/Usage
- Injection Techniques
WHY PROLOATHERAPY?

• Also a Regenerative Injection Technique RIT
• RIT in its most basic form/Immune upregulation
• Prolo is a **concept** of understanding MSK tissue injury and repair
• Prolo is a methodology of treatment application to ensure the injury is completely treated
• More and more RCT’s being published (this really works!)
Where did Prolotherapy come from?

• Lessons from history
  – George Hacket, MD, and others, discover that most MSK pain comes from ligaments and joint capsules- 1935
  – He perfects the treatment process called Prolotherapy capable of resolving these injuries
  – This process is sugar based- much safer to learn and to practice!
Back Slide Into the Dark Ages of MSK Treatment

– 1934 Mixter and Barr discover that you can operate on the lumbar disc, ushering in the "dynasty of the disc".. Hooray?
– Gives a big boost to the surgical treatment of back pain regardless of cause
– We enter the age of spine and other orthopedic surgery and the dark ages of MSK medicine.
HISTORY OF PROLO -cont

• 1982 Prolotherapy is “rediscovered” by physicians who founded the AAOM to teach and promote to other physicians
DEFINITION

- PROLO – To proliferate
- The injection of a substance to stimulate the growth of connective tissue thereby strengthening weakened and painful ligaments, tendons, and joint capsules
- Prolotherapy also known as:
  - “Sclerotherapy”
  - “Ligament Reconstructive Therapy”
HOW PROLO THERAPY WORKS

- Normal healing of wounds occurs in three phases
  - Inflammation phase
  - Proliferative phase
  - Remodeling phase
- Effectively up-regulates the immune system at the site of injection
Wound Healing

NATURAL HEALING CASCADE

INJURY

INFLAMMATION

TISSUE REGENERATION

(Cell Proliferation)

TISSUE REMODELING

COMPLETE HEALING
WOUND HEALING

- Inflammatory Phase
  - Injury to cells (the wound)
  - Cells broken open, spilling contents
  - Debris and chemicals released: kinins, complement cascade, fibrinolysis, prostaglandins, pain
  - Causes influx of leukocytes
  - Lasts one to three days
WOUND HEALING, Continued

- **Proliferative Phase**
  - Hormones and growth factors released which attract macrophages, granulation cells, fibroblasts in succession
  - Macrophages clean up debris
  - New blood vessel growth stimulated
  - Fibroblasts stimulated to make new ligaments by growth factors released by macrophages
  - Can only happen with a fresh injury state
  - Lasts ten days to two weeks
WOUND HEALING, Continued

- Remodeling Phase
  - Collagen fibrils form along stress lines
  - Water squeezed out of fibrils
  - Collagen cross-linked
  - Occurs for two to three months
WOUND HEALING
SUMMARY

- Prolotherapy is a way to jump-start the normal repair process.
- The use of anti-inflammatories given for acute injuries probably not helpful for healing the injury.
HISTORY OF PROLOTHERAPY

- Hippocrates
- 1500 A.D. – French surgeon Paret
- 1927 - First histologic report on animals
- 1939 - Hackett
- Current usage over 50 years
PROLOOTHERAPY AS A THOUGHT PROCESS

• Understands the complexity of MSK injury and pain
  – Eg., sacroiliitis vs SIJ dysfunction and instability
  – Relationship of SS tear to shoulder mechanics and instability
  – Relationship of GT bursitis (really GM tendonopathy) to SIJ instability
  – These are all related to ligament failures
RETHINKING LIGAMENTS

- Limited understanding
- Pain and functional loss related to ligament and tendon injury
  - Well recognized in extremities
  - Largely ignored in axial skeleton
The 5 Origins of Pain

There are only 5 things that can hurt:
• Muscles
• Ligaments
• Joints
• Nerves
• Discs
Prolotherapy causes you to think about Ligaments

• 36 yo female with R cervical pain radiating down the medial aspect of the scapula
  – Non radiciular, nl rom, nl sen, nl st, + tp’s in traps, lev scap, rhomboids, scalenes, cerv ps’s, tender cerv ps’s
  – Poss dx:
    • Myofascial pain
    • Facet syndrome (if you’re and interventionalist)
What about the ligaments?
Think about Ligaments

- 42 yom with lbp and R L5 radicular pain
  - Neg weakness, sensory, reflex changes
  - SLR pos only for prox thigh pain
  - Fairly large bulge at L4/5
- Presumed DX:
  - R L5 Radiculopathy
  - Any other possibilities?
Ligaments make Pain!
Other examples of why ligaments need to be in your differential DX
Headache? Think Ligament!
Implications of adding ligaments to your thought processes

• Myofascial pain tp’s, and spasm become the symptom of ligament failure and joint instability- not their own dx

• A painful joint becomes pain created by the ligaments and joint capsule failure rather than a purely articular problem. Also, the lax ligaments cause the degeneration of the joint

• Radicular and other pain can be actually a ligament referral pattern
PROLO AS A METHODOLOGY

• Teaches you how to treat the entire structure, not just the lesion on MRI or US. This makes cure more likely. For example:
  • Treatment of whiplash involves treating the C2-C7 facet joint capsules, SS/IS ligaments, R and L Nuchal line
  • Treatment of an SIJ requires Bil SIJ ligs (deep and superficial, long and short), ILL, ST.SS ligs, L4/5,L5/S1 facet capsules (at the very least)
  • Has an 80% success rate which tends toward curative (all or none response)
ADVANTAGES OF PROLO

- Simple to perform once learned
- No equipment or preparation
- Treats larger areas: cervical, thoracic, lumbar spines
- As a method of treatment, it addresses the entire organ, insuring stability in the long term
- More affordable for many injuries
- Same outcomes as PRP (tears excepted)
- 5-10% of patients respond to Prolo but not PRP
PROLIFERANT SOLUTION

- 12.5% - 25.0% Dextrose diluted with anesthetic
PROLIFERANT SOLUTIONS,
(historical only)

- Glycerine
- Zinc sulfate
- Phenol 2.5%
- Tannic Acid
- Quinine
- Guaiacol
- Calcium Gluconate
 Tick and Lyme Disease Information Hotline

"Who picked 'I've Got You Under My Skin' to be our on-hold music?"
The Research Basis of Prolotherapy
George keeps at it!
(and others)

• George Stuart Hackett, M.D. (1888 -1969)
• Graduate: Cornell, 1916

• JOINT LIGAMENT RELAXATION TREATED BY FIBRO-OSSEOUS PROLIFERATION

Charles C Thomas Publisher Springfield, Illinois, 1956
CONNECTIVE TISSUE RESEARCH

- Hackett, 1956
  - Showed 40% increase in diameter and size of fibril osseous junction of rabbit tendons two months after injection with proliferant solution
  - Similar studies in medial collateral ligaments
CLINICAL STUDIES

- Hackett, 1960 monograph
  - 1,816 patients
  - Followed for 20 years
  - 82% satisfactorily cured
  - No complications
Others as well


- A double blind study confirmed proliferative influence of sodium morrhuate on rabbit MCL
  - 5 injections in 6 weeks period
  - Electron microscopy demonstrated increased diameter of collagen fibrils to 129.9 nm.; controls were 83.2 nm.
  - Treated MCLs had significantly increased mass, thickness, cross section and junctional strength.
Dextrose based solutions for LBP

- Ongley, 1987 – *Lancet*
  - 81 patients
  - Low back pain greater than one year
  - Experimental group – six weekly injections of P2G proliferant
  - Control group – six weekly injections of NaCl

**RESULTS:** Significant improvement in disability scores and pain ratings
Klein, 1993

- General spinal disorders
- Randomized double-blind study
- 79 patients
- Experimental group – six weekly injections of P2G plus lidocaine
- Control group – six weekly injections of NaCL plus lidocaine

**RESULTS:** 30/39 of experimental group had greater than 50% reduction in pain; only 21/40 of control group showed similar response

- Problem with study – the control was also therapeutic

• Lumbar IVD were injected with combined solution of glucosamine, chondroitin sulfate, dextrose and (DMSO).
• 17 of the 30 patients (57%) improved markedly with an average of 72% improvement in disability and 76% in VAS.
Does Better Than IDET

Comparison of Intradiscal Restorative Injections and Intradiscal Electrothermal Treatment (IDET) in the Treatment of Low Back Pain

- 74 pt.-IDET, 35 pt. –Injected with glucosamine, chondroitin sulfate, dextrose, DMSO.
- Improved after: IDET- 47%; injections - 65%
- Flare up: IDET - 69%, injections - 81%
- Fl. up severity (VAS): IDET- 6.1, injections -7.9
- Fl. up days: IDET - 33.1, injections - 8.6
- Worse after: IDET - 36%; injections - 0 %
Dextrose for Cervical Pain

A Prospective Case Series of Fluoroscopically Guided Cervical Prolotherapy for Instability with Blinded Pre and Post Radiographic Reading.

• Results: post-test VAS score was significantly lower (p=0.04) than the pre-test. The correlation between difference in mean extension at C2-3 and C5-6 was significant (p=0.02 and p=0.03 respectively). Difference in mean flexion at C3-4 and C4-5 was significantly correlated (p=0.02 and 0.01 respectively).

• Conclusions: statistically significant reduction of cervical flexion and extension translation, as well as a reduction in pain VAS score documented after prolotherapy.

• Patients with traumatic cervical instability have few viable treatment options short of surgical fusion, proliferant injections under C-Arm fluoroscope may be a viable treatment option.
Clinical studies, cont

• Dumais, Pain Medicine, Aug 2012
  – Effect of RIT on function and pain in patients with knee OA, RCT with crossover
  – 4 injections Dextrose IA and EA vs home exercise with crossover
  – N=45
  – Level 1 evidence
Dumais 2012
Topol OS Disease 2011

- 3 monthly dextrose injections vs regular treatment vs lidocaine
- N=54
- RCT blinded crossover
- Level 1 evidence
Rabago, Patterson 2013

- Rabago, Patterson, Annals of Family Medicine May/June 2013
- 4 Dextrose IA and EA injections vs saline vs exercise; RCT blinded
- 15 vs 8 vs 8 point improvement in WOMAC score for pain; 16 vs 5 vs 7 for function
- 52 week f/u
- Level 1 evidence
Prolotherapy Research , cont

• 5 Level 1 evidence Prolotherapy studies
• 10 Level 2 evidence Prolotherapy studies as well
• Prolotherapy is taught in many residency training programs in many disciplines
• Many questions remain but Prolotherapy is no longer experimental
• Meets the U.S. Preventative Services Taskforce Recommendations for When Doctors Should Discuss a Treatment (Level 1 or 2 evidence with minimal risk)
“We can get a discount on our health insurance if we list Google as our primary care physician.”
INDICATIONS AND PATIENT SELECTION

- Ligamentous insufficiency or laxity
- Chronic sprain/strain/ unresolved MFS
- Diagnosis of exclusion
- Clinical characteristics
  - Clinically unstable joint (facet/SI) with temporary relief from physical therapy or chiropractic
  - Often hypermobile individual
  - Pain is worse with prolonged sitting or standing
  - Localized reproducible pain
PATIENT SELECTION, Continued

- Clinical characteristics, continued
  - Positive diagnostic blocks (beware of false negatives)
  - Range of motion often, but not always, reduced due to spasm (improves with treatment)
  - No neuro signs
TREATMENT BY PROLOATHERAPY

- Guidelines
  - Usually more conventional forms of treatment first
  - Diagnosis of exclusion
  - Treatment of total area of involvement (e.g., facets, SI joint)
  - Treat in four to six session blocks
  - Repeat sessions every two to six weeks
TREATMENT BY PROLOThERAPY, Continued

- Guidelines, continued
  - Reevaluate two months after four to six sessions are complete
  - Repeat series if greater than 30% but less than 90% improved in pain and/or function
  - Become technically proficient – no substitutes for proper training
  - Know your anatomy! Then study it more!
  - Informed consent
  - Routine sterile prep
  - Discontinue NSAIDS
INJECTION TECHNIQUE

- Advance needle to touch bone at ligament attachment sites – both ends
- **Golden Rule:** Needle always touches bone except intraarticular
- Peppering Technique: 0.5 to 1.0cc at each site
- Sterile prep
INJECTION TECHNIQUE, Continued

- Basic Proliferant:
  - 4cc Dextrose 50%
  - 6cc Procaine 1%
  - Stronger solutions not advisable unless experienced
INJECTION TECHNIQUE, Continued

- Results of Treatment
  - Often curative
  - Significant improvements in function and pain
  - Same outcome endpoints as PRP
SAFETY OF PROЛОTHERAPY

- Just because it’s sugar doesn’t make it harmless!
- As safe as the practitioner performing it.
- Proper training is critical to patient safety and good outcomes
- As safe or as dangerous as any procedure into the same structure done in the same fashion.
- Probably safer than a corticosteroid injection into the same structure
SUMMARY

• Prolotherapy is Regenerative Injection Therapy
• Prolo is a concept of understanding MSK tissue injury and repair
• Prolotherapy is a way of thinking about disease and diagnosing the patient
• Prolotherapy is a treatment methodology to ensure complete treatment of the injury
• Prolotherapy is great to “add on” to other RITs
• Prolotherapy is well researched
• Prolotherapy is not experimental
OTHER ADVANTAGES OF PROLOTHERAPY

• You can treat your Aunt Molly’s arthritic knee when you go visit her!
• You can treat you spouse, kids, relatives, and friends in the comfort of your home!
• You don’t need a collection of machines and expensive equipment to deliver a really powerful treatment for most MSK conditions! (your intellect and training and a syringe of dextrose will serve you fine) Think of the power of that!!